# The Effect Of Age, Sex, And Indications For Operation On The Complications Of Total Thyroidectomy

# Yaş, Cinsiyet Ve Operasyon Endikasyonlarinin Total Tiroidektomi Komplikasyonlari Üzerine Etkisi

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ÖZET	ABSTR
AMAÇ: Total tiroidektomi, tiroidin bir çok benign ve malign hastalıklarında sıkça	AIM: To
yapılmaktadır. En sık görülen komplikasyonları; disfoni, hematom,	maligna
hipoparatiroidi ve rekürren laryngeal sinir hasarıdır. Çalışmamızda total	hemator
tiroidektomi olan hastaların demografik bilgileri ile operasyon	
endikasyonlarının, postoperatif komplikasyonları üzerine etkisi araştırmayı	MATERI
amaçladık.	Baskent

GEREÇ VE YÖNTEM: Çalışmamıza 2011-2022 tarihleri arasında Başkent Üniversitesi Ankara Hastanesine başvuran , 18 yaş üstü, total tiroidektomi operasyonu geçirmiş olan hastalar dahil edildi. Çalışmamız retrospektif, dosya taraması olarak dizayn edildi. Hastaların, yaş cinsiyet, operasyon endikasvonları ve operasvon sonrası komplikasvon bilgileri kavdedildi. Hastalara kalıcı hipoparatiroidi ve kalıcı hipokalsemi diyebilmek için en az 1 yıllık takiplerini değerlendirdik.

BULGULAR: Çalışmaya toplam 580 hasta dahil edildi. Hastaların 422'si (%72,8) kadın, 158'i (%27,2) erkek olup, yaş ortalamaları 49,50±13,91 saptandı. 354 (%61,8) hasta multinoduler guatr, 172 (%29,7) hasta malignite şüphesi, 24 (%4,1) hasta Graves hastalığı, 30 (%5,2) hasta toksik nodul/nodüller nedeni ile opere edilmişti. Operasyon komplikasyonu olarak 1 (%0,02) hastada hematom, 11 (%1,9) hastada vokal kord paralizisi, 10 (%1,7) hastada geçici ses kısıklığı, 7 (%1,2) hastada kalıcı ses kısıklığı, 124 (%21,4) hastada geçici hipoparatiroidi, 11 (%1,9) hastada kalıcı hipoparatiroidi, 263 (%45,3) hastada geçici hipokalsemi, 13 (%2,2) hastada kalıcı hipokalsemi izlendi. Erkeklerde kadınlara göre kalıcı hipokalsemi, kalıcı hipoparatiroidi ve vokal kord paralizisi daha sık izlendi (sırasıyla p=0,009, p=0,010, p=0,502). Malignite şüphesi ile opere edilenlerde kalıcı hipokalsemi, kalıcı hipoparatiroidi, ses kısıklığı ve vokal kord paralizisi daha sık izlendi (sırasıyla p=0,150, p=0,040, p=0,875, p=0,747). ≥65 vas hastalarda postoperatif kalıcı ve geçici ses kısıklığı ayrıca vokal kord paralizisi daha fazla izlendi (sırasıyla p=0,009, p=0.398).

SONUÇ: Postoperatif komplikasyonlar, erkeklerde, ≥65 yaş üstü hastalarda ve malignite şüphesi ile opere edilenlerde daha fazla izlenmektedir.

Anahtar kelimeler: Cinsiyet, komplikasyon, operasyon endikasyonu, total tiroidektomi, yaş

### RACT

Total thyroidectomy is frequently performed in many benign and ant thyroid diseases. The most common complications are; dysphonia, oma, hypoparathyroidism, and recurrent laryngeal nerve injury.

RIAL AND METHOD: Patients over the age of 18 who were admitted to t University Hospital and underwent total thyroidectomy between 2011 and 2022 were included in our study. Our study was designed as a retrospective chart review. Patients' age, sex, indications for operation and postoperative complications were recorded. We evaluated at least 1 year of follow-ups in order to conclude that the patients have permanent hypoparathyroidism and permanent hypocalcemia.

