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Medicine Science International Medical Journal

ORIGINAL ARTICLE

Medicine Science 2022;11(4):1654-9

Retrospective evaluation of patients with thyroidectomy in our region with thyroid

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Received 02 July 2022; Accepted 06 November 2022
Available online 28.11.2022 with doi: 10.5455/medscience.2022.04.086

Abstract

This study presents to evaluate patients with malignant or operated for benign reasons in terms of the Eastern Black Sea region of Turkey which is an endemic region of Goiter. Within the scope of the study, 460 patients over the age of 18 who applied to the RecepTayip Erdoğan University Training and Research Hospital General Surgery Outpatient Clinic between January 2013 and July 2016 and underwent total thyroidectomy or hemithyroidectomy for benign or malign reasons were retrospectively analyzed. Age, gender, TSH values of the patients, preoperative (preop.) Thyroid or neck ultrasonography (USG) reports, thyroid fine-needle aspiration biopsy (FNAB) results, and pathological/morphological examination results were evaluated. 352 of 460 patients were women (76.5%) and the mean age of all patients was calculated as 52.2 (± 11.39). 70 cases (18%) non-diagnostic cytology, 104 cases (26.8%) benign cytology, 59 cases (15.2%) atypia of uncertain significance, 61 cases (15.7%) suspicion of follicular neoplasia/neoplasia, 78 cases (20.1%) were suspected of malignancy and 16 cases (4.1%) were detected as malignant cytology. While malignancy was diagnosed histopathologically in 248 of 352 female patients who were operated on (70.5%), malignancy was detected in 81 of 108 male patients (75%). The most common thyroid papillary microcarcinoma (51.5%) was observed in histopathological examination. While tumor diameter was <1cm in 53% of patients, the multifocality was detected in 57.3%. When comparing the results of patients who underwent thyroidectomy in our city, and its surroundings where is an endemic goiter region, with the results in the literature, it showed heterogeneity, and our study was found to be above the rate of malignancy in the histopathological examination of Turkey and the world average.

Keywords: Thyroid gland, thyroid fine needle aspiration biopsy, bethesda classification, thyroidectomy, histopathological results

Introduction

Benign and malignant diseases of the thyroid continue to be a problem with difficulties and disagreements in diagnosis and treatment among physicians. Thyroid fine-needle aspiration biopsy is a method generally used to investigate nodules at risk of thyroid cancer. Fine-needle aspiration biopsy (FNAB) is the process of taking cell samples and spreading them on the glass for evaluation under the microscope with the help of a fine needle and an injector to diagnose a mass or nodule under imaging guidance (often this is an ultrasound device). In thyroid fine-needle aspiration biopsy, malignant nodules requiring surgery are differentiated from benign ones and unnecessary surgical interventions are prevented. Although FNAB, radionuclide agents and USG have been widely used in the diagnosis of thyroid nodules in recent years, the reliability of diagnostic methods is changing. Clinical and laboratory data should be well evaluated in patient selection for surgery [1-3].

The incidence of thyroid diseases, and especially of nodules, varies according to the population studied and geographical region. In the world, the Himalayas region of India and the eastern Black Sea and Adana region in Turkey are the places where endemic goiter is most common [1]. Thyroid diseases are more common in women [1]. According to the data of the Turkish Endocrine Society, the frequency of palpable nodules is 3 to 7%, while the frequency of nodules that cannot be detected clinically but detected on ultrasonography is reported to be between 20 and 76% [1]. When a thyroid nodule is detected, the most important approach is to determine whether the nodule is benign or malignant. The probability of malignancy in the nodules is 5%. The prevalence of malignancy is similar in goiter with solitary or multiple nodules.

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In children, people who have been exposed to radiation, and the presence of thyroid cancer in the family, the possibility of malignancy of the existing nodule increases. While the probability of malignancy in cold nodules reaches 15%, the malignancy rate in warm nodules is <1% [2,3].

Our aim in this study, in which we evaluated the results of patients who underwent surgery for about four years, is to reveal the current status of thyroid diseases in the Eastern Black Sea region, which is known as the endemic goiter region in Turkey. The aim is to compare the results obtained from the study with the studies in the literature and to lead the studies to be done in the future.

Material and Methods

In our study, 460 patients over the age of 18 who applied to the General Surgery Polyclinic of the RecepTayip Erdoğan University Training and Research Hospital in a 42-month period between 2013 and 2016 and underwent total thyroidectomy or hemithyroidectomy for benign or malignant reasons and underwent a retrospective analysis were analyzed. Approval for the study was obtained from the Medical Research Ethics Committee of the Medical Faculty of RecepTayip Erdoğan University in Turkey. The data of the patients were obtained by scanning the archives retrospectively. Age, gender, TSH values of the patients, preop. thyroid or neck USG reports, FNAB results, pathological/morphological examination results were reviewed and documented. Statistical analyzes of all data were made with the help of SPSS program. The results were discussed and compared with the literature.

