ORIGINAL ARTICLE

# Effect of Inadvertent Parathyroidectomy on Hypocalcemia after Thyroidectomy

Murat Ö Kiliç[1], Ali Sapmaz[2]

## Abstract

**Introduction:** Inadvertent parathyroidectomy (IP) is not a rare condition following total thyroidectomy. However, the clinical relevance of IP is unclear.

**Aim:** The aim of this study was to investigate the clinical effect of IP on postoperative hypocalcemia in patients undergoing total thyroidectomy.

**Materials and methods:** A total of 214 patients who underwent total thyroidectomy for benign or malignant thyroid disease were included in the study. All patients were classified as patients without IP and those with IP. The two groups were then compared between each other in terms of postoperative hypocalcemia and other clinicopathological findings.

**Results:** There were 32 (15%) males and 182 (85%) females, with a mean age of 50.2 years. IP was found in 38 (17.8%) patients. Both postoperative biochemical ($p = 0.001$) and symptomatic ($p = 0.000$) hypocalcemia were found to be more common in patients with IP compared with those without IP. Patients with IP had a significantly higher incidence of permanent hypocalcemia in comparison to those without IP ($p = 0.000$).

**Conclusion:** IP is positively correlated with both transient and permanent hypocalcemia after total thyroidectomy. Careful surgical approach is of great importance to reduce the incidence of this disturbing complication.

**Keywords:** Inadvertent parathyroidectomy, Postoperative hypocalcemia, Total thyroidectomy.

*World Journal of Endocrine Surgery* (2019): 10.5005/jp-journals-10002-1256

## Introduction

Hypocalcemia is among the most frequent complications after total thyroidectomy (TT), with a reported incidence ranging between 1% and 64% for transient hypocalcemia and up to 17% for the permanent form.[1] Although it is multifactorial, parathyroid insufficiency caused by injury to the blood supply or inadvertent removal of parathyroid glands (PGs) was reported as the most frequent reason for this complication.[2–5] The presence of PGs in surgical specimens is not a rare condition, with an incidence of up to 21%.[6] Although most of the postoperative hypoparathyroidies improve within weeks or months after surgery, it is an important cause of concern to both patients and surgeons. Decreased quality of life, increased health costs due to prolonged medications, repeated hospitalizations, loss of surgical motivation, and long-term morbidities such as renal failure and neuropsychiatric disorders are associated with this complication, particularly the permanent form. At this point, the main question needed to be clarified is the effect of inadvertent parathyroidectomy (IP) on the development of a postoperative hypocalcemia.

In this study, we aimed to determine the clinical importance of IP on an early or late postoperative hypocalcemia in a Turkish patient group who underwent TT for benign or malignant thyroid diseases.

## Materials and Methods

### Patients and Study Design

A total of 214 patients who underwent TT for benign and/or malignant thyroid disease in Eskişehir State Hospital between December 2016 and August 2018 were included in this retrospective study. Patients' age and gender, preoperative indirect laryngoscopy, baseline biochemical parameters, sonographic findings, fine needle aspiration biopsies, and final pathology results were recorded. The exclusion criteria were being under 18 years old, previous neck operation, presence of preoperative hypocalcemia, using a drug that interfered with calcium (Ca) homeostasis (Ca or vitamin D supplements, bisphosphonates, diuretics, lithium, etc.), and biochemical findings indicating renal insufficiency.

Total thyroidectomy with or without central/lateral lymph dissection was performed by a single surgeon in all cases. Serum Ca levels were checked at the first day, first month, and sixth month, postoperatively. The definition of postoperative hypocalcemia was accepted as serum-corrected Ca (measured Ca + 0.02 × (40 − serum albumin)) level less than 8.0 mg/dL.

Patients were considered to have symptomatic hypocalcemias in the case of hypocalcemia-related symptoms such as positive Chvostek's or Trousseau's sign, perioral or fingertip, paresthesias or numbness, and cramping.