RESULTS: A total of 580 patients were included in the study.. Observed operative complications included hematoma in 1 (0.02%) patient, vocal cord paralysis in 11 (1.9%) patients, temporary hoarseness in 10 (1.7%) patients, permanent hoarseness in 7 (1.2%) patients, temporary hypoparathyroidism in 124 (21.4%) patients, permanent hypoparathyroidism in 11 (1.9%) patients, temporary hypocalcemia in 263 (45.3%) patients, and permanent hypocalcemia in 13 (2.2%) patients. Permanent hypocalcemia, permanent hypoparathyroidism, and vocal cord paralysis were observed more frequently in men than in women (p=0.009, p=0.010, p=0.502, respectively). Permanent hypocalcemia, permanent hypoparathyroidism, hoarseness and vocal cord paralysis were observed more frequently in patients who were operated with suspicion of malignancy (p=0.150, p=0.040, p=0.875, p=0.747, respectively). Postoperative permanent and temporary hoarseness and vocal cord paralysis were more common in patients aged ≥65 years (p=0.009, p=0.398, respectively).

CONCLUSION: Postoperative complications are more common in men, in patients aged  $\geq$ 65 years, and in those operated for suspected malignancy.

Keywords: Age, complication, indication for operation, sex, total thyroidectomy,

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# INTRODUCTION

Surgeries of the thyroid gland, an important endocrine gland, are frequently performed today and they are becoming more common with the increasing incidence of differentiated thyroid cancer in the recent years. One of the most frequently performed thyroid surgery techniques is total thyroidectomy, that is, the total removal of the thyroid gland. It can be performed for benign or malignant pathologies of the thyroid.<sup>1</sup> Indications for total thyroidectomy can be listed as malignancy and suspicion of malignancy in thyroid nodules, Graves' disease, toxic multinodular goiter, toxic nodule, and signs of compression on the airways and esophagus.<sup>2</sup>

The incidence of complications after thyroidectomy has decreased over the past years thanks to technical developments. Dysphonia, dysphagia, dyspnea, hypoparathyroidism, postoperative bleeding, and recurrent laryngeal nerve (RLN) paralysis are the most feared and common complications. Permanent complications may lead to a significant reduction in the patient's quality of life.<sup>3</sup>

Sex and age have been shown to be the risk factors for the incidence of complications in different studies. Similarly, the indication for operation can also lead to differences in the incidence of complications. The incidence of complications can be higher in those operated with the suspicion of malignancy.<sup>3-6</sup>

By reviewing the demographic information (age, sex), indications for operation, and postoperative complications of patients who underwent total thyroidectomy in our hospital, we evaluated whether age, sex, and indications for operation have any effect on complications.

#### MATERIAL AND METHOD

### **Study Design and Patient Cohort**

Patients who were admitted to Baskent University Faculty of Medicine between 01.01.2011-01.01.2022, were at least 18 years of age, and underwent total thyroidectomy for any indication were included in our study. The study was designed as a retrospective chart review. The patients' age, sex, indications for operation, and postoperative complications were recorded. Since patient charts before 2011 could not be accessed, these data were not included in the evaluation. Exclusion criteria were reoperation and lobectomy.

This study was approved by the Local Ethics Committee of Baskent University, Faculty of Medicine (Approval no. KA21/528). The study adhered to the principles of the Declaration of Helsinki. Since our study was a retrospective study, informed consent was not obtained.

### Definition

Postoperative hypocalcemia was defined as 24-hour postoperative calcium levels <8.5 mg/dL (normal range 8.5-10.2 mg/dL), and hypoparathyroidism was defined as 4-hour post-thyroidectomy serum parathyroid hormone (PTH) levels < 13 pg/mL (normal 13-60 pg/mL). Symptomatic or biochemical hypocalcemia that continues for more than 1 year and requires treatment was classified as permanent hypocalcemia, and hypoparathyroidism with the same conditions was classified as hypoparathyroidism.<sup>5</sup> Hoarseness that continues for more than 1 year was considered permanent hoarseness.<sup>6</sup>

#### Statistical analysis

SPSS 16.0 (IBM, Chicago, USA) software was used to analyze the data. When evaluating study data, descriptive statistical methods (mean, frequency, percentage) were used. Pearson Chi-square and Fisher's Exact tests were used to compare qualitative data. A p value < 0.05 was considered statistically significant.

