



## Evaluation of risk factors for incidental parathyroidectomy during thyroidectomy

### Tiroidektomi sırasında rastlantısal paratiroidektomi için risk faktörlerinin değerlendirilmesi

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#### ABSTRACT

**Objective:** Hypocalcemia remains a common problem after thyroidectomy. One of the most common causes of this condition is incidental parathyroidectomy. This study aimed to evaluate the risk factors for incidental parathyroidectomy and the clinical outcomes of incidental parathyroidectomy in patients undergoing thyroidectomy.

**Methods:** A retrospective analysis was conducted on 817 patients who underwent thyroidectomy at the Department of General Surgery at Gazi University between January 2015 and June 2022. Medical records were reviewed for demographic, pathological, and clinical variables. The primary outcome measure was the factors affecting incidental parathyroidectomy, and the secondary outcome measure was the clinical results of incidental parathyroidectomy.

**Results:** Adding lymph node dissection to thyroidectomy statistically increased the frequency of incidental parathyroidectomy ( $p<0.001$ ). The incidence of incidental parathyroidectomy was significantly higher in patients whose final diagnosis was malignant ( $p=0.006$ ). Considering some characteristics of the malignant group, extrathyroidal spread, lymphatic invasion, vascular invasion, and positive surgical margins were not statistically significant for incidental parathyroidectomy. Post-operative calcium levels were statistically significantly lower in the incidental parathyroidectomy group ( $p<0.001$ ). The incidental parathyroidectomy group had a significantly higher incidence of post-operative biochemical hypocalcemia (calcium level  $<8.5$  mg/dL) ( $p<0.001$ ).

**Conclusion:** Incidental parathyroidectomy may occur during total thyroidectomies. This situation increases with thyroidectomies performed for malignant reasons and lymph node dissection. Moreover, although incidental parathyroidectomy causes post-operative biochemical hypocalcemia, its effect on symptomatic hypocalcemia is low.

**Keywords:** Incidental, parathyroidectomy, thyroidectomy, hypocalcemia

#### ÖZ

**Amaç:** Hipokalsemi tiroidektomi sonrası sık görülen bir sorun olmaya devam etmektedir. Bu durumun en yaygın nedenlerinden biri tesadüfi paratiroidektomidir. Bu çalışmada tiroidektomi yapılan hastalarda insidental paratiroidektomi risk faktörlerini ve insidental paratiroidektominin klinik sonuçlarını değerlendirmeyi amaçladık.

**Yöntemler:** Gazi Üniversitesi Genel Cerrahi Anabilim Dalı'nda Ocak 2015 ile Haziran 2022 tarihleri arasında tiroidektomi yapılan 817 hastanın retrospektif analizi yapıldı. Tıbbi kayıtlar demografik, patolojik ve klinik değişkenler açısından incelendi. Birincil sonuç ölçüsü, tesadüfi paratiroidektomiye etkileyen faktörlerdi ve ikincil sonuç ölçüsü, tesadüfi paratiroidektominin klinik sonuçlarıydı.

**Bulgular:** Tiroidektomiye lenf nodu diseksiyonunun eklenmesi insidental paratiroidektomi sıklığını istatistiksel olarak arttırdı ( $p<0,001$ ). Son tanısı malign olan hastalarda insidental paratiroidektomi sıklığı anlamlı olarak daha yüksekti ( $p=0,006$ ). Malign grubun bazı özellikleri göz önüne alındığında, insidental paratiroidektomi için ekstratiroidal yayılım, lenfatik invazyon, vasküler invazyon ve pozitif cerrahi sınır istatistiksel olarak anlamlı değildi. İnsidental paratiroidektomi yapılan grupta ameliyat sonrası kalsiyum düzeyleri istatistiksel olarak anlamlı derecede düşüktü ( $p<0,001$ ). İnsidental paratiroidektomi grubunda post-operatif biyokimyasal hipokalsemi (kalsiyum düzeyi  $<8,5$  mg/dL) görülme sıklığı anlamlı olarak daha yüksekti ( $p<0,001$ ).