This study was conducted in accordance with the declaration of Helsinki. Written informed consents were not obtained from the patients because of the retrospective nature of the study.

[1]Department of Surgical Oncology, Eskisehir City Hospital, Eskişehir, Turkey

[2]Department of General Surgery, Numune Training and Research Hospital, Ankara, Turkey

**Corresponding Author:** Murat Ö Kiliç, Department of Surgical Oncology, Eskisehir City Hospital, Eskişehir, Turkey, Phone: +90 5053573122, e-mail: murat05ozgur@hotmail.com

**How to cite this article:** Kiliç MÖ, Sapmaz A. Effect of Inadvertent Parathyroidectomy on Hypocalcemia after Thyroidectomy. World J Endoc Surg 2019;11(2):37–40.

**Source of support:** Nil

**Conflict of interest:** None

### 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 ± SD/percentages for continuous variables. Chi-squre test, Mann–Whitney *U* test, and Fisher's exact test were used to evaluate the differences between the two groups. $p < 0.05$ was accepted as significance level.

## Results

A total of 214 patients (ranging from 18 to 76) with a mean age of 50.2 years were included in this study. There were 32 (15%) males and 182 (85%) females. One-hundred and thirty-one (61.2%) patients were operated for a diagnosis of benign thyroid disease, while thyroid cancer was the surgical indication in 83 (38.8%) patients. At least one PG was found in pathological specimens of 38 (17.8%) patients. All the demographic and clinicopathological data were presented in Table 1.

Patients were classified into two groups: patients without IP ($n = 176$, group I) and those with IP ($n = 38$, group II). Both groups were similar in terms of age, preoperative Ca, preoperative vit D, preoperative diagnosis, and type of surgery ($p > 0.5$). Gender was significantly different between the two groups ($p = 0.021$). Postoperative 1st day Ca level was significantly lower in patients with IP than those without IP ($p = 0.005$). Both postoperative biochemical ($p = 0.001$) and symptomatic ($p = 0.000$) hypocalcemia were found to be more common in patients with IP compared with those without IP. Permanent hypocalcemia was observed in eight patients of whom five was in patients of group II. Patients with IP had a significantly higher incidence of permanent hypocalcemia in comparison to those without IP ($p = 0.000$). Comparison of all clinical and pathological findings between the two patient groups were presented in Table 2.

**Table 1:** Baseline clinicopathological characteristics of the patients ($n = 214$)

| *Characteristics* | *n (%)* |
|---|---|
| Age (mean, y) | 50.2 ± 11.8 (18–76) |
| Gender (F/M) | 182 (85)/32 (15) |
| Diagnosis | |
| Toxic goitre (graves + nodulary) | 23 (10.7) |
| Non-toxic multinodulary goitre | 108 (50.5) |
| Cancer | 83 (38.8) |
| Preoperative Ca (mean, ng/mL) | 9.5 ± 0.38 (8.5–10.4) |
| Preoperative vit D (mean, ng/mL) | 16.2 ± 8.2 (2.6–44.04) |
| Type of surgery | |
| TT alone | 188 (87.9) |
| TT + central neck dissection | 26 (12.1) |
| Lateral neck dissection | 6 (2.8) |
| IP | 38 (17.8) |
| Postoperative 1st day Ca (mean, ng/mL) | 8.08 ± 0.63 (6.1–9.5) |
| Postoperative 6th month Ca (mean, ng/mL) | 9.3 ± 0.51 (7.1–10.4) |
| Biochemical hypocalcemia | 91 (42.5) |
| Symptomatic hypocalcemia | 55 (25.7) |
| Permanent hypocalcemia | 8 (3.7) |

Data are presented as mean ± SD for age, preoperative Ca, postoperative Ca, and preoperative vit D, and; *n* (%) for other variables. y, year; F, female; M, male; TT, total thyroidectomy; IP, inadvertent parathyroidectomy

