Original Article

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

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ABSTRACT

Objectives: This study aims 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 (199 males, 685 females; mean age 46.8±12.7 years; range, 16 to 82 years) who underwent total thyroidectomy were included. Thyroid ultrasonography was performed in all 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 microcalcifications, 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 as benign and malignant groups, due to pathological evaluation. Groups were compared in terms of preoperative sonographic findings, FNAB and postoperative histopathological results.

Results: The sonographic malignancy scores were statistically higher in malignant group than in benign group (p=0.001). Nodule size was smaller in malignant group than in benign group (p=0.001). Capsule irregularity rate was statistically higher in malignant group than in benign group (p=0.001). Hypoechogenicity rate was statistically higher in malignant group than in benign group (p=0.001). There was a statistically significant consistency between pathology and FNAB results (kappa=0.478, p=0.001). The sensitivity, specificity, positive predictive and negative predictive values of FNAB were 55.7%, 92.4%, 72.5% and 82.9%, respectively.

Conclusion: Although the thyroid FNAB has acceptable sensitivity and specificity, it is not effective alone in establishing a decision of operation. Risk factors of thyroid malignancy should also be considered when assessing FNAB results.

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 a majority does not reach the size to be examined by palpation, the rates of thyroid nodules differ in epidemiological studies.[5]

Epidemiological studies report the prevalence of palpable thyroid nodules as 5% for females and 1% for males in iodine deficient

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areas.[6] In high-resolution ultrasonography (USG) imaging, 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 primary diagnosed thyroid cancer in 2009, while in 2014, 63,000 cases were diagnosed with thyroid cancer. The frequency of thyroid cancer increased about three times from 1975 to 2009.[8,9] However, although the rate of thyroid cancer diagnosis in thyroid nodules below 1 cm was 25% in 1988-1989, this rate increased to 39% in 2008-2009.[9] As a result of fine-needle aspiration biopsy (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 cause clinicians to experience dilemma in the evaluation of thyroid nodules necessitated developing a standard application for the approach to thyroid nodules.[4] According to the American Thyroid Association (ATA) recommendation, FNAB is the first-line diagnostic tool in the approach to thyroid nodules.[4] Thyroid FNAB is a safe, easy and minimally invasive procedure that can be performed in outpatient setting. According to FNAB results, follow-up or treatment can be decided. Thyroid FNAB sensitivity and specificity were reported between 65-98% and 70-98%, respectively.[12-16] However, thyroid FNAB may not always rule out malignancy and may lead to unnecessary surgical interventions.[17] Therefore, in this study, we aimed to compare the preoperative sonographic findings, FNAB and postoperative histopathological results in patients who underwent total thyroidectomy.

PATIENTS AND METHODS

This retrospective clinical study included 884 patients (199 males, 685 females; mean age 46.8±12.7 years; range, 16 to 82 years) who underwent total thyroidectomy in Bakırköy Dr. Sadi Konuk Training and Research Hospital Otolaryngology and General Surgery clinics between February 2007 and February 2017. 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 collected with FNAB were sent to the pathology clinic for evaluation. The study protocol was approved by the Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee (Ethics Committee No.: 2017/356). A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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 below 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 calculated by adding the ages of all patients. For age score, 1 point was given for those younger than 20 years or older than 45 years of age.

Total thyroidectomy was performed by obtaining the consent of the patients. Patients with cosmetic deformity and those 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 delivered to histopathological examination. According to the histopathological evaluation, patients were divided into two groups as benign and malignant groups. The findings of the two groups were compared for USG score-final histopathology consistency and FNAB-final histopathology consistency.

Statistical analysis

For statistical analysis, Number Cruncher Statistical System (NCSS) 2007 program (Kaysville, Utah, USA) was used. Mean, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of variables

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		
Malignant	239	27.0		
FNAB				
Benign	648	80.1		
Malignant	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		
Multiple	307	34.7		
Microcalcification				
(-)	734	83.0		
(+)	150	17.0		
Echogenicity				
Hyperechogenicity	156	17.6		
Hypoechogenicity	360	40.7		
Isoechogenicity	178	20.1		
Mixed	190	21.5		
Total malignant score			2.4±1.2	0.0-6.0
USG malignant 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 biopsy; USG: Ultrasonography.

Table 2. Histopathological evaluation of patients who 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
Malignant	239	100
Papillary thyroid carcinoma	138	57.8
Follicular cell carcinoma	89	37.2
Hurtle cell carcinoma	12	5.0

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 independent data and Fisher's exact 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

The demographic characteristics of the patients included in the study were summarized in Table 1. Of the patients, 808 (91.40%) underwent total thyroidectomy with FNAB and 76 (8.60%) underwent total thyroidectomy without FNAB. Histopathology results were summarized in Table 2.