**Sonuç:** Total tiroidektomi sırasında tesadüfen paratiroidektomi meydana gelebilir. Malign nedenlerle yapılan tiroidektomiler ve lenf bezi diseksiyonu ile bu durum daha da artmaktadır. Ayrıca insidental paratiroidektomi post-operatif biyokimyasal hipokalsemiye neden olsa da semptomatik hipokalsemiye etkisi düşüktür.

**Anahtar Sözcükler:** İnsidental, paratiroidektomi, tiroidektomi, hipokalsemi

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## INTRODUCTION

Thyroid cancers have been detected more frequently in recent years with the development of ultrasonography. The recommended treatment modality for thyroid cancer is thyroidectomy (1). Although post-operative hypocalcemia has decreased with the development of surgical techniques, it is still a complication that can be seen between 16-55% in patients undergoing thyroidectomy (2,3). In most cases, post-operative hypocalcemia is transient and asymptomatic and is detected only biochemically. However, in a limited number of patients, this condition may be permanent and may require lifelong oral calcium supplementation.

An incidental parathyroidectomy may occur even in an experienced surgeon. There is no consensus on the incidence of incidental parathyroidectomy, its risk factors, and whether it leads to biochemical or symptomatic hypocalcemia (2,4-7). In many previous studies focusing on this issue, different types of surgery have been included (8-10). However, studies on the risk factors and outcomes of incidental parathyroidectomy only during total thyroidectomy are limited. The aim of this study was to determine the risk factors that increase the incidence of incidental parathyroidectomy during total thyroidectomy and the clinical effects of incidental parathyroidectomy.

## MATERIALS AND METHODS

In this study, a retrospective analysis was conducted on 817 patients who underwent thyroidectomy at the Department of General Surgery at Gazi University between January 2015 and June 2022. The study protocol was approved by the Gazi University Institutional Ethics Board (approval number: 15, date: 05.09.2023). Medical records were reviewed for demographic, pathological, and clinical variables. The primary outcome measure was the factors affecting incidental parathyroidectomy, and the secondary outcome measure was the clinical results of incidental parathyroidectomy.

### Statistical Analysis

The data from the study were analyzed using SPSS version 23.0. Initially, descriptive statistics were used. Categorical variables are presented as numbers and percentages, while continuous variables are represented as either mean  $\pm$  standard deviation or median (interquartile range). Continuous variables were assessed for normal distribution using both visual methods (histogram and probability graphs) and analytical techniques (Kolmogorov-Smirnov/Shapiro-Wilk tests). Differences in continuous variables were analyzed using the Mann-Whitney U test, whereas categorical variables were analyzed using chi-square tests.  $P < 0.05$  was considered statistically significant.

## RESULTS

The study included 817 patients who underwent total thyroidectomy at our institution between January 2015 and June 2022. The mean age of the patients was  $49.9 \pm 12.2$  years. Of the patients included in the study, 638 (78.1%) were female and 179 (34.8%) were male. The median nodule size of the patients was 2.0 (1.2- 3.0) cm. Total thyroidectomy was performed in 684 patients (83.7%), total thyroidectomy and central lymph node dissection in 116 patients (14.2%), and total thyroidectomy and neck dissection in

17 patients (2.1%). Post-operative histopathological examination revealed that 452 (55.3%) patients had benign lesions and 365 (44.7%) had malignant lesions. Of the 817 patients who underwent thyroidectomy, 265 (32.4%) underwent lymph node dissection and 158 (19.3%) underwent parathyroidectomy. The median pre-operative calcium level was 9.6 (9.3-9.9) mg/dL and the median post-operative calcium level as 9.3 (8.8-9.7) mg/dL (Table 1).

Table 2 shows a comparison of the frequency of incidental parathyroidectomy according to the descriptive characteristics of the patients. There was no statistically significant difference between the groups of patients with and without incidental parathyroidectomy in terms of age, sex, and nodule size. The incidence of incidental parathyroidectomy was statistically significant according to the surgery performed ( $p < 0.001$ ). The incidence of incidental parathyroidectomy was significantly higher in patients whose final diagnosis was malignant ( $p = 0.006$ ) and those who underwent lymph node dissection ( $p < 0.001$ ). Considering some characteristics of the malignant group, extrathyroidal spread, lymphatic invasion, vascular invasion, and positive surgical margins were not statistically significant for incidental parathyroidectomy.

