

Research Article

The Possibility of Thyroid Cancer May Vary by Age and Gender

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Abstract

Objectives: The aim of this study was to evaluate the possibility of malignancy among thyroid nodules by different age and gender.

Methods: We retrospectively evaluated the biopsy results of 609 consecutive patients who underwent thyroid fine needle aspiration biopsy (FNAB) between 2010 and 2019 according to the Bethesda classification system and tried to determine the possible effect of patient age and gender on thyroid nodule malignancy by FNAB.

Results: The mean age of the whole group was 50.4±13.4 (13-96) years. This study included a total of 609 patients of whom 481 (79%) were women and 128 (21%) were men. The pathology results of the nodules were mostly benign (78.3%) followed by AUS at a rate of 9.5%. There was an inverse relationship between age and malignancy. As in younger ages, malignancy rate increased significantly ($p<0.01$). The risk of malignancy decreased with increasing age in both male and female trend with age showing a statistically significant difference in female ($p=0.002$), but not in male ($p=0.064$).

Conclusion: In the case of a thyroid nodule at any age patients should be informed there may be a risk for thyroid cancer requiring continued monitoring.

Keywords: Age, gender, thyroid cancer

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Thyroid nodules come into clinical attention either when noted by the patient; by a clinician during routine physical examination; or during a radiologic procedure, such as carotid ultrasonography, neck or chest computed tomography, or positron emission tomography scanning. Their clinical importance is primarily related to the need to exclude thyroid cancer, which accounts for 4 to 6.5 percent of all thyroid nodules in non-surgical series.^[1-5] In the last 30

years, there has been a significant increase (2.4-2.9 times) in thyroid cancer frequency. Papillary thyroid carcinoma is considered to be responsible for majority of this increase (3.7 times).^[6,7] The frequency of thyroid cancer is higher among children, adults less than 30 years of age, patients with a history of head and neck irradiation, patients with a family history of thyroid cancer.^[8] Fine needle aspiration biopsy (FNAB) is the standard method for evaluation of thy-

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roid nodules based on pathology criteria. FNAB of a thyroid nodule should be performed in the case of a palpable nodule or asymmetry at the neck and suspicious ultrasonography findings as well as nodule growth.^[8]

The aim of this study was to evaluate the possibility of malignancy among thyroid nodules by different age and gender.

We retrospectively evaluated the biopsy results of patients according to the Bethesda classification and tried to determine the possible effect of patient age and gender on thyroid nodule malignancy by FNAB. There is a limited number of studies analyzing the effect of age and gender on thyroid malignancies. Although thyroid diseases are endemic in our country, there is not a specific study on this subject from our country as well as we could search.

Methods

The study was approved by the Ethics Committee of Bahçeşehir University Faculty of Medicine Ethics Committee (Decision No. 2019/14/01).

Six-hundred forty-nine patients who underwent thyroid FNAB between 2010-2019 were included into the study. Radiology and biopsy reports were recorded and analyzed. FNAB reports of thyroid nodules were evaluated according to the Bethesda criteria as; non-diagnostic, benign, atypia of undetermined significance (AUS) or follicular lesion with undetermined significance (FLUS or AUS), follicular neoplasm or suspicious for follicular neoplasm, suspicious for malignancy and malignant tumour.^[9]

Repeated biopsy results of each initial pathology reports showing atypia of undetermined significance (AUS/FLUS) were evaluated.

Then all patients were sorted to groups by their ages and gender. Among 649 patients pathology outcome reports of 40 patients were regarded as inappropriate and excluded from the study.

A database of 609 consecutive patients who underwent thyroid FNAB between 2010 and 2019 was reviewed. Statistical analysis was performed by using Chi square test, one way Anova test, Mann-Whitney U test and ROC curve test.

Results

This study included a total of 609 patients aged 13 to 96 years, of whom 481 (79%) were women and 128 (21%) were men. Patients' characteristics are given at Table 1. The mean age of the whole group was 50.4±13.4 years. The age of group was not normally distributed. Median ages for women and men were 50 years, and 51 years; respectively. As seen in Table 1, the pathology results of the nodules

Table 1. Some characteristics of patients with thyroid nodules

Characteristic	Number	%
Sex		
Female	481	79,0
Male	128	21,0
The mean age 50.4±13.4 years		
Pathology		
Benign	477	78,3
AUS	58	9,5
Papillary carcinoma	52	8,6
Follicular carcinoma		
Others:	17	2,8
Hurthle cell neoplasia	1	0,2
Oncocytic cell neoplasia	2	0,3
Squamous spindle malignant cells	1	0,2
Papillary oncocytic nodular lesion	1	0,2
Total	609	100

Table 2. Pathology results of thyroid nodules by sex and age

Characteristics	Pathology			p
	Benign	AUS	Malign	
Sex				
Female	377	46	57	0.980*
% within sex	78.5%	9.6%	11.9%	
Male	100	12	16	
% within sex	78.1%	9.4%	12.5%	
Age				
Mean±SD	50.7±13.1	53.6±13.6	46.0±14.7	0.004**
Median	50.0	52.5	44.0	

* Chi-Square test; **One way ANOVA test.

were mostly benign (78.3%) followed by AUS at a rate of 9.5%. Repeated biopsies of AUS patients revealed malignancy in 22.2% of patients.

