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Original Article

Changes in the frequency of thyroid cancer and distribution of some subtypes in our region; Retrospective analysis of 4917 thyroidectomies

Bölgemizde tiroid kanseri sıklığında ve bazı alt tiplerin dağılımında gözlenen değişimler; 4917 tiroidektominin retrospektif analizi

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Abstract

Aim: The aim of this descriptive study is to determine the frequency of thyroid cancer (TC) and evaluate the changing rates of histopathological types, age and sex distribution of thyroid tumours in our region.

Material and Methods: A total of 4917 patients who underwent thyroidectomy for different indications between May 2010 and May 2019 were included in this retrospective study. Patients' age, sex, selected surgical method and postoperative final pathology results were recorded. All data were evaluated using statistical analyses.

Results: Of the 4917 patients, 922 were male (18.8%) and 3995 were female (81.2%). The mean age was 48.3 ± 12.3 (17-84) years. Among all cases 27.1% (1335) of them were malignant and 2.6 % (125) of them were well-differentiated tumours of uncertain malignant potential. The 1335 cases diagnosed with a malignant thyroid tumour had a mean age of 44.7±11.6 years and a female-to-male ratio of 4,3. Of these, 94.9% of them had papillary thyroid carcinoma (PTC), 1.72% had follicular thyroid carcinoma (FTC), 2.32% had medullary thyroid carcinoma (MTC), and 0.45% had anaplastic thyroid carcinoma. Of the cases with PTC, 62.66% of them had microcarcinoma.

Conclusion: Papillary thyroid microcarcinoma (PTMC) frequency increases especially in the younger and female population in our region, FTC frequency decreases significantly and MTC is the second most common type of TCs after papillary cancers. In all TCs, the 59.47% PTMC share (mostly detected incidentally, 83.7%) appears to be the result of pathologists examining more tissue blocks and histological sampling over time.

Keywords: epidemiology; pathology; thyroid cancer; thyroidectomy

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Öz

Amaç: Bu tanımlayıcı çalışmanın amacı, bölgemizdeki tiroid kanseri (TK) sıklığını belirlemek ve histopatolojik tiplerin değişen oranlarını, tiroid tümörlerinin yaş ve cinsiyet dağılımını değerlendirmektir.

Gereç ve Yöntemler: Mayıs 2010 ile Mayıs 2019 tarihlerinde arasında farklı endikasyonlarla tiroidektomi uygulanan 4917 hasta bu retrospektif çalışmaya dahil edildi. Hastaların yaşı, cinsiyeti, seçilen cerrahi yöntem ve postoperatif nihai patoloji sonuçları kaydedildi. Tüm veriler istatistiksel analizler kullanılarak değerlendirildi.

Bulgular: Dörtbindokuzyüzonyedi hastanın 922'si erkek (% 18,8) ve 3995'i kadın (% 81,2) idi. Yaş ortalaması 48,3 ± 12,3 (17-84) idi. Tüm vakaların % 27,1'i (1335) malign,% 2,6'sı (125) malignite potansiyeli belirsiz iyi diferansiye tümördü. Malign tiroid tümörü tanısı konan 1335 olgunun yaş ortalaması 44,7 ± 11,6 yıl, kadın / erkek oranı 4,3 idi. Bunların % 94,9'unda papiller tiroid karsinomu (PTK), % 1,72'sinde foliküler tiroid karsinomu (FTK), % 2,32'sinde medüller tiroid karsinomu (MTK), ve % 0,45'inde anaplastik tiroid karsinomu vardı. PTK olan olguların% 62,66'sında mikrokarsinom vardı.

Sonuç: Bölgemizde özellikle genç ve kadın popülasyonda papiller tiroid mikrokarsinom (PTMK) sıklığı artmakta, FTK sıklığı önemli ölçüde azalmaktadır ve MTK, papiller kanserlerden sonra ikinci en sık görülen TK tipidir. Tüm TK'lerinde, % 59,47 PTMK payı (çoğunlukla tesadüfen saptanmıştır, % 83,7), zaman içinde patologların daha fazla doku bloğunu incelemesi ve histolojik örnekleme yapmasının bir sonucu gibi görünmektedir.