**Table 1.** Characteristics of patients undergoing thyroidectomy

Characteristics	Values
Age (years), mean $\pm$ SD	49.9 $\pm$ 12.2
Sex, n (%)	
Female	638 (78.1%)
Male	179 (21.9%)
Nodule size (cm), median (IQR <sup>b</sup> )	2.0 (1.2-3.0)
Type of operation, n (%)	
Total thyroidectomy	684 (83.7%)
Total thyroidectomy + central lymph node dissection	116 (14.2%)
Total thyroidectomy + radical lymph node dissection	17 (2.1%)
Histopathology, n (%)	
Benign	452 (55.3%)
Malignant	365 (44.7%)
Lymph node removal status, n (%)	
No	552 (67.6%)
Yes	265 (32.4%)
Incidental parathyroidectomy	
No	659 (80.7%)
Yes	158 (19.3%)
Pre-operative calcium level (mg/dL), median (IQR <sup>b</sup> )	9.6 (9.3-9.9%)
Post-operative calcium level (mg/dL), median (IQR <sup>b</sup> )	9.3 (8.8-9.7%)
Post-operative biochemical hypocalcemia	117 (14.3%)
Post-operative symptomatic hypocalcemia	39 (4.8%)
Post-operative persistent hypocalcemia	2 (0.2%)

<sup>a</sup>Standard deviation, <sup>b</sup>Interquartile range, SD: Standard deviation, IQR: Interquartile range.

**Table 2.** Evaluation of the clinicopathological characteristics of patients with incidental parathyroidectomy

	Incidental parathyroidectomy		p
	No	Yes	
Age (years), median (IQR <sup>a</sup> )	51.0 (42.0-59.0)	49.0 (39.0-58.0)	0.059*
<b>Sex, n (%)</b>			
Female	510 (79.9%)	128 (20,1%)	0.323**
Male	149 (83.2%)	30 (16.8%)	
Nodule size (cm), median (IQR <sup>a</sup> )	2.0 (1.3-3.2)	1.8 (1.8-3.0)	0.079*
<b>Type of operation, n (%)</b>			
Total thyroidectomy	573 (83.8%)	111 (16.2%)	<0.001**
Total thyroidectomy + central lymph node dissection	75 (64.7%)	41 (35.3%)	
Total thyroidectomy + radical lymph node dissection	11 (64.7%)	6 (35.3%)	
<b>Histopathology, n (%)</b>			
Benign	380 (84.1%)	72 (15.9%)	0.006**
Malignant	279 (76.4%)	86 (23.6%)	
<b>Extrathyroidal spread, n (%)<sup>b</sup></b>			
No	249 (75.9%)	79 (24.1%)	0.619**
Yes	30 (81.1%)	7 (18.9%)	
<b>Lymphatic invasion, n (%)<sup>b</sup></b>			
No	266 (76.9%)	80 (23.1%)	0.409**
Yes	13 (68.4%)	6 (31.6%)	
<b>Vascular invasion, n (%)<sup>b</sup></b>			
No	260 (76.7%)	79 (23.3%)	0.858**
Yes	19 (73.1%)	7 (26.9%)	
<b>Surgical border positivity, n (%)<sup>b</sup></b>			
No	247 (76.0%)	78 (24.0%)	0.715**
Yes	32 (80.0%)	8 (20.0%)	
<b>Lymph node removal status, n (%)</b>			
No	469 (85.0%)	83 (15.0%)	<0.001**
Yes	190 (71.7%)	75 (28.3%)	
Post-operative calcium level (mg/dL), median (IQR <sup>a</sup> )	9.3 (8.9-9.7)	9.0 (8.5-9.6)	<0.001*
<b>Post-operative biochemical hypocalcemia</b>			
No	579 (82.7%)	121 (17.3%)	<0.001**
Yes	80 (68.4%)	37 (31.6%)	
<b>Post-operative symptomatic hypocalcemia</b>			
No	629 (80.8%)	149 (19.2%)	0.226**
Yes	30 (76.9%)	9 (23.1%)	
<b>Post-operative persistent hypocalcemia</b>			
No	658 (80.7%)	157 (19.3%)	0.798**
Yes	1 (50%)	1 (50%)	

\*Mann-Whitney U test, \*\*Chi-square test, <sup>a</sup>Interquartile range, <sup>b</sup>Comparisons were made only in the malignant group, IQR: Interquartile range.