#### RESULTS

A total of 580 patients were included in the study. Of these patients, 422 (72.8%) were female and 158 (27.2%) were male, with a mean age of 49.50 $\pm$ 13.91 years. Indications for operation were multinodular goiter in 354 (61.8%) patients, suspicion of malignancy in 172 (29.7%) patients, Graves' disease in 24 (4.1%) patients, and toxic nodule/nodules in 30 (5.2%) patients

#### Table 1: Indications for operation and pathology results

	Total	Female	Male	<65	≥65
Number of patients	580	n:422	n:158	n:486, 83.8%	n:94, 16.2%
Mean age (years)	49.5	49.1	50.57	45.43	71.19
Indication for operation					
Multinodular goiter	n:354 (61.0%	n:264 (62.6%	n:90 (57.0%)	n:288 (59.3%	n:66
(%)	)	)	n:58 (36.7%)	)	(70.2%)
Suspicion of		n:114 (27.0%	n:7 (4.4 %)	n:152 (31.3%	
malignancy (%)	)	)		)	(21.3%)
Graves' disease (%)	n:24 (4.1%)	n:17 (4.0%)	n:3 (1.9%)	n:23 (4.7%)	n:1 (1.1%)
Toxic nodule/nodules	n:30 (5.2%)	n:27 (6.4%)		n:23 (4.7%)	n:7 (7.4%)
(%)					
Pathology result					
Nodular hyperplasia	n:281 (48.8%	n:210 (49.8%	n:71 (44.9%)	n:226 (46.5%	
(%)	)	)	n:80 (50.6%)	)	(58.5%)
Papillary carcinoma	n:281 (48.5%	n:201 (47.6%	n:4 (2.5%)	n:246 (50.6%	n:35
(%)	)	)		)	(37.2%)
Follicular carcinoma	n:11 (2.0%)	n:7 (1.7%)	n:1 (0.6%)	n:9 (1.9%)	n:2 (2.1%)
(%)	n:4 (0.7%)	n:3 (0.7%)	n:2 (1.3%)	n:3 (0.6%)	n:1 (1.1%)
Medullar CA (%)	n:3 (0.0%)	n:1 (0.2%)		n:2 (0.4%)	n:1 (1.1%)
Other (%)					

Operation complications were hematoma in 1 (0.02%) patient, vocal cord paralysis in 11 (1.9%) patients, temporary hoarseness in 10 (1.7%) patients, permanent hoarseness in 7 (1.2%) patients, temporary hypoparathyroidism in 124 (21.4%) patients, permanent hypoparathyroidism in 11 (1.9%) patients, temporary hypocalcemia in 263 (45.3%) patients, and permanent hypocalcemia in 13 (2.2%) patients.

Permanent hypocalcemia, permanent hypoparathyroidism and vocal cord paralysis were more common in males than females (p=0.009, p=0.010, p=0.502, respectively). For those operated with the suspicion of malignancy, permanent hypocalcemia, permanent hypoparathyroidism, hoarseness, and vocal cord paralysis were more common (p=0.150, p=0.040, p=0.875, p=0.747, respectively). In patients with ≥65 years of age, postoperative permanent and temporary hoarseness as well as vocal cord paralysis were more common (p=0.009, p=0.398, respectively).

#### Table 1: Indications for operation and pathology results

	Total	Female	Male	<65	≥65
Number of patients	580	n:422	n:158	n:486, 83.8%	n:94, 16.2%
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Indication for operation					
Multinodular goiter (%)	n:354 (61.0%)	n:264 (62.6%)	n:90 (57.0%)	n:288 (59.3%)	n:66 (70.2%
Suspicion of malignancy (%)	n:172 (29.7%)	n:114 (27.0%)	n:58 (36.7%)	n:152 (31.3%)	n:20 (21.3%
Graves' disease (%)	n:24 (4.1%)	n:17 (4.0%)	n:7 (4.4 %)	n:23 (4.7%)	n:1 (1.1%)
Toxic nodule/nodules (%)	n:30 (5.2%)	n:27 (6.4%)	n:3 (1.9%)	n:23 (4.7%)	n:7 (7.4%)
Pathology result					
Nodular hyperplasia (%)	n:281 (48.8%)	n:210 (49.8%)	n:71 (44.9%)	n:226 (46.5%)	n:55 (58.5%
Papillary carcinoma (%)	n:281 (48.5%)	n:201 (47.6%)	n:80 (50.6%)	n:246 (50.6%)	n:35 (37.2%
Follicular carcinoma (%)	n:11 (2.0%)	n:7 (1.7%)	n:4 (2.5%)	n:9 (1.9%)	n:2 (2.1%)
Medullar CA (%)	n:4 (0.7%)	n:3 (0.7%)	n:1 (0.6%)	n:3 (0.6%)	n:1 (1.1%)
Other (%)	n:3 (0.0%)	n:1 (0.2%)	n:2 (1.3%)	n:2 (0.4%)	n:1 (1.1%)

