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Original Article

The Relationship Between Thyroid Ultrasonography and Cytopathology

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Abstract

Background Thyroid fine needle aspiration biopsy (FNAB) is a method performed under ultrasound guidance for diagnosis. The nodule is described according to EU-TIRADS (European Thyroid Imaging and Reporting Data System). FNAB results are classified according to Bethesda system. The aim of this single center retrospective study was to investigate which EU-TIRADS groups had no malignancy based on FNAB results.

Material and Methods Ultrasonography and pathology reports of the patients whom FNAB was performed at the State Hospital between January 2016 and December 2018 were reviewed. 251 patients (201 female, 50 male) who were over 18 years of age (mean age 52.62±12.29) were included. Distribution of EU-TIRADS categories by Bethesda Classification was shown. Numbers and percentages, means, and standard deviation, minimum and maximum for variables were used for descriptive statistics. The level of significance was set at $p<0.05$.

Results Of the 7 cases in Bethesda group V, which were 'suspicious for papillary carcinoma', 42.9% were in EU-TIRADS-5 and 57.1% were in EU-TIRADS-4. None of the EU-TIRADS-2 were in the Bethesda IV, V and VI groups. EU-TIRADS category 4 and 5 ($p=0.003$) and Bethesda category V ($p=0.008$) were significantly higher in the papillary carcinoma diagnosed group as a result of thyroid surgery.

Conclusions With larger number of cases, it can be investigated whether it will be considered safe to follow-up the cases in EU-TIRADS-2 group without applying FNAB.

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Introduction

The European Thyroid Association describes thyroid nodules as space-occupying lesions in the thyroid gland which can be distinguished sonographically from environmental parenchyma.[1]As a result of the widespread use of ultrasonography, the incidence of nodules and malignancies in the thyroid has increased. Thyroid nodules can be detected in 19-68% of randomly selected individuals and are more common in women and the elderly.[2,3] Thyroid fine needle aspiration biopsy (FNAB) results are classified according to the Bethesda system.[4] The prevalence of thyroid nodules in healthy adults is 20–76%.[5] In ultrasonography, the characteristics of the suspicious nodule are determined by the European Thyroid Imaging and Reporting Data System (EU-TIRADS) category developed by the European Thyroid Association.[1,6] The ultrasonography report should include the size of the nodule, its location, structure, echogenicity, calcification, margin and shape, halo presence, colloid content and vascularity, and if any, lymph nodes should also be interpreted. EU-TIRADS categories are: No thyroid nodule is found in EU-TIRADS 1 (Normal); there are pure/ anechoic cysts or entirely spongiform nodules in EU-TIRADS 2 (benign); oval shape, smooth margins, isoechoic or hyperechoic, without any feature of high risk are seen in EU-TIRADS 3 (Low-Risk); oval shape, smooth margins, mildly hypoechoic, without any feature of high risk in EU-TIRADS 4 (Intermediate-Risk); there are nodules with at least 1 of the following high-risk features: non-oval shape, irregular margins, microcalcifications, and marked hypoechogenicity in EU-TIRADS 5 (High-Risk).

The Bethesda System for Reporting Thyroid Cytopathology was first published in 2009 to provide standardization in thyroid cytopathology results and was renewed in 2017.[4] It is recommended to follow-up the patients who had benign cytology at FNAB. Malignancy rate was found to be 54.2% in cases of Bethesda III/IV class who subsequently underwent surgical intervention.[7]

The aim of this study was to investigate which EU-TIRADS groups had no malignancy as a result of FNAB

Material and Methods

In this retrospective study, the hospital records between January 2016 and December 2018 were examined. A total of 251 patients (201 women, 50 men) who had a thyroid FNAB older than 18 years of age (range:18-85 years) were included in the study. Before the biopsy procedure, the patients were questioned for contraindications (anticoagulant use or anxiety not to allow FNA). Informed consent of patients were obtained. FNAB was performed under ultrasound guidance with a 22 Gauge spinal needle using a 20 cc injector. The radiologist sit in front of the screen of the ultrasound equipment, on the right side of patient. The patient was placed supine with the neck hyperextended during the procedure. High-resolution 7.5-14 MHz linear-array transducer was used. The needle tip was placed within the target nodule, 4-5 passes with a negative suction was applied. After FNAB, hemostasis was achieved, after a while bleeding control was done with control USG. The patients were observed for a while and discharged. 1 drop of aspirated material was forced onto several glass slides and smears are prepared by using a second glass slide. The slides were fixed immediately in 95% alcohol. The cytological specimens were stained with the dyes of PAP and Hematoxylin and eosin stain (HE). The FNAC samples were double-read by two experienced pathologists.

