

Strategies to Maintain A Normocalcemic, Asymptomatic Status Following Total Thyroidectomy

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ABSTRACT

Introduction: Hypoparathyroidism is an unintended complication of total thyroidectomy that may result from accidental parathyroid gland excision or devascularization. However, its management remains clinically and surgically challenging. We aimed to investigate associations between postoperative hypoparathyroidism and parathyroid gland excision, vascular integrity, and early replacement therapy.

Methods: We retrospectively analyzed 536 patients who underwent total thyroidectomy between August 2022 and April 2025. Patients with records of preoperative and postoperative parathyroid hormone (PTH) and calcium levels, including 4- and 8-week values, were included in the study. The effects of calcium and active vitamin D replacement therapies were evaluated.

Results: Transient hypoparathyroidism occurred in 18.7% of patients; no cases of permanent hypoparathyroidism were detected. The mean PTH reduction rate was significantly higher in the hypoparathyroidism group (71.71%) than in the non-hypoparathyroidism group (38.44%; $p < 0.05$). No statistically significant difference in PTH reduction was found between patients with and without accidental gland excision. Early calcium and active vitamin D supplementation reduced the incidence of symptomatic hypocalcemia.

Conclusion: Preservation of parathyroid function after thyroid surgery depends on vascular integrity and early replacement therapy with calcium and active vitamin D rather than solely on avoiding gland excision. Early biochemical monitoring and proactive supplementation could mitigate the risk of symptomatic hypocalcemia.

Keywords: Total thyroidectomy, hypoparathyroidism, parathyroid hormone (PTH), hypocalcemia prevention, calcium supplementation

Introduction

Postoperative hypoparathyroidism, a common complication of thyroid surgery, results from accidental excision, devascularization, or trauma-induced functional loss of parathyroid glands. The incidences of transient and permanent hypoparathyroidism following total thyroidectomy range from 10 % to 30 % and from 1 % to 7 %, respectively (1-3). This condition significantly affects patients' quality of life and may lead to serious complications due to hypocalcemia, such as muscle spasms, paresthesia, cardiac arrhythmias, and laryngospasm (4).

Identifying the parathyroid glands *in situ* and preserving their vascular integrity are essential for maintaining parathyroid function. Lorente-Poch et al. (5) demonstrated that *in situ* preservation of parathyroid glands significantly reduced the risk of permanent hypoparathyroidism. Modern surgical tools, such as near-infrared autofluorescence (NIRAF), indocyanine green (ICG) fluorescence imaging, and carbon nanoparticles, have improved gland identification, vascular integrity, and surgical safety (6).

In this study, we retrospectively analyzed the relationship of postoperative hypoparathyroidism with accidental parathyroid gland excision and with the rate of parathyroid hormone (PTH) decline in patients who underwent total thyroidectomy for benign and malignant disease.

Methods

Patients who underwent total thyroidectomy with or without neck dissection for thyroid cancer, follicular nodular disease, or Graves disease between August 2022 and April 2025 were included. PTH and calcium levels were analyzed preoperatively, at 1 h postoperatively, on postoperative day 1, and at weeks 4 and 8.

Patients with PTH levels ≤ 15 pg/mL on postoperative day 0 were classified as having early hypoparathyroidism. Those with PTH levels between 10 and 15 pg/mL received oral elemental calcium (2×600 mg) and calcitriol (2×0.5 μ g) for 1 month, followed by tapering of the doses. Patients with PTH < 10 pg/mL received oral calcium (600 mg three times daily).



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Cite this article as: Ertaş B, Kaya H, Düren Ş, Giray S, Düren M. Strategies to maintain a normocalcemic, asymptomatic status following total thyroidectomy. Istanbul Med J. 2026; 27(1): 27-31

Received: 22.08.2025

Accepted: 22.12.2025

Publication Date: 02.02.2026



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and calcitriol (0.5 µg three times daily), followed by one month of maintenance therapy with calcium (600 mg elemental once daily) and calcitriol (0.5 µg once daily).

Patients who underwent thyroidectomy with or without central neck dissection were hospitalized for one day, whereas those who underwent thyroidectomy with lateral neck dissection were hospitalized for three days. None of the patients required intravenous calcium replacement.

Statistical Analysis

In this study, the mean rate of decline and the arithmetic mean of individual declines were used for statistical analyses, whereas the independent-samples t-test was used for group comparisons. All statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). A p value <0.05 was considered statistically significant.