Table 2: Post-thyroidectomy hypocalcemia and hypoparathyroidism

	None			P value	None	•	Perman	P valu
		ary	ent			ary	ent	
Age								
<65	n:251	n:224	n:11	P=0.701	n:370	n:107	n:9	P=0.691
	51.6%	46.1%	2.3%	а	76.1%	22%	1.9%	а
≥65	n:53	n:39	n:2		n:75	n:17	n:2	
	56.4%	41.5%	2.1%		79.8%	18.1%	2.1%	
			2.1%			18.1%	2.1%	
Sex								
Male	n:87	n:63	n:8	P=0.009	n:124	n:27	n:7	P=0.010
	55.1%	39.9%	5.1%	а	78.5%	17.1%	4%	а
Female	n:217 51.4%	n:200 47.4%	n:5		n:321 76.1%	n:97	n:4	
	51.4%	47.4%	1.2%		76.1%	23%	0.9%	
Indication for operati								
Multinodular goite	n:179	n:170	n:5	P=0.150	n:263	n:87	n:4	P=0.040
	50.6%	48.0%	1.4%	b	74.3%	24.6%	1.1%	а
Suspicion of malignancy	n:98 57.0%	n:66 38.4%	n:8		n:134 77.9%	n:31	n:7	
manglidiity	n:13	n:11	4.7%		n:22	18.0%	4.1%	
	54.2%	45.8%	n:0		91.7%	n:2	n:0	
Gravesdisease	n:14 46.7%	n:16 53.3%	0.0%		n:26 86.7%	8.3%	0.0%	
Toxic			n:0			n:4	n:0	
nodule/nodules			0.0%			13.3%	0.0%	

Table 3: Hoarseness and vocal cord paralysis after total thyroidectomy

			Vocal Cord Paralysis			
	None	Tempoi Permar Pvalue ary ent	⊵ None	Yes	P valu	
Age						
< 6 5	n :476	n:5 1.0 % n:5 1.0 % P=00.0 9	n:478	n :8	P = 0.3	
≥65	97.9%	n:5 5.3 (n:2 2.1 )	98.4%	1.6%	ь	
	n :87		n :9 1	n : 3		
	92.6%		96.8%	3.2%		
Sex						
Male	n:153	n:2 1.3 n:3 1.9 P=0.62	:n:154	n :4	P = 0.5	
Fem ale	96.8%	n:8 1.95 n:40.9% b	97.5%	2.5%	ь	
	n:410		n:415	n :7		
	97.2%		98.3%	1.7%		
Indication for						
operation	n:344	n:6 1.7 n:4 1.1	n:347	n : 7	P = 0.9	
M ultinodular	97.2%	n:4 2.3 n:3 1.7 P=0.94	98.0%	2.0%	b	
goiter	n:165	h:4 2.5: h:5 1.7: F=0.94	n:168	n:4		
Suspicion of	95.9%	n:0 0.05n:0 0.05	97.7%	2.3%		
malignancy	n:24	n:0 0.05 n:0 0.05		n:0		
Graved/îsease	100%		n:24 100.0%			
Toxic	n:30		n :3 0	n :0		
n o d u le / n o d u le s	100%		100.0 %	0.0%		

# DISCUSSION

Today, the incidence of thyroid diseases increases with the increase in the number of imaging and diagnostic methods. In cases of thyroid malignancy or suspicion of malignancy, or in various hyperthyroidism cases such as toxic adenoma and Graves' disease, thyroidectomy appears as a significant treatment option. However, due to the secondary complications of the operation, the decision to surgery constitutes a significant concern for both the clinician and the patient. Due to these concerns, for thyroid cancers in which the normal decision would be to perform thyroidectomy, in the recent years, especially in patients with advanced age, decisions such as nonoperative follow-up or lifetime follow-up with drugs can be taken. This can lead to the deprivation of the patients from absolute permanent treatment even though there is a choice of full recovery and their subjection to medical follow-up. Medical follow-up brings additional anxiety for the patient and the patient's relatives. Similarly, this involves the adverse effects and risks of antithyroid drugs as well as financial problems due to tests and close monitoring at the hospital.