Thyroid ultrasonography findings and pathology reports were examined. In the pathology report, the size of the nodule which FNAB obtained was mentioned. Those who were previously diagnosed with thyroid malignancy were excluded.

Nodules were categorised according to EU-TIRADS. Gender ratio and average age for each group were found. Ultrasonography and pathology results were compared according to gender.

The Bethesda System for Reporting Thyroid Cytopathology was used to categorise thyroid fine-needle aspiration (FNA) specimens: (I) nondiagnostic or unsatisfactory; (II) benign; (III) atypia of undetermined significance (AUS) or follicular lesion of undetermined significance; (IV) follicular neoplasm or suspicious for a follicular neoplasm; (V) suspicious for malignancy; and

(VI) malignant.[4]

Regional Ethics Committee's Approval and informed consent of the patients were obtained (23.07.2019, 1362).

Statistical Analysis

Statistical analysis was performed using SPSS 15.0 software (SPSS Inc, Chicago, IL, USA).

Percentage, frequency, distribution were used to determine the distribution of patients according to

Table 1. Age and gender distribution of patients by EU-TIRADS categories, Bethesda Classification, and having a thyroid surgery condition

			Gender n (%)		Age		
A: Age							
Mean.±SD (min-max)		52.6±12.3 (18-85)					
B: Gender		n (%)					
Male		50 (19.9%)					
Female		201 (80.1%)					
C: EU-TIRADS Categories		n (%)	F	M	min	max	mean±SD
	2	4 (1.6)	1 (25.0)	3 (75.0)	49	73	59.3±10.0
	3	204 (81.3)	164 (80.4)	40 (19.6)	18	84	52.4±12.2
	4	37 (14.7)	30 (81.1)	7 (18.9)	35	85	54.6±12.0
	5	6 (2.4)	6 (100.0)	0 (0.0)	29	62	43.2±14.5
D: Bethesda Classification							
	I	32 (12.7)	26 (81.3)	6 (18.8)	30	85	53.7±12.0
	II	180 (71.7)	141 (78.3)	39 (21.7)	18	84	52.8±12.5
	III	31 (12.4)	26 (83.9)	5 (16.1)	27	72	51.9±11.0
	IV	1 (0.4)	1 (100.0)	0 (0.0)	39	39	39.0
	V	7 (2.8)	7 (100.0)	0 (0.0)	29	63	47.4±13.4
	VI	0 (0)	0 (0)	0 (0)	-	-	-
E: Whether had a thyroid surgery							
	A	179 (91.3)	144 (80.4)	35 (19.6)	26	85	53.8±12.4
	B	8 (4.1)	7 (87.5)	1 (12.5)	29	63	45.9±11.6
	C	8 (4.1)	6 (75.0)	2 (25.0)	32	65	48.3±9.5
	D	1 (0.5)	1 (100)	0 (0)	39	39	39.0±0
F: The group with no information about whether they have thyroid surgery		55 (21.9)	43 (78.2)	12 (21.8)	*18*	*85*	52.6±12.3

TIRADS -4: Intermediate-Risk, EU-TIRADS-5: High-Risk; Bethesda I:Nondiagnostic or unsatisfactory, II:Benign, III: Atypia of Undetermined Significance or Follicular Lesion of indetermined Significance, IV: Follicular Neoplasm or Suspicious for a Follicular Neoplasm, V: Suspicious for papillary carcinoma, VI: Malignant; Whether had a thyroid surgery A: Has not been operated, B:Operated and diagnosed with papillary carcinoma, C:Operated and diagnosed with adenomatous hyperplasia, D: Operated and diagnosed with follicular adenoma

gender, Bethesda class and EU-TIRADS category. Descriptive statistics were used to examine the age of the patients for gender, Bethesda class and EU-TIRADS category. Kruskal-Wallis H test was used to compare the largest nodule size according to the Bethesda class. Cross-tables were prepared to determine the Bethesda classes of the patients according to the EU-TIRADS category, nodule's size, shape, echogenicity, margins, colloid content, vascularity, and thyroid section where the nodule was located. Descriptive statistics, numbers and percentages for each value of a variable, means, standard deviation, minimum and maximum for all variables. p values of <0.05 were considered statistically significant.