Results

352 (76.5%) of the 460 patients included in our study were women. The mean age of women was 51.3 (±11.5), and the mean age of men was 55.16 (±10.332) (Table 1). It was observed that the patients of both sexes, who were operated on, were mostly between the ages of 50-59 (29.5% in females, 38% in males) (Table 2).

Table 1. Demographic data of patients

	Number of patients	Number of patients %	Mean age	Euthyroid	Hyperthyroidism	Hypothyroidism
Female	352	76.5	51.3 (±11.5)	277 (%84.5)	44 (%13.4)	7 (%2.1)
Male	108	23.5	55.1 (±10.332)	67 (%66.3)	33 (%32.7)	1 (%1)

Considering the results of the FNAB results of the patients included in our study according to the Bethesda classification, 104 patients (26.8%) were most frequently diagnosed with benign cytology, while this rate was 24.8%-33.8% in women and men, respectively. It was determined that the sum of Bethesda III-IV-V-VI classes with risk factors for malignancy constituted 58% of all patients in women and 45.3% in men (Table 4).

Malignancy was detected in 248 of 352 female patients (70.5%) and 81 of 108 male patients (75%) (Table 5). Papillary carcinoma was the most common in operated patients (papillary thyroid microcarcinoma-PTmC 51.5%, papillary thyroid carcinoma-PTC 46.4%). The rate of PTmC was 55% and 40.7% in female and male patients, respectively (Table 6). While the follicular variant of papillary carcinoma was detected most frequently (56.1% in females and 62.5% in males), the rates of classical variant (21%) and mixed type variant (12%) were also found to be high.

We detected malignancy in 275 patients (72.4%) with MNG and 29 patients (64.4%) with solitary nodules. While multifocality was observed in 159 patients (58%) with MNG with malignancy in the histopathological examination, bilaterality was not observed in 249 patients (90.9%) with MNG. The conditions mentioned above were found to be statistically significant ($p<0.05$). PTmC was the most common tumor in 147 patients (53.3%) with MNG and 15 patients (51.7%) with solitary nodules.

Major discrepancies were seen in the comparison of FNAB results and histopathological results. Even in Bethesda I and II patients who were considered to be at low risk for malignancy, malignancy rates were found to be 65.7% and 62.5%, respectively (Table 7).

When we examined our series, we found that there was a correlation between tumor diameter and multifocality, and multifocality increased as the diameter increased. While the mean tumor diameter was 1.51cm (±1.31941) in 188 patients with multifocality, the mean tumor diameter was calculated as 1.19cm (±1.34920) in 140 patients without multifocality.

In the presence or absence of multifocality of the patients included in our study, the rates of capsule and lymphatic invasion were found to be close to each other and this rate was statistically significant (respectively; $p=0.0$; $p<0.05$).

Table 2. Frequency and percentage distributions regarding the ages of the patients

Age	Gender			
	Female		Male	
	N	%	N	%
18-29 years	6	1.7	-	-
30-39 years	54	15.3	8	7.4
40-49 years	97	27.6	22	20.4
50-59 years	104	29.5	41	38.0
60-69 years	72	20.5	27	25.0
70-79 years	18	5.1	10	9.3
80 and above	1	0.3	-	-
TOTAL	352	100	108	100

Table 3. Preop. by gender occurrence of multinodular goiter or solitary nodular goiter on USG

		Number of patients	%	$\overline{X}$	ss	t test		
						t	sd	p
Female	MNG	297	84.4	1.09	0.293	1.401	423	0.162
	Solitary nodule	31	8.8					
Male	MNG	83	76.9	1.14	0.353			
	Solitary nodule	14	13.0					

Table 4. Frequency and percentage distributions regarding the ages of the patients

FNAB (Bethesda classification)	Gender			
	Female		Male	
	Number of patients	%	Number of patients	%
I- non-diagnostic cytology	52	17.2	18	20.9
II- Benign cytology	75	24.8	29	33.8
III- atypia of indeterminate significance	48	15.9	11	12.7
IV- Follicular neoplasia or suspected neoplasia	47	15.6	14	16.3
V- Suspicion of malignancy	66	21.9	12	14
VI- Malignant cytology	14	4.6	2	2.3
Total	302		86	