**Table 2:** Comparison of clinical and pathological findings between the two groups

| *Characteristics* | *Group I (n = 176)* | *Group II (n = 38)* | *p* |
|---|---|---|---|
| Age | 50.6 ± 11.9 (18–76) | 48 ± 11.2 (20–68) | 0.301 |
| Gender (F/M) | 145 (82.4%)/31 (17.6%) | 37 (97.4%)/1 (2.6%) | 0.021 |
| Thyroid function status | | | 0.143 |
| Toxic | 16 (9.1%) | 7 (18.4%) | |
| Non-toxic | 160 (90.9%) | 31 (81.6%) | |
| Preoperative Ca (ng/mL) | 9.5 ± 0.39 (8.5–10.4) | 9.6 ± 0.32 (8.8–10.2) | 0.244 |
| Preoperative vit D (ng/mL) | 15.7 ± 7.6 (3.2–44.04) | 18.2 ± 10.4 (2.6–41.3) | 0.356 |
| Type of surgery | | | 1.000 |
| TT alone | 154 (87.5%) | 34 (89.5%) | |
| TT + central ND | 22 (12.5%) | 4 (10.5%) | |
| Lateral ND | 5 (2.8%) | 1 (2.6%) | 1.000 |
| Final histopathology | | | 1.000 |
| Benign | 108 (61.4%) | 23 (60.5%) | |
| Malignant | 68 (38.6%) | 15 (39.5%) | |
| Postoperative 1st day Ca (ng/mL) | 8.1 ± 0.57 (6.1–9.58) | 7.7 ± 0.76 (6.3–9.4) | 0.005 |
| Postoperative 6th month Ca (ng/mL) | 9.3 ± 0.47 (7.88–10.4) | 8.9 ± 0.54 (7.1–9.6) | 0.178 |
| Biochemical hypocalcemia | 65 (36.9%) | 26 (68.4%) | 0.001 |
| Symptomatic hypocalcemia | 33 (18.7%) | 22 (57.9%) | 0.000 |
| Permanent hypocalcemia | 3 (1.7%) | 5 (13.1%) | 0.000 |

Data are presented as mean ± SD for age, preoperative Ca, postoperative Ca, and preoperative vit D; *n* (%) for other variables. y, year; F, female; M, male; TT, total thyroidectomy; ND, neck dissection

## Discussion

As known, traditional rules for the prevention of IP are well recognized, including a meticulous capsular dissection of the thyroid gland, ligation of inferior thyroid artery close to the thyroid capsule, and a high effort for the identification of all PGs.[7,8] However, IP is not an uncommon finding in the pathological evaluation of the thyroidectomy material, and can be even seen in the hands of experienced endocrine surgeons. The incidence of IP in our patient cohort was consistent with those reported from the previous studies.[5,9–11]

To date, various risk factors related to IP (such as female gender, reoperation, thyroiditis, duration of disease, malignancy, neck dissection, and nodal metastases) were determined in the literature.[8–10,12–14] However, it should be stated that those results are highly variable between the published studies. For instance, Cristakis et al. and Zhou et al. reported in their works that female gender was associated with the incidence of IP, while male gender was found to be a risk factor for IP in the study by Manouras et al.[8,14,15] On the other hand, sex was not related to incidental removal of PGs in other studies.[5,11] The results obtained from the present study showed that IP was more common in female

patients. However, age was not a significant risk factor for IP in our patient group, consistent with the majority of the previous studies.[8,11,12] Malignant disease with or without lymph dissection was determined as an associated risk factor for accidental removal of PGs.[5,13,14,16–18] However, neither malignancy nor the extent of surgical procedure was found to be associated with IP in our patient population. This result may be due to the relatively small number of patients who have undergone central or lateral neck dissection (or both). We also consider that a meticulous dissection in accordance with the standard surgical rules might have contributed to this result. It should be stated here that lymph dissection, especially central lymph node dissection, always carries additional risks for the removal or ischemic injury of all PGs.