This was a retrospective analysis of anonymized patient data. The study was approved by the Acibadem University Ethics Committee (approval number: 2025-12/94, date: 10.07.2025). All procedures were performed in accordance with the ethical standards of the institutional and/or national research committees and with the 1964 Declaration of Helsinki and its later amendments.

Results

Our cohort included 536 patients (404 women and 132 men; mean age, 44 years; range, 21-77 years). The diagnoses included papillary thyroid carcinoma (n=316), non-toxic follicular nodular disease (n=152), Graves disease (n=52), and toxic follicular nodular disease (n=16). Among the 316 patients with papillary carcinoma, 68 underwent central neck dissection and 52 underwent additional lateral neck dissection (44 unilateral and 8 bilateral; Table 1).

According to pathology reports, 88 (4.1%) of the 2,144 parathyroid glands excised from 536 patients (16.4%) were removed for the following reasons: 4 for carcinoma invasion, 8 for intrathyroidal location, and 76 due to accidental excision. None of the patients had more than one

gland excised. Parathyroid glands were not autotransplanted.

In our series, the mean preoperative serum vitamin D level was 22.7 nmol/L (range 7.1-46.8 nmol/L).

Postoperative day 1 PTH levels <15 pg/mL were observed in 104 patients (18.7%), of whom 32 had glands accidentally excised (30.7%). Only 12 patients (1.5%) remained symptomatic despite the normalized PTH and calcium levels at the eighth week. This subgroup included eight patients with carcinoma who underwent neck dissection and four patients with Graves' disease.

Among patients with thyroid carcinoma, 68 had PTH levels <15 pg/mL (21.5%). Of the 1,264 parathyroid glands at risk, 64 (5%) were identified in the final pathology reports, with 28 (43.7%) showing PTH levels <15 pg/mL. Of the 32 patients with accidental gland excision and PTH levels <15 pg/mL, 20 (62.5%) underwent lateral neck dissection.

In the follicular nodular disease group, 20 of 152 patients (13.2%) had PTH levels <15 pg/mL. Twenty-four patients (3.9%) had parathyroid tissue in their pathology reports, with only four showing low PTH levels.

Among patients with Graves' disease, 12 of 52 (23.1%) had low PTH levels and had not undergone gland excision. Four of 16 patients with toxic follicular nodular disease (25%) had low PTH levels and no glands excised (Table 2).

In the eighth postoperative week, all patients had normalized PTH and calcium levels, and no cases of permanent hypoparathyroidism were identified.

Among 104 patients with hypoparathyroidism, PTH levels declined by 72.51% in patients with gland excision and by 69.66% in those without (p=0.686). In 88 patients with excised glands, PTH levels decreased by 52.17%; in 448 patients without excised glands, the decrease was 43.5% (p=0.116). The mean PTH reduction was 71.71% among 104 patients with early hypoparathyroidism. Among the remaining 432 patients, the mean PTH reduction was 38.44%, which differed significantly (p<0.05) (Tables 3-5).

None of the patients required readmission after surgical discharge.

Table 1. Demographic and clinical characteristics of the study cohort

Category	Value
Total number of patients	536
Women	404
Men	132
Mean age (range)	44 years (21-77 years)
Diagnoses	
Papillary thyroid carcinoma	316 patients
Nontoxic follicular nodular disease	152 patients
Graves disease	52 patients
Toxic follicular nodular disease	16 patients
Neck dissections (among patients with carcinoma)	
Central neck dissection	68 patients
Lateral + central neck dissection	52 patients (44 unilateral, 8 bilateral)

Table 2. Parathyroid hormone <15 pg/mL and parathyroid gland excision based on diagnosis

Diagnosis	n	PTH <15 pg/mL (n,%)	Parathyroid tissue in pathology (n,%)	With PTH <15 among those (n, %)	Lateral neck dissection (if excised)
Papillary thyroid carcinoma	316	68 (21.5%)	64/1264 glands (5%)	28/64 (43.7%)	20/32 (62.5%)
Follicular nodular disease	152	20 (13.2%)	24 (3.9%)	4/24 (16.7%)	—
Graves disease	52	12 (23.1%)	0	0	—
Toxic follicular nodular disease	16	4 (25%)	0	0	—

PTH: Parathyroid hormone

Table 3. Parathyroid hormone reduction based on gland excision status

Patient subgroup	n	Mean ± SD PTH reduction (%)	p value	Significance
Patients with hypoparathyroidism	104			
With gland excision	32	72.51±13.8	0.686	Not significant
Without gland excision	72	69.66±14.9		
All patients	536			
With gland excision	88	52.17±10.4	0.116	Not significant
Without gland excision	448	43.50±9.7		