Table 5. Comparison of histopathological diagnoses by gender

Histopathological diagnoses	Gender			
	Female		Male	
	N	%	N	%
Benign	104	29.5	27	25.0
Malign	248	70.5	81	75.0
Total	352	100.0	108	100.0

Table 6. Distribution of malignancy results by gender

Types of Malignancies	Gender			
	Female		Male	
	N	%	N	%
Papillary Microca	137	55.0	33	40.8
Papillary Ca	107	43.0	46	56.8
Medullary Ca	2	0.8	1	1.2
Follicular Ca	2	0.8	-	
Anaplastic Ca	-		1	1.2
Metastatic	1	0.4	-	-
Total	249	100	81	100

Table 7. Comparison of FNAB results and histopathological results

FNAB	Histopathological Results		X^2	p
	Benign	Malign		
	Number of patients (%)	Number of patients (%)		
Non-Diagnostic Cytology	24(34.3)	46(65.7)	16.813	<0.001
Benign Cytology	39(37.5)	65(62.5)		
Atypia of Indeterminate Significance	19(32.2)	40(67.8)		
Follicular Neoplasia or Suspected Neoplasia	10(16.4)	51(83.6)		
Suspicion of Malignancy	13(16.7)	65(83.3)		
Malignant Cytology	0(0)	16(100)		

Discussion

352 of the 460 patients (76.5%) included in our study were female, and when we look at the literature, the female / male ratio of patients who underwent thyroidectomy was reported as 71-96 / 6-28%, which is consistent with the literature [4-12].

In the literature, the age range of patients who underwent thyroid surgery was reported as 30-60 years (70.5%), 50-59 years (28%), 41-60 years (56.8%) [11-13]. In Turkey, the age range was 40-59 years (57.4%), which was found to be compatible with the literature. In the literature, it is seen that thyroid diseases occur at earlier ages in female than in male, and the incidence increases with age in male. The mean age values in studies on this subject are heterogeneous and range from 47±14.5 to 59±15. In the study of Vashishta et al., in which they examined 59.478 patients who underwent thyroidectomy in the United States in 2009, the mean age was 53±16.4 [14]. In our series, we calculated the mean age of the patients as 51.3±11.56 for females and 55.1±10.33 for males in our study. Based on this study, as it is the largest number of patient studies, we found that our results were similar to the literature.

The incidence of MNG in operated patients varies in the literature. In a study that included 624 patients who underwent thyroidectomy, researchers found the MNG rate to be 76.1%, regardless of gender [4]. Jena A. et al. [15], in their study of 350 patients who underwent thyroidectomy, the rate of MNG was found to be 39.6%, while the rate of solitary thyroid nodule was higher in their study. Slijepcevic et al. [16] reported the rate of MNG as 46.4% in their study of 2466 patients who had undergone thyroid surgery. In our series, we found the incidence of MNG to be 84.4% in female and 76.9% in male. The incidence of solitary nodules was higher in males (13%) than females (8.8%) (Table 3). These varying rates suggest that the incidence of MNG may differ according to geographical regions. As a matter of fact, the MNG rate in our region, which is an endemic region, was 82.6%, which was found to be higher than other studies.

In the literature, when the results of FNAB (Bethesda) are examined, benign cytology is detected at a higher rate than other diagnoses. Jo V.Y. et al. [17], in which they included 892 patients who underwent surgery, the most common benign cytology (Bethesda-II) was found in 60% of the patients' FNABs, and Wojtczak et al. [18], in which he examined 1078 patients who were operated on, it was found that benign cytology (Bethesda-II) (59.81%) was the most common in FNAB and Uğurluoğlu et al. [13] also found benign cytology (Bethesda-II) (72%) most frequently in 1096 patients. When the FNAB (Bethesda) results of the patients in our series were examined, the most benign cytology (26.8%) was found, while contrary to the literature, there was no big difference between them and the other classes. The distribution of FNAB results between men and women was similar. The incidence of benign cytology in male (33.8%) was higher than in female (24.8%).

Studies have indicated that atypia of uncertain significance (Bethesda-III) according to the Bethesda classification should be between 3-6% of all FNABs in a laboratory. it was emphasized that the higher rates represented the overuse of this category, and the results of atypia of uncertain significance in re-examination

of these preparations were actually more appropriate for other Bethesda classes [19-21]. In our clinic, atypia cytology of uncertain significance was found in 15% of patients who went to surgery, and this value is above the value recommended by Bethesda. These patients were mostly referred for surgery, and we found the malignancy rate to be 67.8% in histopathological examinations in these patients. Considering the situation mentioned in the studies above, we think that the criteria of the pathology unit of our hospital in diagnosing Bethesda-III should be reviewed and excessive use of this category should be prevented. The limiting factor for this situation may be the fact that our study was a surgical study and the patient group diagnosed with atypia of uncertain significance but who did not accept surgery and chose to be under control with repeated follow-ups was not included in the study. We believe that real rates will be reached and more accurate estimations and recommendations can be made with studies including these patients in the future.