The question, which was also the main purpose of the present study, is that how IP effects the clinical course in such patients. The role of IP in the development of a transient or permanent hypocalcemia following TT is still unclear. Some authors reported that IP was associated with hypocalcemia, whereas IP was not found to be correlated to postoperative hypocalcemia in other clinical studies.[9,10,12,15,19–22] First of all, the incidences of the transient and permanent hypocalcemia in our patient group were consistent with those reported by the previous studies.[12,14,22–24] In our work, both biochemical and symptomatic hypocalcemias were significantly more common in patients with IP than those without IP. Similarly, Zheng et al. found that incidental parathyroidectomy was positively correlated with postoperative hypoparathyroidism. Since the postoperative serum PTH measurement was not in our routine clinical approach, this blood test was performed only in patients with a low postoperative Ca. Therefore, PTH levels cannot be statistically evaluated between the groups. Removal of PG is, of course, not the only factor leading to a postoperative hypocalcemia. Ischemic injury to the blood supply of PGs and postoperative fluid resusitation play important roles in the development of hypocalcemia. Nevertheless, the occurrence of hypocalcemia related to hypoparathyroidism is an expected situation following removal of PG. Our results were also in this direction except the correlation between IP and the sixth month Ca levels. Mean Ca level at the sixth month was not significantly different between patients with IP and those without IP. This can be explained by the reactive hypertrophic growth of the remaining PGs, and is not suprising because of the very small number of permanent hypocalcemia in routine practice.

This study has several limitations. First, it was conducted in a single center, which may limit the generalizability of the statistical results. A relatively small number of patients with a permanent hypocalcemia is another limitation, which makes it difficult to interpret subgroup findings. Finally, its retrospective nature may be considered as a limitation. However, a homogeneous cohort of patients by excluding operations other than TT (i.e. lobectomy and reoperations) and performing all operations by a single surgeon with standard surgical techniques may be the strengths of this study.

## Conclusion

IP is positively correlated with both transient and permanent hypocalcemias after TT. Considering the clinical, social, and psychological effects of hypocalcemia, careful surgical approach is of great importance to reduce the incidence of this disturbing complication.