Anahtar kelimeler: epidemiyoloji; patoloji; tiroid kanseri; tiroidektomi

Introduction

Thyroid cancer (TC) is the commonest endocrine system malignancy and its incidence has increased significantly in the last 4 decades [1]. TC is the sixth most common cancer in women in the USA and 52070 new cases occurred in both sexes in 2019. TC is still responsible for 0.3 % of cancer-related deaths, and has an incidence of 3.4 % among all cancers [2]. The reasons for this increase are still controversial. But the advances in imaging techniques for the detection of TC, which allows biopsy of even the smallest nodules, is thought to be main reason. However, it is noteworthy that in many countries of the world, this increase, which is mainly observed in microcancers, is not reflected in the mortality rates caused by TC [3].

More than 95% of all TCs are differentiated TCs originating from the thyroid follicular epithelial and includes papillary, follicular and Hürthle cell TCs. Papillary thyroid cancer (PTC) is the most common subtype and has the best prognosis. Follicular thyroid cancer (FTC), Hürthle cell cancer (HCC), and undifferentiated thyroid cancers are high-risk subtypes and tend to distant metastases. Medullary thyroid cancer (MTC) originating from parafollicular C cells constitutes 1-2% of all TCs. In a quarter of patients, MTC may be a component of multiple endocrine neoplasias (MEN) syndromes [4]. Anaplastic thyroid cancer (ATC) in the undifferentiated group is very rare, and its incidence is less than 1%. Patients often present with a rapidly growing neck mass, often accompanied by lymph nodes (LNs), with hoarseness, dysphagia and dyspnea. It may originate from differentiated cancers, as well as de nova. The prognosis of ATC, where distant metastases such as lung, bone and brain are common, is very poor [5]. Primary thyroid lymphoma (PTL) constitutes 1-5% of all thyroid malignancies and only 2% of extranodal lymphomas. Chronic lymphocytic thyroiditis and Hashimoto's thyroiditis are thought to be the cause of 90% of cases [6]. Well-differentiated tumour of uncertain malignant potential (WDT-UMP) are among the follicular tumours of the thyroid, which encapsulate and do not fully meet the criteria of malignancy, but exhibit suspicious structural and cytological features. Although all these tumour subtypes have unique behavioral characteristics, treatment of thyroid tumours (TTs) is usually surgical and the surgical method to be selected according to the type and stage of the tumour may vary from lobectomy to extended neck dissections.

This descriptive study aims to determine the frequency of TC and evaluate the changing rates of histopathological types, age and sex distribution of TTs in our region, by examining the patients who underwent thyroidectomy for a period of 9 years.

Material and Methods

A total of 4917 patients who underwent thyroidectomy for different indications between May 2010 and May 2019 at the Breast and Endocrine Surgery Clinic of Ankara

Numune Training and Research Hospital were included in this retrospective study. Patients' age, sex, selected surgical method and postoperative final pathology results were recorded. Informed consent was obtained from patients at the time of enrolment in the registry. Local ethics board approval was obtained for this study on December 24, 2019 (Number of ethics committee approval: E1-19-201). This study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

The Statistical package for social science (SPSS 20.0 software, IL-Chicago-USA) standard version was used for data analysis. Descriptive analyses were presented as number/percentage for categorical variables, and mean± standard deviation (SD), percentages, minimum and maximum values for continuous variables. One-way analysis of variance (ANOVA) was used to compare continuous variables. The difference between the ratios was compared using Pearson Chi-square test. In the calculations, $p < 0.05$ was considered statistically significant.