PTH: Parathyroid hormone, SD: Standard deviation

Table 4. Comparison of mean parathyroid hormone reduction between patient groups

Group	Number of patients	Mean ± SD PTH reduction (%)	Statistical significance
Early hypoparathyroidism	104	71.71±12.6	
Others	432	38.44±8.9	
p value	—	—	p<0.05

PTH: Parathyroid hormone, SD: Standard deviation

Table 5. Parathyroid hormone reduction based on gland excision

Patient group	Gland excision	n	Mean ± SD PTH reduction (%)	p value	Significance
Patients with hypoparathyroidism	Yes	32	72.51±13.8	0.686	Not significant
	No	72	69.66±14.9		
All patients	Yes	88	52.17±10.4	0.116	Not significant
	No	448	43.50±9.7		

PTH: Parathyroid hormone, SD: Standard deviation

Discussion

Randomized studies have shown that preserving functional circulation is as crucial as preserving anatomical integrity for maintaining parathyroid function (7,8). Furthermore, intraoperative gland identification reduces the risk of hypoparathyroidism (9). Factors such as age, Graves' disease, and lymph node dissection contribute to clinical outcomes (10,11). Our findings highlight the importance of vascular preservation and early replacement therapy.

The effectiveness of rapid PTH measurement in predicting symptomatic hypocalcemia has been emphasized in previous studies. Düren (12) demonstrated that immediate postoperative assessment of PTH levels in the post-anesthesia care unit offers a reliable and safe method for early detection of at-risk patients. These findings support the use of rapid hormone measurements to guide early supplementation decisions and prevent clinical hypocalcemia, further validating our protocol for early monitoring and intervention.

The transient hypoparathyroidism rate of 18.7% is consistent with that reported in the literature (1,2), while the permanent rate of 0% reflects surgical quality and follow-up.

Wang et al. (3) identified neck dissection in patients with malignancy as a major risk factor for permanent hypoparathyroidism. Even in benign cases, hypoparathyroidism may occur without gland excision, suggesting a key role of devascularization (5).

A decline in PTH after gland excision demonstrates the effectiveness of gland removal. However, a significant decline in PTH levels in patients who did not undergo excision indicates vascular compromise (13).

In our cohort, PTH levels declined by 71.71% from the original value in patients with PTH <15 pg/mL, whereas in patients with accidental gland excision, the decline was 52.17% (p<0.05), confirming that early PTH is a strong predictor.

Selberherr et al. (14) reported that the incidence of biochemical hypoparathyroidism progressively increased with the number of excised parathyroid glands: 13% with no glands excised, 21% with one gland excised, 49% with two glands excised, and 83% with three or more glands excised. In our cohort, although the rate of hypoparathyroidism among patients with gland excision (32/104, 30.7%) was lower than that among those without excision (72/104, 69.2%), the difference in mean PTH reduction between the two groups was not significant (72.51% vs. 69.66%, $p=0.686$). This similarity supports the notion that while accidental gland excision contributes to the risk of hypoparathyroidism, devascularization and intraoperative manipulation may play an equally crucial role. These findings collectively emphasize the importance of preserving both the anatomical integrity and the vascular supply during thyroid surgery.

In our cohort, postoperative hypoparathyroidism in patients with thyroid cancer was mainly attributed to impaired vascularization of the parathyroid glands caused by extensive dissection and/or accidental gland excision. By contrast, in cases of Graves' disease with preserved parathyroid glands and minimal surgical disruption, hypoparathyroidism may be linked to vascular insufficiency secondary to chronic autoimmunity.

Lorente-Poch et al. (15) showed that hypoparathyroidism may occur despite gland preservation, owing to devascularization and manipulation. Therefore, minimizing trauma and preserving vascular integrity are essential.

Calcium-sensing receptors (CaSRs) assist parathyroid cells in responding to calcium changes. Increased CaSR activity may suppress PTH release, thereby weakening compensation for hypocalcemia. This pathway involves both hormonal and receptor-level modulation (16,17).

Routine calcium and active vitamin D supplementation stabilizes calcium levels and supports gland recovery. Meta-analyses by Edeaf et al. (19) and Ritter et al. (18) found that early replacement prevents hypocalcemia and that early PTH measurement is a strong predictor.

In our cohort, 12 patients with normalized PTH and calcium levels exhibited symptoms despite not receiving supplements. We believe that CaSR saturation may explain this discrepancy, and further studies are necessary.