## References


1. Gschwandtner E, Seemann R, et al. How many parathyroid glands can be identified during thyroidectomy?: Evidence-based data for medical experts. Eur Surg 2018;50(1):14–21. DOI: 10.1007/s10353-017-0502-0.
2. Sitges-Serra A, Ruiz S, et al. Outcome of protracted hypoparathyroidism after total thyroidectomy. Br J Surg 2010 Nov;97(11):1687–1695. DOI: 10.1002/bjs.7219.
3. Tredici P, Grosso E, et al. Identifcation of patients at high risk for hypocalcemia after total thyroidectomy. Acta Otorhinolaryngol Ital 2011 Jun;31(3):144–148.
4. McWade MA, Paras C, et al. A novel optical approach to intraoperative detection of parathyroid glands. Surgery 2013 Dec;154(6):1371–1377. DOI: 10.1016/j.surg.2013.06.046.
5. Zheng J, Song H, et al. Evaluation of clinical significance and risk factors of incidental parathyroidectomy due to thyroidectomy. Medicine (Baltimore) 2017 Sep;96(39):e8175. DOI: 10.1097/MD.0000000000008175.
6. Luo H, Zhao W, et al. *In Situ* Preservation Fraction of Parathyroid Gland in Thyroidectomy: A Cohort Retrospective Study. Int J Endocrinol 2018 Mar;2018:7493143. DOI: 10.1155/2018/7493143.
7. Reeve T, Thompson NW. Complications of thyroid surgery: how to avoid them, how to manage them, and observations on their possible effect on the whole patient. World J Surg 2000 Aug;24(8):971–975. DOI: 10.1007/s002680010160.
8. Christakis I, Zacharopoulou P, et al. Inadvertent parathyroidectomy risk factors in 1,373 thyroidectomies—male gender and presence of lymphadenopathy, but not size of gland, independently increase the risk. Gland Surg 2017 Dec;6(6):666–674. DOI: 10.21037/gs.2017.07.06.
9. Lin DT, Patel SG, et al. Incidence of inadvertent parathyroid removal during thyroidectomy. Laryngoscope 2002 Apr;112(4):608–611. DOI: 10.1097/00005537-200204000-00003.
10. Spiliotis J, Vaxevanidou A, et al. Risk factors and consequences of incidental parathyroidectomy during thyroidectomy. Am Surg 2010 Apr;76(4):436–441.
11. Manatakis DK, Balalis D, et al. Incidental Parathyroidectomy during Total Thyroidectomy: Risk Factors and Consequences. Int J Endocrinol 2016;2016:7825305. DOI: 10.1155/2016/7825305.
12. Khairy GA, Al-Saif A. Incidental parathyroidectomy during thyroid resection: incidence, risk factors, and outcome. Ann Saudi Med 2011 May-Jun;31(3):274–278. DOI: 10.4103/0256-4947.81545.
13. Applewhite MK, White MG, et al. Incidence, Risk Factors, and Clinical Outcomes of Incidental Parathyroidectomy During Thyroid Surgery. Ann Surg Oncol 2016 Dec;23(13):4310–4315. DOI: 10.1245/s10434-016-5439-1.
14. Zhou HY, He JC, et al. Inadvertent parathyroidectomy: incidence, risk factors, and outcomes. J Surg Res 2016 Sep;205(1):70–75. DOI: 10.1016/j.jss.2016.06.019.
15. Manouras A, Markogiannakis H, et al. Unintentional parathyroidectomy during total thyroidectomy. Head Neck 2008 Apr;30(4):497–502. DOI: 10.1002/hed.20728.
16. Sippel RS, Ozgul O, et al. Risks and consequences of incidental parathyroidectomy during thyroid resection. ANZ J Surg 2007 Jan-Feb; 77(1-2):33–36. DOI: 10.1111/j.1445-2197.2006.03972.x.
17. Campos NS, Cardoso LP, et al. Risk factors for incidental parathyroidectomy during thyroidectomy. Braz J Otorhinolaryngol 2012 Feb;78(1):57–61. DOI: 10.1590/S1808-86942012000100009.
18. McGoldrick DM, Majeed M, et al. Inadvertent parathyroidectomy during thyroid surgery. Ir J Med Sci 2017 Nov;186(4):1019–1022. DOI: 10.1007/s11845-017-1560-9.
19. Özoğul B, Akçay MN, et al. Incidental parathyroidectomy during thyroid surgery: risk factors, incidence, and outcomes. Turk J Med Sci 2014;44(1):84–88. DOI: 10.3906/sag-1211-56.
20. Sorgato N, Pennelli G, et al. Can we avoid inadvertent parathyroidectomy during thyroid surgery? In Vivo 2009 May-Jun; 23(3):433–440.

21. Youssef T, Gaballah G, et al. Assessment of risk factors of incidental parathyroidectomy during thyroid surgery: a prospective study. Int J Surg 2010;8(3):207–211. DOI: 10.1016/j.ijsu.2009.12.008.
22. Sheahan P, Mehanna R, et al. Is systematic identification of all four parathyroid glands necessary during total thyroidectomy?: a prospective study. Laryngoscope 2013 Sep;123(9):2324–2328. DOI: 10.1002/lary.23954.
23. Del Rio P, De Simone B, et al. Unintentional parathyroidectomy and postoperative hypocalcaemia. Conventional thyroidectomy versus miniinvasive thyroidectomy. Ann Ital Chir 2014 Sep-Oct;85(5):470–473.
24. Eismontas V, Slepavicius A, et al. Predictors of postoperative hypocalcemia occurring after a total thyroidectomy: results of prospective multicenter study. BMC Surg 2018 Aug 9;18(1):55. DOI: 10.1186/s12893-018-0387-2.