Results

The mean age was 52.62±12.29. Age and gender distribution of patients by EU-TIRADS categories, Bethesda classification,and having a thyroid surgery condition are shown in Table 1, and correlation of EU-TIRADS categories with Bethesda classification is shown in Table 2. The patients were divided in groups according to whether they had thyroid surgery or not and diagnosis after tyroid surgery, according to EU-TIRADS category and Bethesda classification *(Table 3 and 4, respectively)*. The distribution of those patients who had thyroid surgery and not according to EU-TIRADS categories and Bethesda Classification are shown in Table 5 and 6 respectively. The gender distribution and correlation of those who underwent thyroid surgery according to EU-TIRADS categories and Bethesda classification are shown at Table 7. Correlation between the findings on EU-TIRADS categories with Bethesda classification is shown at Table 8.

There were no results in the Bethesda class VI. 42.9% of the 7 cases in the Bethesda class V (Suspicious for papillary carcinoma) were in the EU-TIRADS-5 and 57.1% were in the EU-TIRADS-4 categories. The only case in the Bethesda IV class was in the EU-TIRADS-3 category. None of those in EU-TIRADS-2 category were in Bethesda classes V and VI *(Table 2)*.

No information could be obtained in 55 of 251 patients whether they had thyroid surgery or not. Of the 196 patients whose information

Table 2. Correlation of EU-TIRADS categories with Bethesda Classification

		EU-TIRADS Categories				
n (%)		**2**	**3**	**4**	**5**	**Total**
Bethesda Classification	**I**	2 (50.0%)	21 (10.3%)	8 (21.6%)	1 (16.7%)	32 (12.7%)
	II	1 (25.0%)	154 (75.5%)	23 (62.2%)	2 (33.3%)	180 (71.7%)
	III	1 (25.0%)	28 (13.7%)	2 (5.4%)	0 (0.0%)	31 (12.4%)
	IV	0 (0.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	1 (0.4%)
	V	0 (0.0%)	0 (0.0%)	4 (10.8%)	3 (50.0%)	7 (2.8%)
	VI	-	-	-	-	-
	Total	4 (1.6%)	201 (80.1%)	37 (14.7%)	6 (2.4%)	251

EU-TIRADS: Thyroid Imaging Reporting and Data System, EU-TIRADS-2: benign, EU-TIRADS-3: Low-Risk, EU-TIRADS-4: Intermediate-Risk, EU-TIRADS-5: High-Risk; Bethesda Classification I: Nondiagnostic or unsatisfactory, II: Benign, III: Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance, IV: Follicular Neoplasm or Suspicious for a Follicular Neoplasm, V: Suspicious for papillary carcinoma VI: Malignant.

Table 3. The distribution of the groups formed according to whether the patients had thyroid surgery and the diagnosis of those who underwent thyroid surgery, according to EU-TIRADS category

		EU-TIRADS Categories			
n (%)		**2**	**3**	**4**	**5**
Whether had a thyroid surgery	Has not been operated	2 (100%)	154 (94.5%)	21 (80.8%)	2 (40.0%)
	Papillary carcinoma	0 (0.0%)	1 (0.6%)	4 (15.4%)	3 (60.0%)
	Adenomatous hyperplasia	0 (0.0%)	7 (4.3%)	1 (3.8%)	0 (0.0%)
	Follicular adenoma	0 (0.0%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
	No information	2 (50.0%)	41 (20.1%)	11 (29.7%)	1 (16.7%)

EU-TIRADS-2: Benign, EU-TIRADS-3: Low-Risk, EU-TIRADS-4: Intermediate-Risk, EU-TIRADS-5: High-Risk

Table 4. The distribution of the groups formed according to whether the patients had thyroid surgery and the diagnosis of those who underwent thyroid surgery, according to Bethesda Classification

