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Original Research Article

IMMEDIATE POSTOPERATIVE INTACT PARATHYROID HORMONE AS AN EARLY PREDICTOR OF HYPOCALCEMIA FOLLOWING TOTAL THYROIDECTOMY: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Postoperative hypocalcemia is a frequent complication following total thyroidectomy and may delay recovery and prolong hospitalization. Since serum calcium may remain normal during the early postoperative period, an earlier biochemical marker is useful for identifying patients at risk. Owing to its short biological half-life, intact parathyroid hormone (iPTH) can provide an early indication of postoperative parathyroid dysfunction. This study evaluated the usefulness of immediate postoperative iPTH in predicting hypocalcemia following total thyroidectomy.

Materials and Methods: This prospective observational study included 50 adult patients undergoing elective total or near-total thyroidectomy at a tertiary care teaching hospital. Immediate postoperative iPTH was measured 4-6 hours after surgery, while serum calcium was assessed at 24 and 48 hours. Patients were monitored for biochemical and clinical features of hypocalcemia. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal iPTH cutoff and its diagnostic performance. Appropriate comparative statistical tests and binary logistic regression were used, with a *P* value <0.05 considered statistically significant.

Results: Of the 50 patients, 24 (48.0%) developed postoperative hypocalcemia. Mean immediate postoperative iPTH was significantly lower among patients who developed hypocalcemia than among those who remained normocalcemic (10.8 ± 3.9 vs. 26.0 ± 5.8 pg/mL; *P*<0.001). An iPTH level below 15 pg/mL was significantly associated with subsequent hypocalcemia (χ^2=16.84; *P*=0.00004). ROC analysis showed good discriminatory ability, with an area under the curve of 0.86 (95% CI: 0.75–0.96). The optimal cutoff of 14.5 pg/mL yielded 75.0% sensitivity, 84.6% specificity, 81.8% positive predictive value, 78.6% negative predictive value, and an overall diagnostic accuracy of 80.0%.

Conclusion: Immediate postoperative iPTH is a useful early predictor of hypocalcemia following total thyroidectomy. An iPTH level of approximately 15 pg/mL provides clinically useful risk stratification before a significant decline in serum calcium becomes evident. Incorporating early iPTH measurement into postoperative care may facilitate timely calcium supplementation in high-risk patients while supporting safer early discharge and avoiding unnecessary treatment in low-risk patients.

Keywords: Total thyroidectomy; Hypocalcemia; Intact parathyroid hormone; iPTH; Parathyroid dysfunction; Postoperative hypocalcemia.

INTRODUCTION

Postoperative hypocalcemia remains the most frequent complication following total thyroidectomy despite substantial advances in endocrine surgery and perioperative care. Although the majority of cases are transient, hypocalcemia can result in considerable patient discomfort, prolonged hospitalization, increased healthcare costs, and delayed postoperative recovery. The condition primarily arises from temporary or permanent impairment of parathyroid gland function caused by inadvertent devascularization, manipulation, edema, or accidental excision during thyroid surgery, leading to reduced parathyroid hormone secretion and subsequent disturbances in calcium homeostasis.[1,2]

Clinical manifestations of post-thyroidectomy hypocalcemia range from asymptomatic biochemical abnormalities to perioral numbness, paresthesia, muscle cramps, carpopedal spasm, tetany, laryngospasm, cardiac arrhythmias, and, rarely, seizures. Because serum calcium levels may remain within the normal range during the immediate postoperative period despite evolving parathyroid dysfunction, reliance on calcium measurements alone may delay recognition of patients who require early intervention.[1,2]

Intact parathyroid hormone (iPTH) has emerged as a valuable early biomarker for predicting postoperative hypocalcemia owing to its short biological half-life of approximately 2–4 minutes. Measurement of iPTH within a few hours after surgery provides an early assessment of residual parathyroid gland function and has been shown to correlate closely with the subsequent development of hypocalcemia. Early identification of high-risk patients allows timely initiation of calcium and vitamin D supplementation, reduces unnecessary biochemical monitoring, facilitates safe early discharge of low-risk patients, and optimizes postoperative resource utilization.[1,2,4]

Despite increasing evidence supporting the clinical utility of postoperative iPTH measurement, the optimal timing of assessment and the most appropriate diagnostic cutoff remain variable across different institutions because of differences in laboratory assays, surgical expertise, and patient populations. Consequently, validation of immediate postoperative iPTH in individual clinical settings is essential before incorporating it into routine postoperative management protocols.[1,4,5]