Fifty-two patients with nodular goiter had papillary carcinoma (8.6%) and 17 patients had follicular carcinoma (2.8%). Other neoplasms (Hurthle cell neoplasia, oncocytic cell neoplasia, squamous spindle malignant cells, papillary oncocytic nodular lesion) were detected in the remaining 5 patients (0.9%). The age and gender based on cytopathology are represented at Table 2. Pathology results were evaluated in three categories as benign, AUS and malignant. Both genders had similar distribution in terms of benign, malignant or AUS results (p=0.980). There was an inverse relationship between age and malignancy. As in younger ages, malignancy rate increased significantly (p<0.01). In ROC analysis of age to determine a critical value for malignancy in thyroid nodules, the area under the curve was

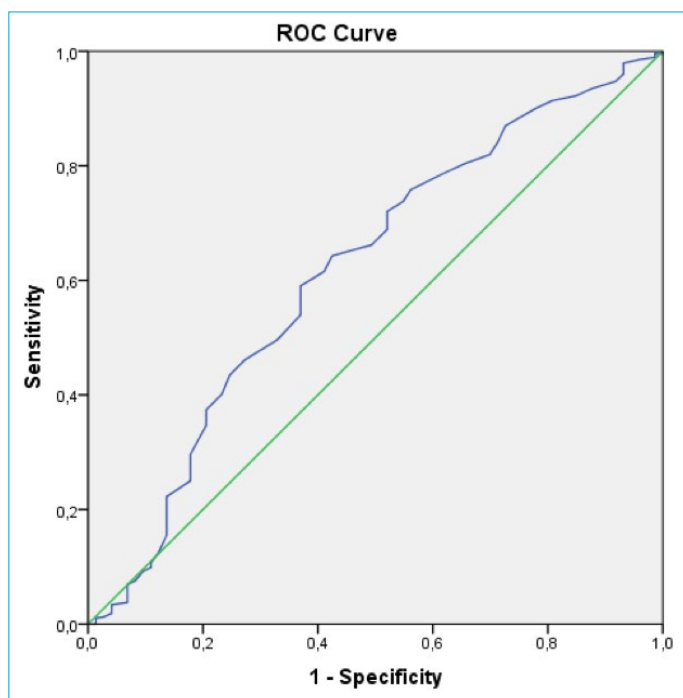


Figure 1. ROC Curve of age for malignancy in thyroid nodules.

calculated as 0.617 (95% CI: 0.545-0.690) (Fig. 1). The age of 45.5 (sensitivity = 0.643, 1-specificity = 0.425) was found to be the closest value to the upper left corner of ROC curve. When 45.5 were taken as cut-off, the risk of malignancy was found to be statistically higher in patients with $45.5 >$ age group (9.2%) than those with $45.5 \leq$ (19.8%) ($p=0.000$, OR = 2.43, 95% CI: 1.478-4.023).

When we grouped the ages according to the quartiles of the malignant group (Fig. 2), it is seen that the highest malignancy rate is in the age group below 35 years, followed by age of 35-44 (Table 3). The risk of malignancy at age 53 and over, which corresponds to the seventy-fifth percentile, is almost halved. Table 4 presents the pathology results based on age groups classified by age quartiles. It is seen that the risk of malignancy decreases with increasing age in both male and female. This decreasing trend with age showed a statistically significant difference in female ($p=0.002$), but not in male ($p=0.064$).

Age groups (years)	Pathology			
	Benign		Malign	
	No	%	No	%
35>	47	74.6	16	25.4
35-44	114	84.4	21	15.6
45-52	108	84.7	18	14.3
53≤	207	92.0	18	8.0