		Bethesda Classification					
n (%)		**I**	**II**	**III**	**IV**	**V**	**VI**
Whether had a thyroid surgery	Has not been operated	25 (100%)	135 (95.1%)	19 (86.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Papillary carcinoma	0 (0.0%)	1 (0.7%)	1 (4.5%)	0 (0.0%)	6 (100%)	0 (0.0%)
	Adenomatous hyperplasia	0 (0.0%)	6 (4.2%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Follicular adenoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100%)	0 (0.0%)	0 (0.0%)
	No information	7 (21.9%)	38 (21.1%)	9 (29.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)

Bethesda Classification I: Nondiagnostic or unsatisfactory, II: Benign, III: Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance, IV: Follicular Neoplasm or Suspicious for a Follicular Neoplasm, V: Suspicious for papillary carcinoma, VI: Malignant

Table 5. The distribution of those who had not thyroid surgery by EU-TIRADS Categories and Bethesda Classification

		n (%)
Gender	M	35 (19.6)
	F	144 (80.4)
EU-TIRADS Categories	2	2 (1.1)
	3	154 (86.0)
	4	21 (11.7)
	5	2 (1.1)
Bethesda Classification	I	25 (14.0)
	II	135 (75.4)
	III	19 (10.6)

F: Female, M: Male; EU-TIRADS-2: Benign, EU-TIRADS-3: Low-Risk, EU-TIRADS-4: Intermediate-Risk, EU-TIRADS-5: High-Risk; Bethesda I: Nondiagnostic or unsatisfactory, II: Benign, III: Atypia of Undetermined Significance or Follicular Lesion of indetermined Significance

Table 6. The distribution of those who had thyroid surgery by EU-TIRADS Categories and Bethesda Classification

		n (%)
Gender	M	3 (17.6)
	F	14 (82.4)
EU-TIRADS Categories	3	9 (52.9)
	4	5 (29.4)
	5	3 (17.6)
Bethesda Classification	II	7 (41.2)
	III	3 (17.6)
	IV	1 (5.9)
	V	6 (35.3)

F: Female, M: Male; EU-TIRADS-2: Benign, EU-TIRADS-3: Low-Risk, EU-TIRADS-4: Intermediate-Risk, EU-TIRADS-5: High-Risk; Bethesda I: Nondiagnostic or unsatisfactory, II: Benign, III: Atypia of Undetermined Significance or Follicular Lesion of indetermined Significance

Table 7. The distribution of those who underwent thyroid surgery according to EU-TIRADS Categories, Bethesda Classification and gender

		Diagnosis of Malignancy in Pathological Examination After Surgery				
		Yes		No		
		n	%	n	%	p
Gender	M	1	12.5	2	22.2	1.000
	F	7	87.5	7	77.8	
EU-TIRADS Categories	3	1	12.5	8	88.9	0.003
	4	4	50.0	1	11.1	
	5	3	37.5	0	0.0	
Bethesda Classification	II	1	12.5	6	66.7	0.008
	III	1	12.5	2	22.2	
	IV	0	0.0	1	11.1	
	V	6	75.0	0	0.0	

was available, only 17 of them had undergone thyroid surgery. Of these patients, 8 had papillary carcinoma, 1 had follicular adenoma, 8 had adenomatous hyperplasia.

Of the 8 patients diagnosed with papillary carcinoma, 6 of them had a suspicion of papillary carcinoma in FNAB, one patient was a 55-year-old female patient with a diagnosis of atypia of indeterminate significance in FNAB, classified in Bethesda III and EU-TIRADS 3 categories, with a nodule of 17×10 mm in the left lobe inferior. The other patient who was diagnosed with papillary carcinoma was a 42-year-old male patient who was in the Bethesda II and EU-TIRADS 4 category and had an isoechoic nodule with coarse calcifications in the left lobe, without atypical cells in FNAB. No information could be obtained whether 1 out of 7 patients with suspected papillary carcinoma in FNAB was operated.

One patient with follicular neoplasia in FNAB was diagnosed histopathologically as follicular adenoma.

In 8 patients who were histopathologically diagnosed as adenomatous hyperplasia after surgery, 6 had no atypical cells in FNAB, 1 was compatible with follicular lesion, 1 had atypia of indeterminate significance.

Among the patients who underwent thyroid surgery, there was a significant difference between benign and malignant cases, both EU-TIRADS categories (p=0.003) and Bethesda classifications (p=0.008). EU-TIRADS categories 4 and 5 and Bethesda category V were significantly higher in papillary carcinoma group than the others.

