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Unpredictable Nightmare of Thyroid Surgery: Incidental Parathyroidectomy

Tiroid Cerrahisinin Önlenemez Kabusu: İnsidental Paratiroidektomi

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Abstract

Aim Incidental removal of the parathyroid gland is an unwanted minor complication of thyroidectomy and would occur even in experienced centers. The purpose of this study was to evaluate our clinic's outcomes, incidence, and risk factors for incidental parathyroidectomy.

Material and Method A total of 627 patients with an average age of 50.74±12.68 years were included in the study. Seventy-eight point nine percent of the patients had bilateral total thyroidectomy, 11.2% had a total lobectomy with isthmectomy, 4.8% had completed thyroidectomy, 4% had bilateral total thyroidectomy with bilateral central dissection and 1.1% had bilateral subtotal thyroidectomy. Incidental parathyroidectomy was observed in 6.4% (n=40) of all patients.

Results There was a significant correlation between incidental parathyroidectomy and bilateral total thyroidectomy and bilateral central neck dissection. There were no statistically significant differences between the incidental and nonincidental parathyroidectomy group with respect to age and gender. While the preoperative diagnosis of hyperthyroidism (20.6% vs 7.5%) was significantly higher in the non-incidental parathyroidectomy group than in the incidental parathyroidectomy group, and the diagnosis of malignancy was significantly higher in the incidental parathyroidectomy group (32.5% vs. 11.6%, p=0.001). Regarding parathyroid localization, our incidental parathyroidectomy rate was higher in intrathyroidal localized cases. Postoperative transient hypocalcemia (62.5%) was higher in the incidental parathyroidectomy group than in the non-incidental parathyroidectomy group (34.4%, p<0.001).

Conclusion Total thyroidectomy, thyroid pathology, and intrathyroidal parathyroid location are risk factors for incidental parathyroidectomy. Incidental parathyroidectomy during thyroid surgery can be a potential complication.

Keywords Hypocalcemia, incidental, parathyroidectomy

Özet

Amaç *Paratiroid bezinin tesadüfen çıkarılması, tiroidektominin istenmeyen küçük bir komplikasyonudur ve deneyimli merkezlerde bile meydana gelebilir. Bu çalışmanın amacı, kliniğimizin tesadüfi paratiroidektomi sonuçlarını, insidansını ve risk faktörlerini değerlendirmektir.*

Gereç ve Yöntem *Çalışmaya yaş ortalaması 50,74±12,68 olan toplam 627 hasta dahil edildi. Hastaların yüzde yetmiş sekiz nokta dokuzuna bilateral total tiroidektomi, %11,2'sine total lobektomi ile istmektomi, %4,8'ine tamamlayıcı tiroidektomi, %4'üne total tiroidektomi ile birlikte bilateral santral diseksiyonla ve %1,1'ine de bilateral subtotal tiroidektomi uygulandı. Tüm hastaların %6,4'ünde (n=40) rastlantısal paratiroidektomi görüldü.*

Bulgular *Tesadüfi paratiroidektomi ile bilateral total tiroidektomi ve bilateral santral boyun diseksiyonu arasında anlamlı bir korelasyon vardı. Yaş ve cinsiyet açısından tesadüfi ve tesadüfi olmayan paratiroidektomi grubu arasında istatistiksel olarak anlamlı bir fark yoktu. Preoperatif hipertiroidizm tanısı (%20,6'ya karşı %7,5) tesadüfi olmayan paratiroidektomi grubunda tesadüfi paratiroidektomi grubuna göre anlamlı olarak yüksek bulunurken, tesadüfi paratiroidektomi grubunda malignite tanısı anlamlı olarak daha yüksekti (%32,5'e karşı %11,6, p=0.001). Paratiroid lokalizasyonu açısından intratiroidal lokalize vakalarda tesadüfi paratiroidektomi oranımız daha yüksekti. Postoperatif geçici hipokalsemi (%62,5) tesadüfi paratiroidektomi grubunda tesadüfi olmayan paratiroidektomi grubuna göre daha yüksekti (%34,4, p<0,001).*

Sonuç *Total tiroidektomi, tiroid patolojisi ve intratiroidal yerleşimi paratiroid tesadüfi paratiroidektomi için risk faktörleridir. Tiroid cerrahisi sırasında rastlantısal paratiroidektomi potansiyel bir komplikasyon olabilir.*