Table 3. Comparison of groups according to pathological evaluation

	Benign			Malignant			
	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 malignant score			2.2±1.1			3.0±1.3	0.001*
USG malignant score			1.6±0.9			2.4±1.2	0.001*
Nodule size (mm)			27.9±15.7			20.4±13.5	0.001*
Nodule size (cm)							0.001**
>1.5	159	24.7		106	44.4		
≥1.5	486	75.3		133	55.6		
Capsule irregularity							0.001**
(-)	621	96.3		194	81.2		
(+)	24	3.7		45	18.8		
Number of nodules							0.001**
Isolated	443	68.7		134	56.1		
Multiple	202	31.3		105	43.9		
Microcalcification							0.001**
(-)	559	86.7		175	73.2		
(+)	86	13.3		64	26.8		
Echogenity							
Hyperechogenicity	130	20.2		26	10.9		0.001**
Hypoechogenicity	208	32.2		152	63.6		0.001**
Isoechogenicity	151	23.4		27	11.3		0.001**
Mixed	156	24.2		34	14.2		0.001**

SD: Standard deviation; USG: Ultrasonography; * Mann-Whitney U test; ** Chi-square-test.

Table 4. Diagnostic value of fine-needle aspiration biopsy

	Benign		Malignant				Sensitivity	Positive predictive value	Specificity	Negative predictive value	
	n	%	n	%	Kappa	*p*	%	%	%	%	*p*
FNAB											
Benign	537	83.3	111	46.4	0.478	0.001*	55.1	72.5	92.4	82.9	0.001**
Malignant	44	6.8	116	48.5							

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

There were no statistically significant differences in the age and gender 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			Malignant			
	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 malignant score			2.4±1.2			2.6±1.1	0.001*
USG malignant score			1.8±1.1			2.0±1.1	0.001*
FNAB results							0.003**
Benign	537	82.2		111	71.6		
Malignant	116	17.8		44	28.4		
Nodule size (mm)			26.5±15.6			23.0±15.3	0.001*
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							
Hyperechogenicity	126	19.3		25	16.1		0.363**
Hypoechogenicity	255	39.1		87	56.1		0.001**
Isoechogenicity	131	20.1		17	11.0		0.009**
Mixed	141	21.6		26	16.8		0.183**

FNAB: Fine-needle aspiration biopsy; USG: Ultrasonography; * 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, isoechogenicity ratio and mixed echogenicity ratio were significantly lower than the benign group ($p=0.001$, $p=0.001$, $p=0.001$ and $p=0.001$, respectively) (Table 3).

There was a statistically significant correlation between pathology and FNAB results (kappa=0.478, $p=0.001$). 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 ($p=0.703$, $p=0.984$ and $p=0.406$, respectively) between FNAB consistent and inconsistent groups. The nodule size, isoechogenicity rate, total malignancy score, and USG malignancy score were significantly lower in the FNAB consistent group than FNAB inconsistent group (for all comparisons, $p=0.001$). The rate of hypoechogenicity and FNAB malignancy predictive rate were significantly higher in FNAB consistent group ($p=0.001$ and $p=0.003$, respectively). There was no significant difference in terms of the number of capsular irregularities, number of nodules and microcalcification rates between 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[20] reported that the routine usage of thyroid FNAB leads to an increased rate of detection of cancer in thyroid nodules. However, 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.[21] 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%.

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 thyroid FNAB has acceptable 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]

Significant information was obtained in studies investigating the compliance of sonographic findings with thyroid FNAB. Akhawan et al.[17] 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. Uçler et al.[22] reported that the size of the nodule had no effect on the correct outcome of FNAB. Moreover, Samulski et al.[23] reported that sonographic findings such as nodule size, echogenicity and vascularity did not have any significant effect on the diagnosis of malignancy. In their study, Tutuncu et al.[24] 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. Furthermore, Shin et al.[25] reported that the nodule size, nodule borders and microcalcifications were effective in the diagnosis of malignancy, while Na et al.[26] reported that isolated macrocalcific thyroid nodules may have low malignancy potential and should not be considered as benign lesions.

Studies comparing the diagnostic power of FNAB with sonographic findings indicate that these two diagnostic tests are relatively reliable. All published guidelines recommend thyroid FNAB in cases with suspicion of malignancy. American Thyroid Society 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 of thyroid cancer history, in patients with a history of radiation, in syndromic cases such as those with multiple endocrine neoplasia type 2 syndrome, or in patients with calcitonin higher than 100 pg/mL, ATA 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 ATA association were considered. All patients in our study were followed-up with thyroid USG and patients with nodules below 1 cm without risk factors did not undergo FNAB. In cases with the aforementioned risk factors, if the size of the thyroid nodule was smaller than 5 mm, FNAB was not performed because of the small size of the nodule. Fine-needle aspiration biopsy was recommended for patients with larger nodules in the case of the 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 performing FNAB even in small-sized nodules in patients with malignancy suspicion resulted in this finding. In this study, the number and size of nodules, capsular irregularity, presence of microcalcifications and echogenicity were the sonographic findings.

In this study sonographic findings consistency with FNAB results was compared. Larger and isoechogenic nodules ratio were higher in the consistent group than inconsistent group. No significant difference was found between groups for the other sonographic findings. According to the findings of this study, the presence of capsular irregularity, hypoechogenicity and microcalcification in thyroid nodules should induce suspicion of malignancy.

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

In conclusion, although thyroid FNAB has acceptable sensitivity and specificity, it is not effective by itself in establishing a decision of operation. Risk factors of thyroid malignancy should be considered when evaluating the results of FNAB.

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