Discussion

Thyroid nodules are more common in women,[2] 80.1% of our cases were women.

Statistically significant malignant features include microcalcification, irregular or amorphous morphology, long but not wide shape, irregular margins, vascularity and presence of a pathological-looking lymph node.[8,9] In a retrospective cohort study, 495 nodules with a non-diagnostic result were followed-up for 2.7 years and thyroid cancer was found in 3%. The presence of nodular calcifications was the strongest predictor of thyroid malignancy. Initial nodule size was inversely associated with malignancy. Nodules

Table 8. Correlation of the findings on EU-TIRADS with Bethesda Classification

Nodule's			Bethesda					
			I	II	III	IV	V	Total
Size	0.5-0.9 cm	n	3	10	3	0	0	16
		%	(18.8%)	(62.5%)	(18.8%)	(0.0%)	(0.0%)	(100.0%)
	1.0-2.0 cm	n	20	97	16	1	6	140
		%	(14.3%)	(69.3%)	(11.4%)	(0.7%)	(4.3%)	(100.0%)
	≥ 2.1 cm	n	7	73	12	0	1	93
		%	(7.5%)	(78.5%)	(12.9%)	(0.0%)	(1.1%)	(100.0%)
	Total	n	30	180	31	1	7	249
		%	(12.0%)	(72.3%)	(12.4%)	(0.4%)	(2.8%)	(100.0%)
Composition	Solid	n	0	8	0	0	0	8
		%	(0.0%)	(100.0%)	(0.0%)	(0.0%)	(0.0%)	(100.0%)
	Predominant solid	n	1	2	0	0	0	3
		%	(33.3%)	(66.7%)	(0.0%)	(0.0%)	(0.0%)	(100.0%)
	Predominant cystic	n	13	129	22	0	1	165
		%	(7.9%)	(78.2%)	(13.3%)	(0.0%)	(0.6%)	(100.0%)
	Cystic	n	2	4	1	0	0	7
		%	(28.6%)	(57.1%)	(14.3%)	(0.0%)	(0.0%)	(100.0%)
	Total	n	16	143	23	0	1	183
		%	(8.7%)	(78.1%)	(12.6%)	(0.0%)	(0.5%)	(100.0%)
Echogenicity	Markedly hypoechoic	n	1	10	3	0	3	17
		%	(5.9%)	(58.8%)	(17.6%)	(0.0%)	(17.6%)	(100.0%)
	Mildly hypoechoic	n	1	5	3	0	0	9
		%	(11.1%)	(55.6%)	(33.3%)	(0.0%)	(0.0%)	(100.0%)
	Isoechoic	n	25	153	24	0	4	206
		%	(12.1%)	(74.3%)	(11.7%)	(0.0%)	(1.9%)	(100.0%)
	Hyperechoic	n	0	7	0	0	0	7
		%	(0.0%)	(100.0%)	(0.0%)	(0.0%)	(0.0%)	(100.0%)
	Total	n	27	175	30	0	7	239
		%	(11.3%)	(73.2%)	(12.6%)	(0.0%)	(2.9%)	(100.0%)
Margins	Irregular	n	1	2	2	0	3	8
		%	(12.5%)	(25.0%)	(25.0%)	(0.0%)	(37.5%)	(100.0%)
	Smooth	n	2	11	2	0	1	16
		%	(12.5%)	(68.8%)	(12.5%)	(0.0%)	(6.3%)	(100.0%)
	Ill-defined	n	1	1	0	0	0	2
		%	(50.0%)	(50.0%)	(0.0%)	(0.0%)	(0.0%)	(100.0%)
	Total	n	4	14	4	0	4	26
		%	(15.4%)	(53.8%)	(15.4%)	(0.0%)	(15.4%)	(100.0%)
Calcifications	Microcalcifications	n	1	5	0	0	1	7
		%	(14.3%)	(71.4%)	(0.0%)	(0.0%)	(14.3%)	(100.0%)
	Macrocalcifications	n	7	29	2	0	2	40
		%	(17.5%)	(72.5%)	(5.0%)	(0.0%)	(5.0%)	(100.0%)
	Rim calcifications	n	1	3	0	0	0	4
		%	(25.0%)	(75.0%)	(0.0%)	(0.0%)	(0.0%)	(100.0%)
	Total	n	9	37	2	0	3	51
		%	(17.6%)	(72.5%)	(3.9%)	(0.0%)	(5.9%)	(100.0%)
Colloid inclusions	Yes	n	1	14	2	0	1	18
		%	(5.6%)	(77.8%)	(11.1%)	(0.0%)	(5.6%)	(100.0%)
	No	n	0	0	29	0	6	35
		%	(0.0%)	(0.0%)	(82.9%)	(0.0%)	(17.1%)	(100.0%)
	Total	n	1	14	31	0	7	53
		%	(1.9%)	(26.4%)	(58.5%)	(0.0%)	(13.2%)	(100.0%)
Vascularity	No	n	1	3	n	0	1	5
		%	(20.0%)	(60.0%)	%	(0.0%)	(20.0%)	(100.0%)
	Peripheral	n	1	1	n	0	0	2
		%	(50.0%)	(50.0%)	%	(0.0%)	(0.0%)	(100.0%)
	Mildly intranodular	n	0	4	n	0	0	4
		%	(0.0%)	(100.0%)	%	(0.0%)	(0.0%)	(100.0%)
	Marked intranodular	n	6	15	n	0	3	24
		%	(25.0%)	(62.5%)	%	(0.0%)	(12.5%)	(100.0%)
	Total	n	8	23	n	0	4	35
		%	(22.9%)	(65.7%)	%	(0.0%)	(11.4%)	(100.0%)
Location	Right lobe	n	22	86	9	0	6	123
		%	(17.9%)	(69.9%)	(7.3%)	(0.0%)	(4.9%)	(100.0%)
	Left lobe	n	9	87	17	0	1	114
		%	(7.9%)	(76.3%)	(14.9%)	(0.0%)	(0.9%)	(100.0%)
	Isthmus	n	1	7	5	0	0	13
		%	(7.7%)	(53.8%)	(38.5%)	(0.0%)	(0.0%)	(100.0%)
	Total	n	32	180	31	0	7	250
		%	(12.8%)	(72.0%)	(12.4%)	(0.0%)	(2.8%)	(100.0%)