Results

Of the 4917 patients included in the study, 922 were male (18.8%) and 3995 were female (81.2%). The mean age of all patients was 48.3 ± 12.3 (17-84) years. Bilateral total thyroidectomy was performed in 4257 (86.58%) patients, total lobectomy in 324 (6.59%) patients and complementary thyroidectomy in 269 (5.47%) patients. The number of substernal and intrathoracic goitre cases performed by sternotomy or thoracotomy was 39 (0.79%). The selected surgical methods in patients operated for different indications are summarized in Table 1. When the final pathologies of the patients were examined, it was found that 70.3% (3457) of the patients were benign and multinodular goiter was in the first place with 1982 patients (40.31%), lymphocytic thyroiditis was seen in 522 patients (10.61%), nodular goiter was observed in 353 patients (7.19%) and Hashimoto thyroiditis was seen in 245 patients (4.98%). The histopathological results of 4917 patients who underwent thyroidectomy are presented in Table 2. Among all TTs; 15.06% (259) of the tumours were benign, 77.66% (1335) of them were malignant and 7.28% (125) of them were TTs with uncertain malignancy potential (Table 3). The most common malignant diagnosis was papillary thyroid microcarcinoma (PTMC) with 16.14% (n = 794), while PTC was seen in 9.61% (n = 473). When PTCs were detected with fine needle aspiration cytology before surgery (469 patients, 97.05%), the vast majority of the PTMCs (665 patients, 83.7%) were diagnosed incidentally. MTC was identified in 31(0.63%) patients, FTC in 23 (0.46%), ATC in 6 (0.12%) and lymphoma in only 3 (0.06%) patients. The detailed age and sex distribution of the cases are presented in Tables 3 and 4.

Table 1. Selected Surgical Methods in Patients Included in the Study

Operation method	n	%
Bilateral total thyroidectomy	4257	86.58
Total lobectomy	324	6.59
Complementary thyroidectomy	269	5.47
Substernal-intrathoracic	39	0.79
One side total, opposite side subtotal thyroidectomy	16	0.32
Subtotal lobectomy	9	0.18
Bilateral subtotal thyroidectomy	3	0.06
Central neck dissection	378	7.68
Lateral neck dissection	108	2.19
Total number of patients	4917	100

Table 2. Histopathological Results of 4917 Thyroidectomy Cases

Pathological diagnosis	n	%
MNG	1982	40.31
PTMC	794	16.15
LT	522	10.61
PTC	473	9.63
NG	353	7.19
HT	245	4.98
FA	176	3.58
WDT-UMP	125	2.55
HCA	83	1.68
TDG	96	1.95
MTC	31	0.63
FTC	23	0.46
ATC	6	0.12
HCC	5	0.10
PTL	3	0.06
Total	4917	100

Abbreviations: MNG, Multinodular goiter; PTMC, Papillary thyroid microcarcinoma; LT, Lymphocytic thyroiditis; PTC, Papillary thyroid carcinoma; NG, Nodular goiter; HT, Hashimoto's thyroiditis; FA, Follicular adenoma; WDT-UMP, Well- differentiated tumour of uncertain malignant potential; HCA, Hürthle cell adenoma; TDG, Toxic diffuse goiter; MTC, Medullary thyroid carcinoma; FTC, Follicular thyroid carcinoma; ATC, Anaplastic thyroid carcinoma; HCC, Hürthle cell carcinoma; PTL, Primary thyroid lymphoma.

Table 3. Age and sex characteristics of benign and malignant thyroid tumours

	Number of cases n (%)	Age mean ± ss (min-max)	p(age)	Female n (%)	Male n (%)	p(sex)
Benign (FA, HCA)	259 (15.06)	36.9.1±12.6 (18-72)	0.048	202 (78)	57 (22)	0.001
Malignant (PTMC, PTC, FTC, MTC, ATC, HCC,PTL)	1335 (77.66)	44.7±11.6 (17-84)		1084 (81.2)	251 (18.8)	
WDT-UMP	125 (7.28)	42.4±9.2 (28-61)		92 (73.6)	33 (26.4)	
Total	1719 (100)	43.8±13.2 (17-84)		1378 (80.2)	341 (19.8)	

Abbreviations: FA, Follicular adenoma; HCA, Hürthle cell adenoma; PTMC, Papillary thyroid microcarcinoma; PTC, Papillary thyroid carcinoma; FTC, Follicular thyroid carcinoma; MTC, Medullary thyroid carcinoma; ATC, Anaplastic thyroid carcinoma; HCC, Hürthle cell carcinoma; PTL, Primary thyroid lymphoma; WDT-UMP, Well- differentiated tumour of uncertain malignant potential.