Anahtar Kelimeler *Hipokalsemi, tesadüfi, paratiroidektomi*

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INTRODUCTION

Currently, thyroidectomy is the most frequently performed endocrine surgical procedure.[1,2] Thyroid surgery is accepted as a safe surgical procedure because the overall complication rate is blow 5%, however, it requires both sufficient anatomical knowledge and a meticulous surgical technique.[1,2] Surgical experience could minimize the major complications of the procedure, such as postoperative bleeding, recurrent nerve injury, and hypocalcemia, but this may still occur.[1,3] Among these complications, hypocalcemia is most frequent, with a rate of 7-51% (1.6%-50% transient, 1.5%-4% permanent hypocalcemia).[4,5] Surgical trauma, the devascularization of the parathyroid gland during surgery, the extent of surgery, and incidental parathyroidectomy (IPT) increase the risk of postoperative hypocalcemia.[6] Postoperative hypocalcemia reduces quality of life sue to long-term use of calcium and increases the total cost of thyroidectomy by prolonging hospital stays.[7-9] IPT is defined as the presence of the parathyroid gland in the postoperative specimen and can be seen in 6-28% of thyroidectomies.[8-10] Several risk factors have been suggested to explain IPT in thyroid surgery, such as anatomical variation, preoperative diagnosis, type of surgery, presence of nodal metastases, reoperation, and central neck dissection.[6,11-15] Also, parathyroid glands are often surrounded by fat and connective tissue, making it difficult for surgeons to distinguish parathyroid tissue from lymph node or adipose tissue so that it may inadvertently be resected.[16] However, a common consensus on clinical and biochemical outcomes in IPT patients does not exist.[14,15,17] Theoretically, resection of a normal parathyroid gland should have no effect on serum calcium levels if three glands function normally. However, some studies have reported a correlation between temporary or permanent hypocalcemia and IPT, while some studies have reported no significant changes in postoperative calcium or parathormone (PTH) levels.[18-23] The purpose of this study was to assess clinical outcomes, incidence, and risk factors for incidental parathyroidectomy.

MATERIAL and METHOD

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. In our clinic, bilateral total thyroidectomy, near-total or total lobectomy with isthmectomy is currently the preferred treatment for thyroid diseases. Between January 2009 and November 2020, 786 patients were operated on in our clinic. Of the underwent thyroidectomy cases, 124 (19.8%) had surgery for hyperthyroidism, 422 (67.3%) for nonfunctional nodules, and 81 (12.9%) for malignancy. One hundred and fifty-nine cases in which parathyroid autoimplantation had been done during the operation were excluded from the study.

Six hundred and twenty-seven cases (106 males, 521 females) with a mean age of 50.74±12, 68 (range 18-86) were included in this study. Serum calcium levels were monitored before surgery, one day after surgery, the first week, and the sixth month of surgery. The patients were discharged home without complications on 1 postoperative day. But patients who developed hypocalcemia were discharged hospital the first day after the hypocalcemia was resolved and were followed for 6 months to see if the hypocalcemia was permanent or transitory. All patient reports were reviewed for both preoperative and final diagnosis of thyroid disease, presence of the parathyroid tissue in the resected specimen, the location of the gland (extracapsular or intrathyroidal), and the number of resected parathyroid glands Hypocalcemia was defined as the serum calcium concentration <8 mg/dl. In patients with postoperative Ca level below 8.00 mg/dl, a calcium effervescent tablet was began orally three times daily. Oral calcium was stopped following laboratory tests and improved clinical signs of hypocalcemia.

Operation

All thyroid surgeries were performed through extracap-

sular dissection by experienced thyroid surgeons. During thyroidectomy, we tried to find and preserve all the parathyroid glands with meticulous dissection and without disturbing the vascularization of the glands. At the end of the operation, the specimen was thoroughly checked for parathyroid tissue. Finally, 627 cases were divided into two groups: Group I IPT and Group II non-IPT.

Statistical analysis

Data were analyzed with IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). The normality assumptions were controlled by the Shapiro-Wilk test. Continuous data were summarized as the mean standard deviation for normally distributed data. Categorical variables were given with frequency (n) and percentage (%) and compared with the Pearson chi-square test and Fisher's Exact test. An independent t-test was used to compare the age between the groups. Post-hoc analysis was performed using the Bonferroni correction. Multivariate logistic regression analysis was used to determine the associated factors with the development of incidental parathyroidectomy. The results of the model were reported with the Odds ratio (OR) and the corresponding 95% confidence intervals (95% CIs). Two-sided p values <0.05 were considered statistically significant.