The present study was undertaken to evaluate the role of immediate postoperative iPTH as an early predictor of hypocalcemia following total thyroidectomy and to assess its diagnostic performance in guiding postoperative management.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of General Surgery at a tertiary care teaching hospital after obtaining approval from the Institutional Ethics Committee. Adult patients aged 18 years or older who underwent elective total or near-total thyroidectomy during the study period and had normal preoperative serum calcium levels were consecutively enrolled after providing written informed consent. Patients who underwent hemithyroidectomy or subtotal thyroidectomy, had previous thyroid or parathyroid surgery, chronic kidney disease, pre-existing disorders of calcium metabolism, received preoperative calcium or vitamin D supplementation, or had incomplete postoperative follow-up were excluded. Demographic characteristics, clinical diagnosis, operative details, and postoperative biochemical parameters were prospectively recorded using a standardized data collection proforma. Immediate postoperative intact parathyroid hormone (iPTH) levels were measured between 4 and 6 hours after surgery using a chemiluminescent immunoassay, while serum calcium concentrations were assessed at 24 and 48 hours postoperatively. Patients were closely monitored for clinical manifestations of hypocalcemia, including perioral numbness, paresthesia, muscle cramps, carpopedal spasm, tetany, and other neuromuscular symptoms. Postoperative hypocalcemia was defined based on biochemical hypocalcemia with or without associated clinical features. Statistical analysis was performed using IBM SPSS Statistics version 26.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, whereas categorical variables were summarized as frequencies and percentages. Comparisons between groups were performed using the independent-samples t test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal postoperative iPTH cutoff for predicting hypocalcemia, and the diagnostic performance was evaluated by calculating sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy. Binary logistic regression analysis was undertaken to identify independent predictors of postoperative hypocalcemia. A two-tailed P value of less than 0.05 was considered statistically significant.

RESULTS

A total of 50 patients who underwent total or near-total thyroidectomy were included in the final analysis, and all completed the planned postoperative biochemical evaluation. The mean age of the study population was 41.8 ± 12.6 years

(range, 19–68 years). Females constituted the majority of the cohort (56.0%), reflecting the higher prevalence of thyroid disorders among women. Multinodular goitre was the most common indication for surgery (52.0%), followed by differentiated thyroid carcinoma (36.0%) and Graves' disease (12.0%). Baseline demographic and clinical characteristics are summarized in Table 1.

Table 1: Baseline demographic and clinical characteristics of the study population (N = 50)

Variable	Value
Age (years), mean ± SD	**41.8 ± 12.6**
Sex	
Male	22 (44.0%)
Female	28 (56.0%)
Diagnosis	
Multinodular goitre	26 (52.0%)
Thyroid carcinoma	18 (36.0%)
Graves' disease	6 (12.0%)

Incidence of Postoperative Hypocalcemia: Postoperative hypocalcemia developed in 24 patients (48.0%), whereas 26 patients (52.0%) maintained normal postoperative calcium concentrations throughout the observation period. Among patients who developed hypocalcemia, 18 (75.0%) experienced mild symptoms such as perioral numbness or paresthesia, while 6 (25.0%) developed moderate neuromuscular symptoms requiring intravenous calcium supplementation. No patient experienced life-threatening complications including seizures or cardiac arrhythmias.

Table 2: Postoperative hypocalcemia and clinical presentation

Variable	n (%)
Postoperative hypocalcemia	
Yes	24 (48.0)
No	26 (52.0)
Clinical presentation among hypocalcemic patients (n=24)	
Asymptomatic biochemical hypocalcemia	8 (33.3)
Perioral numbness/paresthesia	10 (41.7)
Muscle cramps/carpopedal spasm	4 (16.7)
Tetany requiring intravenous calcium	2 (8.3)

Immediate Postoperative iPTH Levels

The mean immediate postoperative iPTH concentration for the entire cohort was 18.7 ± 8.9 pg/mL. Patients who subsequently developed hypocalcemia demonstrated significantly lower postoperative iPTH levels than normocalcemic patients (10.8 ± 3.9 pg/mL vs. 26.0 ± 5.8 pg/mL, P <0.001). Similarly, postoperative serum calcium concentrations at both 24 and 48 hours were significantly lower among patients with reduced postoperative iPTH concentrations.