Table 4. Distribution of malignant thyroid tumours by age and sex characteristics

Tumour type	Number of cases n (%)	Age (yıl)	p(age)	Female (F)	Male (E)	F/M	p(sex)
PTMC	794 (% 59.47)	43.8±11.7 (20-79)	0.032	659	135	4.8	<0.001
PTC	473 (% 35.43)	45.1±13.2 (17-81)		366	107	3.4	0.039
FTC	23 (% 1.72)	44.2±15.3 (21-67)		21	2	10.5	0.034
MTC	31 (% 2.32)	49.4±16.8 (22-69)		19	12	1.5	0.168
ATC	6 (% 0.45)	69.2±7.8 (58-84)		0	6	0	-
HCC	5 (% 0.38)	44.0±10.2 (38-63)		4	1	4	0.428
PTL	3 (% 0.23)	58.0±26.1 (39-76)		1	2	0.5	0.588
Total	1335 (%100)	44.7±11.6 (17-84)		1070	265	4.0	<0.001

Abbreviations: PTMC, Papillary thyroid microcarcinoma; PTC, Papillary thyroid carcinoma; FTC, Follicular thyroid carcinoma; MTC, Medullary thyroid carcinoma; ATC, Anaplastic thyroid carcinoma; HCC, Hürthle cell carcinoma; PTL, Primary thyroid lymphoma.

Discussion

In our country, the incidence of TC has increased by 14% in recent years. It is still the second most common cancer in women after breast cancer, and it is among the first fifteen in men [7]. In our study, which aims to show the changing trends of TC in our region; 1335 (27.1%) of 4917 patients were diagnosed with TC. In a 2008 study of 1632 thyroidectomy specimens from Turkey, the rate of malignant cases was reported to be 16% [8]. Compared with this study, the difference between TC rates, reflecting the same population over a 10-year period, is striking. Similarly, a study from Spain reporting a significant increase in the proportion of TC, which increased from 16.7% in 1978 to 43% in 2001 [9]. Another remarkable issue in TC is gender inequality. In a review of 2016 combining many important studies, TC is reported to be approximately 3 times more common in women than men [10]. In our study, the mean age of thyroid malignancies was 44.7 ± 11.6 years and the female/male (F/M) ratio was 4.3. We found that the female gender was slightly more dominant than the literature.

PTC, which constitutes more than 80% of TCs, is observed 3 times more in women and the average age at first diagnosis is between 40-50 [11]. In the current study, we examined PTMC and PTC as two different subtypes and we found their ratio among all TCs to be 94.9% in total. While the mean age for PTMC and PTC was 43.8 ± 11.7 and 45.1 ± 13.2, respectively, F/M ratios were 4.8 and 3.42. Compared to PTC, it can be said that PTMC is a little more common in young people and women. The predominance of PTMC to make up 59.47% of all thyroid malignancies may be a response to the overall increase in the incidence of TCs.

Contrary to decreases in mortality from TC, in recent years, the incidence of this neoplasm has increased in many countries around the world [2]. Considering that there is no defined change in the known risk factors for TC in our region, it is not wrong to explain this increase in TC incidence (predominantly PTMC) by overdiagnosis and treatment. It is reported in many studies that there is an increase in the detection of micropapillary lesions as a result of increased diagnostic imaging and ultrasound-guided needle biopsies, increased thyroid surgery rates and further cross-sectional examination of histopathological specimens [12, 13]. In this way, thyroid lesions are over-treated and at the same time, other subtype lesions, which may have a worse prognosis, are treated without further growth. All these processes are likely to be associated with an increased incidence of TC and decreased mortality.