Bethesda I- Nondiagnostic or unsatisfactory II- Benign III- Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance IV- Follicular Neoplasm or Suspicious for a Follicular Neoplasm V- Suspicious for papillary carcinoma VI- Malignant

containing calcifications should be followed-up.10

Calcification status of the nodule was mentioned in 20.3% of our cases. 25% of patients with rim calcification were in the nondiagnostic or unsatisfactory and 75% in the 'Benign' group. Calcification was observed in 28.1% of our nondiagnostic patients and 11.1% of them were rim calcification. Malignancy was detected in 27% of those with peripheral calcification in the literature.[11]

The largest nodule size measurements of our cases did not differ significantly between Bethesda classes (p>0.05). In a retrospective cohort analysis at Boston, of those 1.0 to 1.9 cm in diameter, 10.5% were cancerous, of those >2.0 cm, 15% were cancerous, no graded increase in risk beyond the 2-cm threshold. When malignant, the proportion of papillary carcinoma decreased (nodules 1.0-1.9 cm, 92% of cases; >4 cm, 74% (p<.01).[12] In 85.7% of our 'suspicious for papillary carcinoma' cases, the nodule size was between 1.0-2.0 cm. 1,104 patients who underwent thyroid FNAB and subsequent thyroidectomy retrospectively reviewed, it was found that nodule size alone was not predictive of malignancy in patients except for Hürthle cell neoplasms.[13] As the nodule is low/intermediate/high-risk, the probability of malignancy may increase as the size of the nodule increases.[14,15]

In this study, 49.2% of the nodules were located in the right lobe, 45.6% in the left lobe and 5.2% in isthmus. Six of the 7 nodules in the group 'suspicious for papillary carcinoma'were in the right lobe and 1 in the left lobe. In the literature, it has been reported that the prevalence of malignancy in isthmus, right or left lobe was not significantly different.[16] According to the location of the nodules, the incidence of malignancy was higher in those located in the upper pole,[17] however, in our cases, no information was found about the pole where the nodule was located.