Advanced imaging techniques, such as ICG angiography, allow real-time intraoperative assessment of parathyroid gland perfusion and have shown promise in reducing postoperative hypoparathyroidism. Zaidi et al. (6) reported that ICG angiography correctly predicted parathyroid viability, with a sensitivity of 97% and a specificity of 95%, and that its use was associated with a hypoparathyroidism rate as low as 5%. Similarly, other studies have shown that identifying at least one well-perfused gland using ICG may significantly reduce the risk of transient and permanent hypoparathyroidism.

In our study, ICG was not used. Instead, surgical outcomes were achieved through meticulous dissection and early replacement therapy. Even without perfusion imaging, we achieved a transient hypoparathyroidism rate of 18.7% and a permanent rate of 0%, underscoring the critical

role of surgical experience and early intervention. Although ICG may be a valuable adjunct, our findings suggest that its absence does not preclude excellent outcomes when fundamental surgical principles are applied rigorously.

NIRAF enables intraoperative parathyroid identification by intrinsic tissue fluorescence at ~ 820 nm. Previous studies demonstrated improved gland detection and reduced postoperative hypoparathyroidism, with Falco et al. (20) reporting a decline in transient hypoparathyroidism from 23% to 8% under NIRAF guidance. Despite these advantages, heterogeneity among studies, equipment costs, and limited accessibility have restricted its routine use (21).

In our series, transient and permanent hypoparathyroidism rates were 18.7% and 0%, respectively; these outcomes were achieved without NIRAF or other imaging technologies. These results, which fall between conventional rates (20-30%) and NIRAF-assisted rates (as low as 8%), suggest that meticulous surgical dissection combined with early supplementation can yield outcomes comparable to technology-assisted approaches.

Our findings suggest that early replacement of calcium and active vitamin D, rather than sole reliance on visual identification, plays a crucial role in prevention. Timely physiological support allows for the recovery of gland function and prevents hypocalcemia.

Our results are consistent with the findings of Ertaş et al. (22), who reported a transient hypoparathyroidism rate of 19.2% following total thyroidectomy for benign thyroid diseases, with no cases of permanent hypoparathyroidism. Their study, which reported findings similar to those in our cohort, emphasized that meticulous surgical technique and early supplementation with calcium and vitamin D significantly reduced the incidence of symptomatic hypocalcemia. This supports the effectiveness of a proactive replacement strategy and careful tissue handling, even in the absence of advanced imaging technologies, to preserve parathyroid function and minimize complications.

Study Limitations

Hypoparathyroidism not only affects patients' quality of life but also imposes a substantial economic burden on healthcare systems. A comprehensive French national cohort study showed that patients who developed postoperative hypoparathyroidism incurred significantly higher medical costs in the first postoperative year than those without the condition (4). These costs were primarily driven by frequent emergency visits, repeated biochemical monitoring, prolonged medication use (e.g., calcium and active vitamin D analogs), and hospital readmissions owing to symptomatic hypocalcemia. In addition, chronic hypoparathyroidism often necessitates long-term endocrinological follow-up, placing a persistent strain on healthcare resources. From a broad perspective, this condition contributes to indirect costs, including loss of productivity, patient anxiety, and reduced work capacity. Therefore, effective prevention through meticulous surgical techniques and early biochemical support is not only clinically prudent but also economically advantageous, reducing the financial impact on both patients and health systems.

Conclusion

Hypoparathyroidism remains a common complication of thyroid surgery. Identification and preservation of the parathyroid glands and their vascularity, and autotransplantation in cases of complete excision, are needed. Early postoperative PTH levels are useful predictors. Routine calcium and active vitamin D supplementation effectively prevents symptoms of hypoparathyroidism. Meticulous surgical planning and multidisciplinary monitoring are essential to ensure patient safety and quality of life.

Ethics

Ethics Committee Approval: The study was approved by the Acibadem University Ethics Committee (approval number: 2025-12/94, date: 10.07.2025).

Informed Consent: This was a retrospective analysis of anonymized patient data.

Acknowledgments

We thank Ms. Buse Çalık for her assistance in data processing.

Footnotes

Authorship Contributions: Surgical and Medical Practices - B.E., H.K., Ş.D., S.G., M.D.; Concept - B.E., M.D.; Design - B.E., M.D.; Data Collection or Processing - B.E., H.K., Ş.D., S.G.; Analysis or Interpretation - B.E., H.K., Ş.D., S.G.; Literature Search - B.E., Ş.D., S.G.; Writing - B.E., M.D.

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