With the advancement in surgical techniques in recent years, there has been a significant reduction in post-thyroidectomy complications. However, despite these advancements, the incidence of post-thyroidectomy complications may occasionally vary depending on the patient's or the condition's characteristics.

The most common post-operative symptoms can be listed as dysphonia, vocal cord paralysis, hypocalcemia, hypoparathyroidism, and hematoma. The frequency of hoarseness varies between 0.7-5.65% in the literature.<sup>1</sup> In our study, similar to the literature, the frequency of temporary hoarseness was 1.7% and the permanent hoarseness was 1.2%. Post-operative hoarseness was observed more frequently in patients above 65 years of age than in patients below 65 years of age (5.3% and %1, respectively). Possible delays in the operation and related nerve damage were thought to be among the reasons why hoarseness was observed more frequently over the age of 65.The effect of indication for operation and sex on hoarseness was not found significant.

Vocal cord paralysis was observed in 1.9% of the patients. In males, although it was observed more commonly in those above 65 years of age and in those operated due to malignancy, the difference was not statistically significant. Previously, in an Italian study analyzing 14934 patients, the frequency of recurrent laryngeal nerve injury that resulted in vocal cord paralysis after total thyroidectomy was 4.3%.<sup>6</sup> Moreover, similarly, in a meta-analysis of 23512 patients, the frequency of recurrent laryngeal nerve injury after total thyroidectomy performed using different techniques varied between 3.47% and 3.67%.<sup>7</sup>

In our study, the rates of transient hypocalcemia and hypoparathyroidism were found to be 45.3% and 21.4%, respectively. In similar studies in the literature, rates of transient hypocalcemia and hypoparathyroidism were found to be 36.4% and 16.5%, respectively.<sup>5</sup> In our study, this rate was slightly higher than in the literature, and one of the reasons may be the high vitamin D deficiency in our society. In our study, permanent hypocalcemia frequency was 2.2% and permanent hypoparathyroidism frequency was 1.9%. In males and in those operated due to malignancy, these frequencies were much higher. Permanent hypocalcemia frequency was 5.1% in males and 4.7% in those operated due to malignancy. Permanent hypoparathyroidism was 4% in males and 4.1% in those operated due to malignancy. In those operated due to malignancy, the addition of central lymph node dissection is a significant risk factor for hypoparathyroidism and hypocalcemia and can be the reason behind increased frequencies of these conditions. However, in the literature, hypocalcemia, and hypoparathyroidism were observed more commonly in females than in males.<sup>5-9</sup> Similarly, in the literature, in a series including 14934 patients, the frequency of permanent hypocalcemia after total thyroidectomy was 2.2%, and this can be as high as 3.3% in cases operated due to malignancy.6

Several previous studies have shown that the risk of hypocalcemia and hypoparathyroidism after total thyroidectomy due to Graves' disease was much higher. This was attributed to increased bone loss due to thyrotoxicosis and the increased risk of hungry bone syndrome.<sup>10-12</sup> However, in our patients, the frequency of temporary hypocalcemia in those operated due to Graves' disease was similar to in those operated due to other reasons, and the risk of

permanent hypoparathyroidism and hypocalcemia did not increase. Restoring euthyroidism prior to surgery in patients to be operated due to Graves' disease can be considered as the factor that resulted in no increase in the risk.

Hematoma was observed in only 1 patient (0.02%) in our study, but its frequency in the literature varies between 1-3.7%.<sup>16</sup>

Our study had some limitations. The most important one was that although we are a tertiary healthcare center, the sample size of some groups was low. With larger sizes, intergroup differences can be more significant. Moreover, data on factors that can result in significant differences in postoperative hypocalcemia and postoperative hypoparathyroidism risks, such as the patient's comorbidities, preoperative vitamin D, and calcium levels, were not available. In addition, the lack of preoperative vocal cord evaluation information of the patients and the lack of information about whether lymph node dissection was performed during the operation are among the limitations of the study.

# CONCLUSION

In conclusion, complications following total thyroidectomy are more common in those operated due to malignancies. The increase in complication risk following operations due to benign indications such as Graves' disease and toxic nodule was not substantial. In those operated due to Graves' disease and toxic nodule, concerns regarding this complication should not withhold the clinicians and patients this treatment if the best treatment option is surgery. Multi-center studies with a larger sample size are required to relieve the concerns regarding this subject. Considering the fact that concerns regarding complications following thyroidectomy are often weighty enough to influence the treatment decisions, we believe that this study is significant.

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