There are studies linking echogenicity and vascularity of the nodule with malignancy.[18,19,20] The majority of malignant thyroid tumors are 62.5-87.2% hypoechoic and hypoechoic nodules have a higher risk of malignancy (%20.6-70.4).[3] In our cases, 57.1% isoechoic and 42.9% markedly hypoechoic nodules were detected in the 'suspicious for papillary carcinoma' group.

Vascularity status was noted in 13.9% of our cases, 11.4% of all cases whose vascularization status was stated were 'suspicious for papillary carcinoma', and 75% of them showed significant intranodular vascularization, while 25% did not show vascularization. To draw conclusions from vascularity is not feasible as only 35 cases have been studied here. There are publications showing that there is a relationship between intranodular vascularization and malignancy.[21,22]

Irregular shapes and margins differ significantly between groups in a study compared with Bethesda II to III-IV.[23] In our study, nodule margins were determined in 10.3% of cases, 25% of patients with irregular nodule margins were 'AUSor follicular lesion of undetermined significance', and 37.5% of them were 'suspicious for papillary carcinoma'. Margins were noted in 57.1% of cases with 'suspicious for papillary carcinoma', of which 75% were irregular margins.

The presence of colloid-filled cyst on ultrasonography showed 100% benignity in a prospective study conducted among American elderly veterans.[8] In 21.1% of our cases, there was information about the colloid content of the nodule. 5.6% of patients with nodule colloid were nondiagnostic or unsatisfactory, 77.8% of patients with nodule colloid were benign, 11.1% were 'AUS or follicular lesion of undetermined significance, and 5.6% were 'suspicious for papillary carcinoma'.

In 27.1% of our cases, solid or cystic composition of the nodule was not specified in the ultrasonography report. Only 1 of the 7 cases with 'suspicious for papillary carcinoma' has been identified, and it is predominant cystic. Of the nodules whose composition was mentioned, 4.4% were solid and all of them were Bethesda II. When we searched the literature, 81.6-93% of malignant thyroid tumors were solid.[3]

In the axial plan, the definition of nodules as height>width was not made in any of our cases.

According to the Bethesda classification, 12.7% of patients were nondiagnostic or unsatisfactory. In the literature, this rate is up to 20%.24 71.7% of them were 'benign', 12.4% were of 'AUS or 'follicular lesion of undetermined significance' and were compatible with the literature.[25] Papillary thyroid carcinoma is the most common thyroid malignancy in the literature,[3] it can be found at a rate of 9.2 -13% after FNAB,26 2.8% of our cases were in the group 'suspicious for papillary carcinoma'. Other malignancies were not found.

In an article published in 2018, 184 patients were prospectively included, and malignancy risk

in EU-TIRADS was 0, 2.2, 38.5 and 77.8% in benign, low risk, intermediate risk, and high risk groups, respectively.[27]

In our study, none of the cases in the benign group in EU-TIRADS was found to be malignant as a result of FNAB (0%). In EU-TIRADS, 0.49% of those in the low risk group, 10.8% of the intermediate risk, and 50% of the high risk were found at Bethesda IV and V. The malignancy rate of the intermediate risk group is 22 times higher than that of the low risk group, and the malignancy rate of those in the high risk group is 102 times higher than the low risk group.

Conclusions

None of the cases in the 'Benign group' in EU-TIRADS were found to be malignant as a result of FNAB. By carrying out studies with larger number of cases, it can be investigated whether it will be considered safe to follow-up the cases in 'Benign' EU-TIRADS group without applying FNAB.

Conflict of Interest

All authors declare that they have no confict of interest.

Limitations

According to EU-TIRADS, it was seen that detailed information was not included in every ultrasonography report in our cases. This may be due to the excessive workload of radiologists. While we were making the statistical evaluation, we took into account what was stated in the report. Other limitations are that it is a retrospective study and the number of cases is low. There are many studies on this subject, but this findings can be considered as local data.Better results can be obtained in a prospective study with higher number of cases.

Authors' Contribution

Study Conception: AA, RK, SK, MNG; Study Design: AA, RK, SK, MNG; Supervision: AA, RK, SK, MNG; Funding: AA, RK; Materials: AA, RK, SK, MNG; Data Collection and/or Processing: AA, RK; Statistical Analysis and/or Data Interpretation: AA, RK; Literature Review: AA, RK; Manuscript Preparation: AA, RK; and Critical Review: AA, RK.

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