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Original Research Article

Evaluating the predictive value of early postoperative parathyroid hormone levels for hypocalcemia in total thyroidectomy patients: a retrospective cohort study

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ABSTRACT

Background: Hypocalcemia is a common complication following total thyroidectomy, often resulting from transient or permanent parathyroid gland dysfunction. Identifying early predictors is essential to prevent morbidity and guide timely supplementation. The retrospective single-center study evaluated the predictive value of immediate postoperative parathyroid hormone (PTH) levels for early hypocalcemia.
Methods: A total of 54 patients aged ≥18 years were included. PTH was measured within 1 hour postoperatively, while baseline serum calcium (Ca) levels were monitored every 8 hours for 24-48 hours. Patients were categorized by PTH level as low (<10 pg/ml), borderline (10-20 pg/ml), or normal (>20 pg/ml). Hypocalcemia was defined as Ca <8 mg/dl. Statistical analyses included the Kruskal-Wallis test with Tukey adjustment and Chi-square or Fisher's exact test.
Results: Most patients had normal PTH levels (77.8%, n=42), and hypocalcemia occurred in 20.4% (n=11). A significant association was observed between low PTH levels and hypocalcemia, with 66.7% of patients with low PTH developing hypocalcemia compared to 9.5% in the normal group (p=0.0022). ROC curve analysis using a PTH cutoff of <20 pg/mL yielded an AUC of 0.76, with 58.3% sensitivity and 90.5% specificity. Pairwise comparisons showed that low PTH (Mdn=7.67, IQR=1.2, p<0.001) differed significantly from normal PTH but not from borderline low PTH (p=0.436). A significant difference was also observed between borderline low and normal PTH (p=0.0313).
Conclusions: Early postoperative PTH measurement is a valuable predictor of hypocalcemia after thyroidectomy. Patients with PTH ≤20 pg/ml should be closely monitored and managed proactively to ensure safe recovery and facilitate early discharge.

Keywords: Thyroidectomy, Hypocalcemia, Parathyroid hormone, Post-operative complications

INTRODUCTION

Thyroidectomy has become increasingly common with the rising incidence of thyroid cancer, particularly papillary carcinoma, largely driven by the frequent incidental detection of thyroid nodules in up to 70% of adults.[1,2] Advances in surgical techniques, especially the adoption of capsular dissection, have reduced the rates of permanent hypocalcemia and recurrent laryngeal nerve injury. Despite these improvements, transient hypocalcemia remains a common postoperative complication, with reported rates ranging from 3% to 40%.[3] Postoperative hypocalcemia is primarily attributed to parathyroid gland dysfunction resulting from devascularization, inadvertent removal, or surgical trauma, leading to a decline in parathyroid hormone (PTH) levels and, subsequently,

serum calcium.[4-6] Clinical manifestations of hypocalcemia may be delayed, sometimes appearing up to 48 hours after surgery.[7,8] Therefore, early postoperative measurement of PTH has been proposed as a reliable predictor for identifying patients at risk and enabling timely intervention. This study aims to evaluate the role of early postoperative parathyroid hormone measurement in predicting the development of hypocalcemia following thyroidectomy, and to assess its utility in guiding postoperative management.

METHODS

This retrospective study was conducted at the John Hopkins Center in Dammam, Saudi Arabia, between January 2022 and January 2023. Ethical approval was obtained from the institutional review board, and informed consent was collected from all participants involved in the study. The study was sponsored by the John Hopkins Center.

All patients aged ≥18 years who underwent total thyroidectomy were included in the study.

Patients with preoperative parathyroid disorders, hypocalcemia, regular use of calcium supplements, chronic kidney disease, or bone mineralization disorders were excluded.

Within 1 h in the recover Postoperative PTH levels were measured within 1 h in the recovery room, alongside baseline calcium levels. Subsequently, calcium levels were measured every 8 h during admission. Patients were observed for 24-48 h for any hypocalcemia symptoms before discharge.

PTH levels of <10 pg/ml were classified as low, while levels between 10 and 20 pg/ml were considered borderline low. Normal PTH levels were defined as >20 pg/ml.[1] Additionally, normal Ca levels were defined as 8-10 mg/dl, with levels below 8 mg/dl considered low.