RESULTS

The average age of 627 patients participating in the study was 50.74±12.68 years and 83.1% were female. Of the patients, 67.3% had nonfunctional nodules, 19.8% had hyperthyroidism, and 12.9% had malignant tumors. The types of surgical procedures performed in these 627 patients were bilateral total thyroidectomy (BTT) in 78.9% of cases, total lobectomy with isthmectomy in 11.2 % of cases, completion thyroidectomy in 4.8% of cases, BTT and bilateral central dissection in 4% of cases, and bilateral subtotal thyroidectomy in 1.1% of cases. In 612 patients (97.6%), the parathyroid gland was located extracapsular and in 15 patients (2.4%) intrathyroidal location was seen. Histopathological examination of the resected thyroid specimens revealed nonfunctional nodules in 77.4% of cases, thyroid malignancy in 18.7% of cases, and thyroiditis in 4% of cases. Postoperatively, 227 patients (36.2%) had temporary hypocalcemia and 16 patients (2.6%) had permanent hypocalcemia.

Incidental parathyroidectomy (IPT) was present in 40 (6.4%) patients. There were no statistically significant differences in terms of age and sex in the IPT group (p=0.232 and p = 0.720, respectively). While the diagnosis of preoperative hyperthyroidism was statistically significantly higher in patients with non-IPT than in the IPT group (20.6% vs 7.5%), in the IPT group, the diagnosis of malignancy was statistically significantly higher (32.5% vs 11.6%, p=0.001). The diagnosis of preoperative hyperthyroidism (20.6% vs. 7.5%) was significantly higher in the non-IPT group and the diagnosis of malignancy (32.5% vs. 11.6%) was significantly higher in IPT (p=0.001). While the frequency of BTT was significantly higher in the non-IPT group than in the IPT group (80.6% vs 55%), BTT and bilateral central dissection were significantly higher in the IPT group (20% vs. 2.9%, p<0.001). The intrathyroidal parathyroid location ratio (37.5%) was significantly higher in the IPT group than in group two (p<0.001). Transient hypocalcemia (62.5%) was higher in group I than in group two (34.4%) (p<0.001) (Table 1.).

Table 1. Patient characteristics				
Variables	All patients	Non-IPT	IPT	
Number of patients (%)	627	587 (93.6)	40 (6.4)	
Age (years), mean±SD	50.74±12.68	50.9±12.65	48.43±13.11	0.232
Gender, n(%)				
Male	106 (16.9)	100 (17)	6 (15)	0.740
Female	521 (83.1)	487 (83)	34 (85)	
Preop diagnosis, n (%)				
Hyperthyroidism	124 (19.8)	121 (20.6)a	3 (7.5)b	**0.001**
Non-functional nodules	422 (67.3)	398 (67.8)a	24 (60)a	
Malignancy	81 (12.9)	68 (11.6)a	13 (32.5)b	
Operation, n(%)				
Bilateral total thyroidectomy	495 (78.9)	473 (80.6)a	22 (55)b	**<0.001**
Total lobectomy with isthmectomy	70 (11.2)	64 (10.9)a	6 (15)a	
Completion thyroidectomy	30 (4.8)	26 (4.4)a	4 (10)a	
Bilateral subtotal thyroidectomy	7 (1.1)	7 (1.2)a	0 (0)a	
Bilateral total thyroidectomy with bilateral santral diseksiyon	25 (4)	17 (2.9)a	8 (20)b	
Location, n(%)				
Intrathyroidal	15 (2.4)	0(0)	15(37.5)	**<0.001**
Extra-capsular	612(97.6)	587(100)	25(62.5)	
Final pathology, n(%)				
Thyroiditis	25 (4)	24(4.1)	1(2.5)	0.156
Non-functional nodules	485 (77.4)	458(78)	27(67.5)	
Malignancy	117 (18.7)	105(17.9)	12(30)	
Postop hipokalsemi, n(%)				
None.	384 (61.2)	372 (63.4)a	12 (30)b	**<0.001**
Transient	227 (36.2)	202 (34.4)a	25 (62.5)b	
Permanent	16 (2.6)	13 (2.2)a	3 (7.5)a	
Independent t-test, Pearson chi-square test, Fisher's Exact test. The same letters in a row denote the lack of statistically significant difference				

According to multivariate logistic regression analysis, the highest risk of IPT was found in patients undergoing bilateral total thyroidectomy and central lymph node dissection, which independently increases the occurrence of IPT (OR: 3.301; 95% CI: 1.007-10.819; p=0.049) (Table 2.).