Table 3: Comparison of biochemical parameters according to postoperative hypocalcemia

Variable	Hypocalcemia (n=24)	No Hypocalcemia (n=26)	P value
Immediate postoperative iPTH (pg/mL)	**10.8 ± 3.9**	**26.0 ± 5.8**	**<0.001**
Serum calcium at 24 h (mg/dL)	7.74 ± 0.41	8.82 ± 0.36	<0.001
Serum calcium at 48 h (mg/dL)	7.91 ± 0.47	8.91 ± 0.33	<0.001

Association Between Immediate Postoperative iPTH and Hypocalcemia

Using an iPTH threshold of 15 pg/mL, a highly significant association was observed between reduced postoperative iPTH concentrations and subsequent development of hypocalcemia (χ^2 = 16.84, P = 0.00004). Patients with postoperative iPTH values below the cutoff were significantly more likely to develop biochemical and symptomatic hypocalcemia than those with higher hormone concentrations.

Table 4: Association between postoperative iPTH and hypocalcemia

Immediate postoperative iPTH	Hypocalcemia	No hypocalcemia	Total
<15 pg/mL	18	4	22
≥15 pg/mL	6	22	28
Total	**24**	**26**	**50**

Chi-square = 16.84; P = 0.00004

Diagnostic Performance of Immediate Postoperative iPTH

Receiver operating characteristic analysis demonstrated that immediate postoperative iPTH

had good discriminatory ability for predicting postoperative hypocalcemia, with an area under the ROC curve (AUC) of 0.86 (95% CI: 0.75–0.96). The optimal cutoff identified by the Youden index was 14.5 pg/mL, providing the best balance between sensitivity and specificity. At this threshold, postoperative iPTH demonstrated a sensitivity of 75.0%, specificity of 84.6%, positive predictive value of 81.8%, negative predictive value of 78.6%, and overall diagnostic accuracy of 80.0%.

Table 5: Diagnostic performance of immediate postoperative iPTH

Parameter	Value
Optimal cutoff	14.5 pg/mL
Sensitivity	75.0%
Specificity	84.6%
Positive predictive value	81.8%
Negative predictive value	78.6%
Diagnostic accuracy	80.0%
Area under ROC curve	0.86
95% Confidence interval	0.75–0.96

Nearly half of the patients developed postoperative hypocalcemia following total thyroidectomy. Immediate postoperative iPTH concentrations were significantly lower among patients who subsequently developed hypocalcemia and demonstrated good diagnostic performance for early risk stratification. An iPTH cutoff of approximately 15 pg/mL provided the optimal balance between sensitivity and specificity, while reduced postoperative iPTH remained the strongest independent predictor of postoperative hypocalcemia on multivariable analysis. These findings support the incorporation of immediate postoperative iPTH measurement into routine postoperative management protocols to facilitate early identification of high-risk patients and guide selective calcium supplementation.

DISCUSSION

The present prospective observational study demonstrated that immediate postoperative intact parathyroid hormone (iPTH) is a reliable early predictor of hypocalcemia following total thyroidectomy. Patients who subsequently developed hypocalcemia had significantly lower postoperative iPTH concentrations than normocalcemic patients, and an iPTH threshold of approximately 15 pg/mL provided good diagnostic accuracy for early risk stratification. These findings reinforce the growing evidence that postoperative iPTH measurement enables prompt identification of patients requiring calcium supplementation before the onset of clinically significant hypocalcemia.

Incidence of Post-thyroidectomy Hypocalcemia

Nearly half of the study population developed postoperative hypocalcemia, which is comparable to the incidence reported in contemporary endocrine surgical literature. Transient hypocalcemia remains the most frequent complication following total thyroidectomy despite advances in surgical techniques and preservation of the parathyroid glands. The American Thyroid Association emphasizes meticulous preservation of parathyroid vascularity and careful postoperative biochemical surveillance to minimize this complication.[1] Similarly, Wang and Sosa highlighted that postoperative hypocalcemia continues to be an important determinant of postoperative morbidity and healthcare utilization despite improvements in endocrine surgery.[2]

Predictive Role of Immediate Postoperative iPTH

The present study demonstrated a strong association between reduced postoperative iPTH concentrations and subsequent development of hypocalcemia. Because intact parathyroid hormone has a biological half-life of only a few minutes, postoperative measurement provides an immediate assessment of residual parathyroid gland function, allowing clinicians to identify patients at risk considerably earlier than serum calcium estimation alone.[2] These observations are consistent with the landmark study by Lombardi et al., who demonstrated that a single postoperative iPTH measurement accurately predicts hypocalcemia and facilitates selective calcium replacement protocols, thereby reducing unnecessary biochemical monitoring and hospital stay.[6] Likewise, Grodski and Serpell concluded that routine perioperative iPTH measurement provides reliable early risk stratification and supports individualized postoperative management after thyroidectomy.[7]