Radiation exposure is stated as the most important factor in the etiology of thyroid malignancies [22]. The effects of the Chernobyl nuclear power plant accident, especially in the Eastern Black Sea Region of our region, were investigated and the increase in the incidence of cancer was attributed to this accident [22]. After the accident in 1986, a remarkable increase in the ionized isotope density was detected in the surface measurements made by the Turkish Atomic Energy Agency in our region. However, after 30 years, it has been reported that radioactive isotopes have expired in our region and do not pose a risk anymore [22]. Zengi et al. [24] also argued that the Chernobyl accident was not effective on increasing thyroid carcinoma. Considering that thyroid malignancies, especially PTC, is a slowly progressive tumor, it should be kept in mind that individuals exposed to radiation 30 years ago may cause an increase in today's cancer incidence. As a matter of fact, while the rate of thyroid papillary carcinoma was 15.4% in the series performed in the same center as our study between 2008 and 2012 [25], this rate increased to 71.5% in the last 4 years. As determined in our study and in the literature, the average age of thyroid diseases is the 5th and 6th decades [11,13,26]. For this reason, we think that the effects of the Chernobyl accident cannot be ignored in the increase in cancer incidence. However, we do not have any research on the etiological factor, family history, and radiation exposure of our patients in the year of the accident in the patients we included in our study. For this reason, we think that studies should be carried out to support our view.

According to 2008 data in the United States, the incidence of thyroid cancer was found to be 15.1% and 4.6% in male and female, respectively [22]. In the literature review, malignancy rates are in between a wide range of 3%-50.07% [4, 5, 7, 9, 27-29]. The data in Turkey also show differences. According to the data of the Public Health Agency of Turkey, it is one of the 7 most common cancers diagnosed in women and constitutes 3% of all cancers in female. Yıldız et al. [23] found the incidence of thyroid carcinoma to be 13.6% in their retrospective study examining 14-year data including 1585 patients who had undergone thyroid surgery. While the researchers calculated the thyroid carcinoma rate as 8.4% between 1996 and 2002, they reported that this rate increased to 16.9% between 2003 and 2009. This change has been attributed to the Chernobyl nuclear accident, the mandatory household salt iodization program for endemic iodine deficiency that came into effect in 1999, increased diagnostic studies, developments in pathological examinations, and changing surgical techniques. Karagulle et al. [30] found the rate of thyroid carcinoma to be 10.1% in the histopathological examination of 344 patients who underwent surgery, while they found the rate of occult carcinoma to be 62.9%. Bozkurt et al. [31] found thyroid carcinoma in 11 of 241 patients (4.56%) who underwent thyroid surgery in their cancer frequency research in Şırnak province in Turkey and its environs, which is considered endemic due to iodine deficiency. Karatzas et al. [32] in their study in which 2019 patients who underwent total thyroidectomy were examined, the rate of thyroid carcinoma was found to be 29.1%. Albasri et al. [33] found the malignancy rate to be 25.3% in 292 patients who underwent thyroidectomy. When the occult carcinoma rates detected in cadaver series are added, these rates increase even more. Taniover et al. [34] examined 36 thyroid glands in 108 cadaver autopsies in their study in Istanbul and Marmara Region, and they found occult thyroid carcinoma in 4 of them. In their study, they found the rate of occult thyroid carcinoma to be 11.1%. In our study, on the basis of patients undergoing surgery, our malignancy rates seem to be much higher than the average of Turkey compared to similar studies. In our study, the malignancy rate was calculated as 71.5% in all patients who underwent surgery. We think that this height is due to the patient selection due to the developments in the field of diagnosis and treatment, increase in medical facilities, clinical and technical improvements, and especially in our region, due to the developments in access to health services, in our region as well as in the whole world, rather than a real height. The shortcomings of our study are that it is a single-center study, the samples were examined by the same pathology unit, and the patients' family history and radiation exposure histories are lacking.