Follicular adenoma (FA) and FTCs are defined as follicular neoplasms of the thyroid gland and are seen in 5 to 1 ratio in surgical specimens [14]. FTCs, which constitute 5-10% of TCs, are 3 times more common in women and peak at the 5th decade [11]. In our series, the mean age of the FTC was 44.2 ± 15.3, while the F/M ratio was found to be 10,5. More interestingly, the FA/FTC ratio was 176/23 [7,6] in this study, which was higher than the literature and the incidence of FTC in all TCs was 1.72%. These results show that the female predominance in FTC is increased, but its incidence among TCs is significantly decreased. There may be three reasons for this decline. Firstly, It is a known fact that FTC develops more in patients with iodine deficiency, and PTC predominates in those given excess dietary iodine [14]. As a result of the iodization of household salt, which was started in 1994 and made compulsory in 2000, in Turkey [15]; It can be thought that there has been a significant increase in the frequency of PTC and a relative decrease in FTC over the years. Secondly, a more accurate diagnosis of the follicular variant of papillary cancer and Hürtle cell cancer may also have been effective in this decrease. And finally, the evolution of FAs to FTCs caused by oncogenic mutations. Approximately 20% of patients with FA may develop FTC as a result of N-RAS and K-RAS mutations [14]. Early treatment of these patients with FA by lobectomy or total thyroidectomy may end this transformation before it begins. Similarly, in 2008, Netea-maier et al. emphasized the decrease in other TC subtypes such as FTC and ATC, despite the increase in the incidence of PTC in their study involving 5080 patients [16].

In our study, MTC had a share of 2.32% among all TCs and became the second most common subtype after PTC. Although it can be seen at any age, the mean age for MTC in this study was 49.4 ± 16.8 years, and no significant gender superiority was detected. And ATC, the worst type of TC was 0.45%. The ages of the patients ranged from 58 to 84 years (mean: 69.2 ± 7.8) and all 6 patients were male. In a study of 635 cases reported from our country, Erten et al. detected PTC in 93.2%, FTC in 3.3%, MTC in 2.2% and ATC in 0.6% of TCs [17]. These findings support our study in terms of the decrease in the incidence of FTC and ATC. HCC is another rare type of well-differentiated TC, which accounts for approximately 5% of TC diagnoses. In our series, the HCC rate was 0,38%. Four of 5 patients with HCC were female and the mean age was 44 years. The decreasing percentage of subtypes (such as FTC, HCC and ATC) with poor prognosis, as a result of an increase in the incidence of TC thought to be caused by over-detection may explain this decline. Another hypothesis may be that; As a result of over-treatment of millimetric nodules detected, possible subtypes originating from these nodules disappear before they are formed.

In our study, the diagnosis of PTL was 0.23% of all TCs. Unlike other lymphomas, PTL is a rare entity that accounts for 1% to %5 of all thyroid malignancies, frequently seen in older women and is 2-6 times more common in women [6]. Of the 3 patients, 2 were male and the mean age was 58 years. There was no significant difference between the sexes due to the small number of patients.

The strong sides of this study can be expressed as follows. We reviewed 4917 thyroidectomy cases as one of the most important reference hospitals in our country. While 1/4 of our patients were from Ankara, 3/4 were from local hospitals in other parts of the country. Therefore, the current study, which summarized the data of 1335 TC cases that we encountered in a 9-year period, is also important in terms of reflecting the general characteristics of TC cases in the whole country. A limitation to our study is retrospective nature and has a limited number of variables that did not allow us to compare the risk factors of TCs, such as radiation exposure, family history or dietary factors.

Data collected from 2010 to 2019 showed that more patients who had undergone thyroidectomy had benign thyroid disease (70.3%). But an increased cancer rate (27.1%) is remarkable compared to previous years. This study shows that PTMC frequency increases especially in the younger and female population in our region, FTC frequency decreases significantly and MTC is the second most common type of TCs after papillary cancers. In all TCs, although the share of TMPCs is 59.47%, the vast majority (83.7%) were detected incidentally. This seems to be the result of pathologists examining more tissue blocks over time and an increase in direct histological sampling.

Conclusion

This study confirms an increase in the incidence of TC in our region in recent years. This increase is largely due to an increase in the diagnosis of the PTMCs detected incidentally in the thyroid glands removed for benign thyroid diseases. However, further studies are needed to determine if this increase in the incidence of TC is due to overdiagnosis and detailed cross-sectional examination of histopathological specimens or an increase in TC risk factors.

Declaration of conflict of interest

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