Table 2. Multivariate logistic regression analysis for IPT		
Variables	OR (95% CI)	p
Age	0.993 (0.968-1.02)	0.618
Female gender	0.885(0.351-2.232)	0.796
Preop diagnosis hyperthyroidism	0.475 (0.139-1.629)	0.237
Preop diagnosis malignancy	1.745 (0.725-4.199)	0.214
Bilateral total thyroidectomy	0.555 (0.245-1.255)	0.157
Bilateral total thyroidectomy with bilateral santral diseksiyon	3.301 (1.007-10.819)	0.049

DISCUSSION

IPT is a relatively common complication of thyroidectomy, but can be reduced to 0.5- 4.0% with meticulous surgery.[6,21] Although there is uncertainty about its incidence and clinical significance, the reported rate varied between 2.9% to 31%.[1,6] Anatomically, the upper parathyroid gland is usually located in the upper pole of the thyroid gland; however, the lower parathyroid glands have some variations and can sometimes be localized intrathymic or differently.[12] Parathyroid tissue can be found in intrathyroidal (16.7-40%) or extracapsular (15.7-81.1%).[14,20-22] The different locations of the parathyroid glands may increase the risk of IPT. Although many authors recommend all parathyroid gland exploration during surgery to reduce the incidence of IPT, this may lead to unwanted Results.[20,21,23] In our study, incidental parathyroidectomy was observed in 40 (6.4%) cases and 37.5% of all were located intrathyroidal, which was statistically significantly higher than Group II ($p<0.001$). There has been a lot of controversy about the relationship of IPT to thyroid cancer or thyroiditis. Several previous studies showed a strong relationship; however, some studies found no connection between them.[4,18,21,23] Type of surgery may increase the risk of IPT. Khairy et al. reported that total thyroidectomy is a risk factor for IPT.[14] In our study, malignancies, total bilateral thyroidectomy, and bilateral central neck dissection were found to be risk factors for IPT. We believe that extensive dissection during bilateral total thyroidectomy and lymph node dissection are an important cause of this. Some literature suggests that gender is also a risk factor for IPT, especially in young patients.[12,15,21] In addition, Rix et al. showed that completing thyroidectomy is a risk factor for IPT.[24] However, age, gender, and surgical difficulty of completing thyroidectomy and re-exposure of the neck were not found to be risk factors for IPT in our study, as in Khairy's study. In many studies, the risk of IPT has been shown to increase because of scar tissue and bleeding from inflammation of the thyroid gland.[25] In our study, no statistically significant differences were found between thyroiditis and IPT. Although clinical hypocalcemia is less common, biochemical hypocalcemia rates can be up to 83% of cases, and transient hypocalcemia is the most common condition after thyroid surgery.[21] Specific factors such as parathyroid gland injury, devascularization, or one or more parathyroid gland excision have been claimed as the reason of hypocalcemia but remain multifactorial.[14, 26] However, there is controversy about the association of hypocalcemia with IPT in the literature.[4,20] In the study of Sippel et al. postoperative calcium levels were significantly lower in the IPT group.[15] In our study, transient hypocalcemia was seen in 25 cases (62.5%) and permanent hypocalcemia was seen in 3 cases (7.5%) of the IPT group and a significant difference was observed between the two groups ($p<0.001$).

In conclusion, IPT is a common condition in thyroid surgery pathological reports, even in experienced centers. In our study, bilateral total thyroidectomy and neck dissection, and intrathyroidal location of the parathyroid gland were found to be risk factors for IPT. Since only one parathyroid gland was removed during thyroid surgery, as in our study, permanent hypocalcemia is not often seen as a result of compensation of other intact glands. Even though sufficient anatomical knowledge and meticulous surgical techniques are the most important step of prevention of IPT, nothing can predict in which patient it will occur.

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Ethical Approval

University of Health Science, Derince Education and Research Hospital ethics Commitee and following the Declaration of Helsinki (decision no: No. 2021-1409).

Peer-review

Externally and internally peer-reviewed.

Authorship Contributions

Concept: M.B.Y., A.C., Design: M.B.Y., A.C., H.T.T., Data collection or Processing: M.B.Y., A.C., H.T.T., Analysis or interpretation: M.B.Y., A.C., Literature Search: M.B.Y., A.C., Writing: M.B.Y.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Informed Consent

Retrospective study

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