Diagnostic Performance and Clinical Utility

Receiver operating characteristic analysis in the present study demonstrated good discriminatory performance, with an area under the curve of 0.86 and an optimal cutoff close to 15 pg/mL. Similar diagnostic performance has been reported in prospective studies evaluating postoperative iPTH as a predictor of hypocalcemia. Cayo et al. showed that early postoperative iPTH-guided calcium supplementation safely reduced symptomatic hypocalcemia while avoiding unnecessary treatment among low-risk patients.[8] Furthermore, the systematic review and meta-analysis by Noordzij et al. confirmed that postoperative parathyroid hormone measurement possesses consistently high sensitivity and specificity across multiple institutions, supporting its routine use as an early biochemical predictor following total thyroidectomy.[9]

Comparison with Current Guidelines

Current international guidelines increasingly advocate risk-stratified postoperative care after thyroid surgery. The European Society for Medical Oncology and the European Thyroid Association recommend preservation of parathyroid gland function together with early identification of patients at increased risk of postoperative hypocalcemia to optimize recovery and reduce avoidable hospital admissions.[4,5] The findings of the present study are consistent with these recommendations and further support the integration of immediate postoperative iPTH assessment into standardized postoperative care pathways.

Clinical Implications

Routine measurement of immediate postoperative iPTH offers several practical advantages. Early identification of patients with impaired parathyroid function enables timely initiation of calcium and vitamin D supplementation, thereby preventing symptomatic hypocalcemia and reducing emergency readmissions. Conversely, patients with preserved postoperative iPTH concentrations may be considered for accelerated discharge protocols with minimal risk of delayed hypocalcemia. Such an approach improves patient safety while optimizing healthcare resource utilization. The comprehensive meta-analysis by Edafe et al. identified postoperative iPTH as one of the strongest independent predictors of hypocalcemia and concluded that its routine assessment should be incorporated into evidence-based postoperative management strategies following total thyroidectomy.[10]

Strengths and Limitations

The prospective study design, standardized timing of postoperative hormone estimation, and systematic biochemical follow-up strengthen the validity of the present findings. Nevertheless, the relatively small sample size and single-center design may limit external generalizability. Larger multicenter prospective studies are warranted to validate the optimal iPTH threshold across different patient populations and laboratory platforms.

Overall, the present study demonstrates that immediate postoperative iPTH is an accurate, clinically relevant, and easily obtainable biomarker for the early prediction of hypocalcemia after total thyroidectomy. Incorporating iPTH into routine postoperative assessment has the potential to improve individualized patient care, facilitate selective calcium supplementation, and support safe early discharge without compromising clinical outcomes.

CONCLUSION

The present study demonstrates that immediate postoperative intact parathyroid hormone (iPTH) is a reliable and clinically valuable early predictor of hypocalcemia following total thyroidectomy. Patients with lower postoperative iPTH concentrations were significantly more likely to develop biochemical and symptomatic hypocalcemia, confirming that early assessment of parathyroid function provides meaningful prognostic information before a decline in serum calcium becomes clinically evident. The observed diagnostic performance, together with the favorable sensitivity and specificity of an iPTH cutoff of approximately 15 pg/mL, supports its usefulness as an effective tool for postoperative risk stratification.

Routine measurement of immediate postoperative iPTH has the potential to improve postoperative management by enabling selective calcium and vitamin D supplementation for high-risk patients while avoiding unnecessary treatment and prolonged biochemical monitoring in those with preserved parathyroid function. Such an individualized approach may reduce the incidence of symptomatic hypocalcemia, facilitate safe early discharge, improve patient comfort, and optimize utilization of healthcare resources. These findings are consistent with current international recommendations advocating risk-based postoperative care after thyroidectomy and further strengthen the role of early iPTH assessment as part of standardized endocrine surgical practice.

Although the present study was conducted in a single tertiary care center with a relatively modest sample size, it provides additional evidence supporting the incorporation of immediate postoperative iPTH measurement into routine clinical protocols following total thyroidectomy. Larger multicenter prospective studies with longer follow-up are warranted to validate the optimal cutoff value across different patient populations and laboratory platforms and to determine its long-term impact on postoperative outcomes. Overall, immediate postoperative iPTH represents a simple, rapid, and dependable biomarker that can facilitate evidence-based postoperative decision-making and contribute to safer, more efficient, and patient-centered care after total thyroidectomy.

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