Statistical methods

Data were analyzed using descriptive statistics. For continuous variables (iPTH and Ca levels), the mean (M), standard deviation (SD), median (Mdn), and interquartile range (IQR) were calculated. Categorical variables (PTH category, hypocalcemia, and neck dissection) were summarized using frequencies and percentages. Hypocalcemia was defined as a Ca level of <8 mg/dl within 48 h postoperatively. The Kruskal-Wallis test was used to assess differences in minimum Ca levels within 48 h across PTH categories (low: <10 pg/ml; borderline low: 10-20 pg/ml, normal: >20 pg/ml), followed by pairwise comparisons with Tukey's adjustment for multiple comparisons. The association between PTH categories and hypocalcemia within 48 h was evaluated using a chi-square test of independence with the likelihood ratio statistic. Fisher's exact test was used to examine the relationship between neck dissection and hypocalcemia within 48 h. Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the predictive ability of the PTH category (coded as normal=1, borderline low, and low=2) for hypocalcemia, calculating the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratio (LR+ and LR-) at various cutpoints. Confidence intervals (CIs) [95%] were computed for the AUC, sensitivity, specificity, PPV, and NPV. All analyses were performed in RStudio (2023.06.0+421) with a sample size of 54. Statistical significance was set at $p<0.05$.

RESULTS

The mean age of the participants was 42.5±12.3 years, with a median age of 41 years (IQR 33-52). The majority of patients were female (64.8%). The indications for surgery included thyroid cancer (21 patients, 38.9%), multinodular goiter (26 patients, 48.1%), and diffuse goiter (7 patients, 13.0%). All patients underwent total thyroidectomy. The baseline demographic characteristics of the study population are summarized in (Table 1).

The mean iPTH level was 50.00 pg/ml (SD=35.48, Mdn=42.25), with calcium levels remaining stable (M=8.66-8.84 mg/dl). Most patients had normal PTH levels (77.77%, n=42), while 20.37% experienced hypocalcemia (Ca<8 mg/dl).

A significant association was observed between PTH levels and hypocalcemia. Among patients with low PTH levels (<10 pg/ml), 66.67% (n=4) developed hypocalcemia compared with 9.52% (n=4) of those with normal PTH levels (Table 2). Patients with borderline low PTH levels (10-20 pg/ml) had a 50% risk of developing hypocalcemia.

No significant association was found between central neck dissection and hypocalcemia ($p = 0.2$); 29.41% (n=5) of patients with hypocalcemia had undergone neck dissection compared with 16.22% (n=6) of patients without hypocalcemia (Table 3).

The Kruskal-Wallis test revealed significant differences in calcium levels within 48 hours across PTH categories (Figure 1). Pairwise comparisons showed that low PTH (Mdn=7.67, IQR=1.2, $p<0.001$) differed significantly from normal PTH but not from borderline low PTH ($p=0.436$). A significant difference was also observed between borderline low and normal PTH ($p=0.0313$).

Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the predictive ability of PTH categories for hypocalcemia (Figure 2). The area under the curve (AUC) was 76% [95% CI (60.7%, 92.6%)]. Sensitivity was 58.33% [95% CI (45.18%, 71.48%)], and specificity was 90.48% [95% CI (82.65%, 98.31%)]. The positive predictive value (PPV) was 63.64% [95% CI (50.81%, 76.47%)], and the negative predictive value (NPV) was 88.37% [95% CI (79.82%, 96.92%)]. Using a

PTH≥2 cutpoint (borderline low or low), 83.33% of cases were correctly classified, with LR+=5.47 and LR−=0.41.

DISCUSSION

The parathyroid glands produce PTH, an essential hormone that plays a significant role in regulating serum calcium levels. Following post-thyroidectomy, one of the most serious complications reported is hypocalcemia, which is attributed to transient or permanent damage to the parathyroid glands. Early detection and prompt management of hypocalcemia can reduce patient morbidity and shorten postoperative hospital stays.[9] Therefore, serum PTH has been proposed as a predictor of post-thyroidectomy hypocalcemia, since biochemical or clinical signs of hypocalcemia may not become apparent until 24-48 h postoperatively.[10,11]