The Bethesda classification currently has a very important place in the determination of follow-up and treatment. There are many studies in the literature examining the correlation of cytological and histopathological results. Sharma C et al. [35] found the malignancy rate of 1.41% in patients with benign cytology in their study of 724 patients, in which they compared FNAB and histopathological results, while Deniwar A et al. [36] found 15% malignancy in benign cytology. Jo V. Y. et al. [37] in their study, some of the patients with non-diagnostic cytology results were operated on for the first time and the other part after biopsy repetition, and they stated that there was no significant difference in the malignancy results. However, Uğurluoğlu et al. [13] found the malignancy rate as 16% as a result of repetitive biopsy in the non-diagnostic cytology class, and emphasized the importance of repeat FNAB. Arul P et al. [38] investigated many publications in the literature and found the malignancy rate to be higher especially in atypia cytology of uncertain significance (24.4%). Researchers attributed the low rates of malignancy in non-diagnostic and benign cytology results according to the Bethesda classification to improvements in medical and technical facilities, increased success of clinicians in selecting patients to be referred for surgery, and improvements in pathologists' cytological examinations. Kiernan et al. [39] included 1625 patients who underwent thyroidectomy and found the malignancy rate to be 15% in patients diagnosed with atypia of uncertain significance (Bethesda-III). In their study, they saw that the rate of FNAB use increased, and patients with uncertain results in their biopsies were more often referred for surgery. Therefore, interdepartmental communication should be

strengthened to minimize the differences between FNAB and histopathological correlation. Our different correlation results in our series can be attributed to the small number of cases, the difference in the reference classification system, and the way the pathologist described the lesions. In addition, the nodule in which FNAB was taken and the nodule in which malignancy was detected may be two different nodules. We do not have data on this. In our hospital, different doctors in the radiology department perform TIAP procedures. This situation makes the work dependent on the person and affects the results. In addition, our study is a surgical study and it should be kept in mind that the data of the patients who were followed up and did not undergo surgery may affect our rates. All these factors may explain the differences in the correlation of FNAB and histopathological results in our study. However, it is not difficult to meet the mentioned conditions and researches in this direction should be done in the future.

When the malignancy results in all Bethesda classes were examined in our study, it was seen that PTC was mostly (>90%). Kleiman DA et al. [10] In the Bethesda VI correlation, PTC was found to be 76.9%, while Uğurluoğlu C et al. [13] Bethesda stated the rate of PTC in V and VI correlations of 72% and 97%, respectively. Baynes AL et al. [40] the rate of PTC in Bethesda V class was 83%. In our study, Bethesda found the most common PTC in the V and VI categories, which is similar to the literature.

When we look at the results of our study, the most striking situation is that the malignancy rates of the thyroidectomy material in the last pathology result are considerably higher than the country and world data, regardless of the FNAB result. Although it seems logical to attribute this situation to the radioactive accident that took place 30 years ago, it is not possible to prove the accuracy of this fact. The location of the patients included in the case 30 years ago or the presence of other risk factors that may affect the malignancy (radiotherapy history, family history, iodine deficiency, etc.) were not questioned. Therefore, it does not seem possible to attribute the high malignancy rate to a single cause. However, the results of the presented data are also clear. Plus preop. malignancy was also found in the vast majority of patients whose FNAB results were not interpreted as 'malignant'. For this reason, we believe that patients with MNG should be more prone to thyroidectomy, due to the high incidence of malignancy, regardless of the TIAB result, in areas where endemic goiter is common, and even where there is a history of radioactivity, such as our region. One of the most important factors limiting the study is that the surgical method applied is not homogeneous. Results of hemithyroidectomy cases such as total thyroidectomy were also included in our study. In other words, the pathology of the remaining thyroid tissue in some of the patients is unknown. Although we do not think that it will affect the results, we believe that it should be taken into account in the evaluation.

Conclusion

The results of patients who underwent thyroidectomy in and around our city, which is an endemic goiter region, show heterogeneity when compared with the results in the literature, and in our study, we found that the malignancy rates were above the average of Turkey and the world, in the histopathological examination. Rather than a real increase in the high malignancy rates we have achieved, more careful selection of patients to be operated on, more accurate and guiding USG findings, an increase in technical possibilities and molecular analyzes, application of FNAB to suspected patients during follow-up, changes in the examination conditions and methods of pathologists, We think that it is due to factors such as thin section study, awareness of patients and compliance with their follow-up. Therefore, it was concluded that a multidisciplinary study is needed to prevent unnecessary operations in patient follow-up and not to miss patients who need to be operated.

Limitations

It is a surgical study, patients followed up without surgery were not included in the study, biopsy and pathology evaluations were performed by different clinicians, radiation exposure of patients was not investigated.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
Approval for the study was obtained from the Medical Research Ethics Committee of the Medical Faculty of RecepTayip Erdoğan University in Turkey.

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