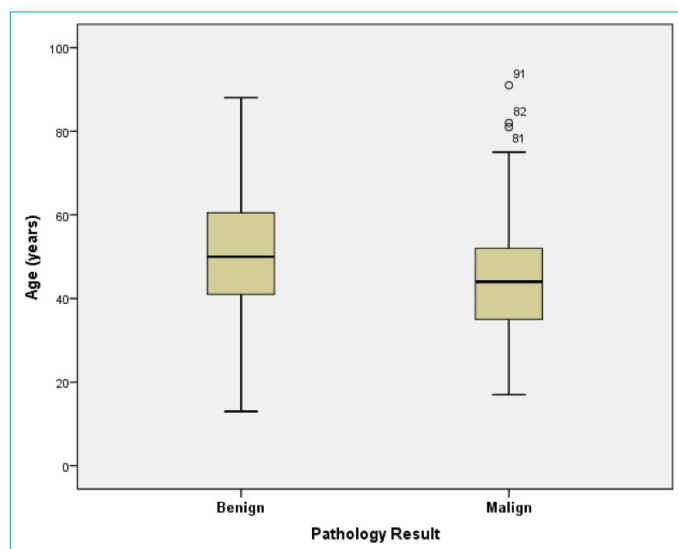


Figure 2. Boxplot graph of age by pathology results.

Discussion

Medical history and physical examination of thyroid nodules fail to predict cancer. None of the sonographic findings have a high level of sensitivity and specificity in the diagnosis of malignancy.^[10] FNAB is the most useful method to differentiate benign and malignant thyroid nodules.^[11-13]

The National Cancer Institute published the Bethesda System for Reporting Thyroid Cytopathology, which is recommended for cytological classification of thyroid nodules.^[9]

Earlier studies have reported that 20% of thyroid nodules were categorized as AUS based on cytological examination of an FNA biopsy specimen.^[14-15] There is a 5% to 15% risk of malignancy in these cases.^[16] In our study, approximately 10% of thyroid nodules were malignant and 10% of them were AUS. Repeat biopsy findings revealed thyroid cancer in 22.2% of AUS patients. In various studies especially in Western population, up to 4-6.5% of thyroid nodules were found to be cancerous.^[1-5]

In the literature, investigation of malignancy by age and gender was rare and had various results. Also, in our country the relationship between age/gender and thyroid cancer has never been explored.

Kwong N et al., evaluated 6391 patients (20-95 years) according to their age groups. Thyroid cancer was detected in 16% of the patients. The younger (youngest) group (20-29 years) had 43% more thyroid nodules than the older (oldest) group (≥ 70 years) in comparison.^[5] The youngest group of the patients had a 14.8% risk of cancer per thyroid nodule at diagnosis, while the oldest group had a 5.6% risk of cancer per nodule. However, the number of high-risk thyroid cancer significantly increased with advancing age, ranging from 0% in the youngest group to

Table 4. Pathology results of thyroid nodules by age and gender groups

	Pathology							
	Female				Male			
	Benign		Malign		Benign		Malign	
	No	%	No	%	No	%	No	%
Age groups (years)								
35>	40	75.5	13	24.5	7	70.0	3	30.0
35–44	90	84.9	16	15.1	24	82.8	5	17.2
45–52	85	85.9	14	14.1	23	85.2	4	14.8
53≤	162	92.0	14	8.0	45	91.8	4	8.2
Total	377	86.9	57	13.1	99	86.1	16	13.9

16% in the oldest group.^[5] Bessey et al., performed FNAB to 3981 patients, of whom 2766 were women and 964 were men between 2002–2009. Among the 3981 patients 196 (5.3%) had malignant FNAB cytology. The frequency of having malignant FNAB was two times higher in those under the age of 45. Men showed a higher incidence of cancer than women, and given the age group, it was found to be over 45 years old. Although the peak age of malignancy in women is 30s (10.4%), this increase has occurred in the male population after 10 years (12.1%). In both sexes, malignancy rate decreased at the age of 70 (M: 2.3% and F: 1.9%).^[17]

In our study, the risk of malignancy under the age of 45 was significantly higher than over the age of 45 (9.2% vs. 19.8%, $p=0.0000$). Table 4 represents the pathology results based on age groups classified by age quartiles (Fig. 2). It is seen that the risk of malignancy decreases with increasing age in both male and female. This decreasing trend with age showed a statistically significant difference in female ($p=0.002$), but not in male ($p=0,064$). Nodule was more common in women (434/115). It was seen that malignant nodules are more common under the age of 35 (25.4%). It was the rarest in ages above 53 years (9.8%). The incidence of nodules increases with age in both sexes but the probability of malignancy decreases. As a result, similar to previous studies although thyroid nodule frequency increase with age, it has been determined that malignancy is more common at young ages and there is no gender difference in terms of malignancy. Malignancy was detected in approximately 1/5 of the control biopsies performed after a while in patients with AUS.

Conclusion

In the case of a thyroid nodule at any age patients should be informed there may be a risk for thyroid cancer requiring continued monitoring.

Disclosures

Ethics Committee Approval: The study was approved by the Ethics Committee of Bahçeşehir University Faculty of Medicine Ethics Committee (Decision No. 2019/14/01).

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Conflict of Interest: None declared.

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