The median post-operative calcium level was 9.3 (8.9-9.7) mg/dL in patients in whom no parathyroid was found on histopathological examination and 9.0 (8.5-9.6) mg/dL in patients with incidental parathyroidectomy. Post-operative calcium levels were significantly lower in the incidental parathyroidectomy group ( $p<0.001$ ). The incidental parathyroidectomy group had a significantly higher

incidence of post-operative biochemical hypocalcemia (calcium level  $<8.5$  mg/dL) ( $p<0.001$ ). Post-operative symptomatic hypocalcemia occurred in 9 patients in the incidental parathyroidectomy group, whereas symptomatic hypocalcemia occurred in 30 patients in the non-incidental parathyroidectomy group. There was no statistically significant difference between the two groups ( $p=0.226$ ).

## DISCUSSION

Previous studies have shown that the incidence of incidental parathyroidectomy in thyroid surgery depends on the surgical procedure performed (5-7). However, the number of studies focusing on incidental parathyroidectomy in total thyroidectomy is limited. Manouras et al. (5) reported an incidence of incidental parathyroidectomy of 19.7% in patients undergoing total thyroidectomy. In the study by Du et al. (11), this rate was 10.3%. Manatakis et al. (2) reported an incidental parathyroidectomy rate of 24.9%. In our study, similar to previous studies, we determined the frequency of incidental parathyroidectomy in total thyroidectomies to be 19.3%.

Studies have identified several potential risk factors for incidental parathyroidectomy. Youssef et al. (12) showed that the addition of simultaneous central lymph node dissection to thyroidectomy increased the risk of incidental parathyroidectomy. Sippel et al. (13) reported that younger age, malignant pathology, and bilateral thyroid resection were risk factors for incidental parathyroidectomy. Du et al. (11) reported lateral cervical lymph node dissection, Song et al. (14) reported nodule size, and Khairy and Al-Saif (10) found that extrathyroidal tumor spread was a risk factor for incidental parathyroidectomy. In the present study, we found that the addition of lymph node dissection to total thyroidectomy or lymph node detection on histopathological examination and malignant pathology were risk factors for incidental parathyroidectomy. However, age, sex, nodule size, extrathyroidal spread, and positive surgical margin were not evaluated as risk factors for incidental parathyroidectomy.

The frequency of biochemical hypocalcemia after thyroidectomy varies between 5 % and 55% in the literature (6,11,15,16). In our study, the frequency was recorded as 14.3%. In our study, we also showed that incidental parathyroidectomy decreased post-operative calcium levels and significantly increased biochemical hypocalcemia. However, consistent with previous studies, we did not detect a significant increase in the frequency of symptomatic hypocalcemia and permanent hypocalcemia in patients who underwent incidental parathyroidectomy (6,11). We believe that this is because the remaining parathyroid glands continue to meet physiological needs, similar to other authors.

### Study Limitations

The limitation of our study is that it is retrospective in nature.

## CONCLUSION

In conclusion, incidental parathyroidectomy may occur during total thyroidectomies. This situation increases with thyroidectomies performed for malignant reasons and lymph node dissection. Moreover, although incidental parathyroidectomy causes post-operative biochemical hypocalcemia, its effect on symptomatic hypocalcemia is low.

### Ethics

**Ethics Committee Approval:** The study protocol was approved by the Gazi University Institutional Ethics Board (approval number: 15, date: 05.09.2023).

**Informed Consent:** Retrospective study.

**Peer-Review:** Externally peer-reviewed.

## Authorship Contributions

Concept: Ç.B., Design: Ç.B., H.B., Supervision: K.D., H.B., Resources: H.B., Materials: A.Y., Data Collection or Processing: Ç.B., A.Y., Analysis or Interpretation: K.D., H.B., Literature Search: Ç.B., Writing: H.B.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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