Lam and Kerr observed that all patients with a PTH level of <8 pg/ml, measured 1 h after thyroidectomy, developed hypocalcemia, whereas those with a PTH level of <9 pg/ml remained normocalcemic.[12] Lombardi et al reported that measuring PTH at 4 and 6 h postoperatively provided the highest accuracy in predicting hypocalcemia.[13] However, the optimal timing for measuring intraoperative or postoperative PTH levels remains controversial in the literature, with no clear guidelines.[14] In this study, serum PTH was measured 1 h postoperatively for all patients, which we considered the best timing to guide early hypocalcemia management and safe patient discharge, as supported in various studies to have excellent reliability.[12,15,16]

Furthermore, patients were categorized based on their postoperative PTH levels. Those with levels of >20 pg/ml were considered to have normal parathyroid function, while those with levels of <10 pg/ml were considered to have abnormal parathyroid function. Another group was categorized separately for patients with borderline low PTH levels (10-20 pg/ml), as it remains unclear whether their parathyroid function is adequate.[17]

The PTH threshold used to predict hypocalcemia varies across studies.[16,18-20] Payne et al identified serum PTH levels of <10 pg/ml as the strongest indicator of postoperative hypocalcemia, a finding that aligns with our results. In our study, patients with postoperative PTH levels of <10 pg/ml had a serum mean Ca level of 7.67 mg/dl.[20]

Noordzij et al reported a mean PTH level of 13.52 pg/ml in patients who developed postoperative hypocalcemia.[16] Roh and Park observed that some patients experienced postoperative hypocalcemia with higher PTH levels, stating that the most accurate predictor of hypocalcemia was a PTH level ≤15 pg/ml, with similar findings reported by Asari et al.[21,22] In a review by Bashir et al the optimal PTH threshold cutoff for predicting postoperative hypocalcemia was 19.95 pg/ml with 100% sensitivity.[23] Interestingly, in this study, 50% of patients in the borderline low PTH group (PTH levels between 10 and 20 pg/ml) developed postoperative hypocalcemia. Among these patients with hypocalcemia, PTH levels ranged between 16.9 and 20 pg/ml. Additionally, the mean Ca levels of patients in the borderline low PTH group were 8.02 mg/ml, which differed significantly (p=0.0313) from the mean of patients with normal PTH levels of >20 pg/ml. Therefore, caution should be exercised when managing patients with PTH levels of ≤20 pg/ml, particularly when there are no other available parameters for Ca status prediction. Such serum PTH levels may indicate inadequate parathyroid gland function, especially in the postoperative setting.[24,25]

Our results align with several Saudi studies demonstrating that early postoperative PTH measurement is a reliable indicator of hypocalcemia after thyroidectomy. A multicenter study by Argan et al reported that low immediate postoperative PTH levels were independent predictors of hypoparathyroidism, while Althoubaity et al. found a strong association between low PTH and postoperative calcium decline.[15,26] Similarly, studies by AlQahtani et al. and Algarni et al showed that PTH levels measured within the first few postoperative hours accurately predicted hypocalcemia.[28,29] Together, these regional findings support the clinical value of early PTH monitoring and reinforce our recommendation for individualized postoperative management that considers all relevant risk factors.

In addition to the importance of PTH as a measurable predictor of postoprative hypocalcemia, patient-specific risk factors identified in previous studies should also be considered to individualize postoperative care. Central neck dissection is recognized as one of these risk factors, along with the female sex, malignant disease, and incidental parathyroidectomy.[14]

Central neck dissection was analyzed as a risk factor for hypocalcemia in various studies; however, our data did not show a strong association between central neck dissection and postoperative hypocalcemia (p=0.2).[25]

Limitations

This study has some limitations that should be considered. The sample size was relatively small, which may affect the strength and generalizability of the findings. In addition, as this was a single-center study, the results may not be fully representative of other populations. PTH and calcium levels were measured at limited postoperative time points, so some variations may not have been captured. Pre-operative PTH levels were not measured, which limits our ability to compare baseline parathyroid function. We also did not assess other factors that can influence calcium levels, such as vitamin D or magnesium. Further studies with larger, multicenter cohorts and more comprehensive assessments are needed to confirm these findings.

CONCLUSION

The variability in PTH thresholds and timing reported in the literature highlights the complexity of predicting hypocalcemia following thyroidectomy. While our study

supports the utility of a 1-h postoperative PTH measurement, the observed cases of hypocalcemia in patients with borderline low PTH levels underscore the need for cautious monitoring and individualized clinical judgment considering all reported risk factors for hypocalcemia.

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