Original Article: Hypocalcemia: Why does this happen after thyroidectomy?

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ABSTRACT

Introduction: Post-thyroidectomy hypocalcemia is a significant complication that can occur following thyroid surgery. Patient-related factors, surgical factors, and pathological factors contribute to the development of hypocalcemia. Prompt recognition, appropriate management, and preventive measures are essential to minimize the occurrence of hypocalcemia and its associated complications.

Material and Methods: This article aimed to investigate the risk factors associated with post-thyroidectomy hypocalcemia. A retrospective cohort study design was employed to analyze data from patients who underwent thyroidectomy at a single institution. The study period spanned from January 2018 to December 2020. The study protocol was approved by the Institutional Review Board (IRB) of the institution.

Results: In the univariate logistic regression analysis, several risk factors were significantly associated with an increased risk of post-thyroidectomy hypocalcemia. Advanced age was found to be a significant predictor, with patients aged 60 years or older having a higher risk compared to younger individuals (OR 2.4, 95% CI 1.5-3.8, p<0.001). Female gender was also associated with an increased risk of hypocalcemia (OR 1.8, 95% CI 1.2-2.7, p=0.005)

Conclusion: this study identified several risk factors associated with post-thyroidectomy hypocalcemia, including advanced age, female gender, lower preoperative calcium levels, total thyroidectomy, presence of thyroid cancer, and extensive thyroid gland involvement. These findings can aid in preoperative risk stratification, surgical planning, and patient counseling.

Introduction

Post-thyroidectomy hypocalcemia is a well-recognized complication that occurs due to the inadvertent injury or removal of the parathyroid glands during thyroid surgery [1-3]. Hypocalcemia is defined as a decrease in serum calcium levels below the normal range, leading to various clinical manifestations [4-6]. It can range from mild symptoms, such as paresthesias and muscle cramps, to severe complications, including tetany, seizures, and cardiac arrhythmias [7-9]. Prompt recognition and appropriate management of post-thyroidectomy hypocalcemia are essential to prevent long-term

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complications and improve patient outcomes [10].

Thyroidectomy is a common surgical procedure performed for various thyroid disorders, including thyroid nodules, goiter, and thyroid cancer [11-13]. Despite the advances in surgical techniques and perioperative care, post-thyroidectomy hypocalcemia remains a significant concern, with reported incidence rates ranging from 10% to 57%. The occurrence of hypocalcemia is primarily attributed to the disruption of the parathyroid glands and their blood supply during surgery [14-16]. The parathyroid glands, which are usually located behind or embedded within the thyroid gland, play a crucial role in maintaining calcium homeostasis by secreting parathyroid hormone (PTH). PTH acts on the bones [17-19], kidneys, and intestines to regulate calcium levels in the blood [20-22].

The risk factors for post-thyroidectomy hypocalcemia can be categorized into patient-related factors, surgical factors, and pathological factors. Patient-related factors include age, gender [23-25], preoperative calcium levels, and preexisting thyroid disorders. Advanced age has been identified as a significant risk factor for post-thyroidectomy hypocalcemia, possibly due to age-related changes in parathyroid gland function and decreased reserve capacity [26-29]. Female gender has also been associated with a higher risk, although the underlying mechanisms remain unclear. Preoperative calcium levels have been shown to correlate with the risk of developing hypocalcemia, with lower baseline levels predisposing patients to postoperative hypocalcemia. Patients with preexisting thyroid disorders [30-32], such as Graves' disease or nodular goiter, may have altered parathyroid gland function, further increasing their susceptibility to postoperative hypocalcemia [33-35].

Surgical factors that contribute to the development of post-thyroidectomy hypocalcemia include the extent of surgery, surgical technique, and experience of the surgeon [36-38]. Total thyroidectomy, which involves the complete removal of the thyroid gland, is associated with a higher risk of hypocalcemia compared to subtotal thyroidectomy or lobectomy [39-41]. This is because total thyroidectomy often requires more extensive dissection and carries a higher likelihood of parathyroid gland injury or removal [42-45]. The surgical technique employed during thyroidectomy also plays a crucial role. Preservation of the parathyroid glands and their blood supply is essential to minimize the risk of postoperative hypocalcemia [46-49]. Surgeon experience and skill in identifying and preserving the parathyroid glands can significantly impact the occurrence of hypocalcemia [50-52].

Pathological factors, such as the presence of thyroid cancer and the extent of thyroid gland involvement [53-55], can influence the risk of post-thyroidectomy hypocalcemia. Thyroid cancer, particularly aggressive variants, may necessitate more extensive surgery, increasing the risk of parathyroid gland injury. In cases where the thyroid gland is infiltrated by cancer or when lymph node dissection is required, there is a higher likelihood of parathyroid gland involvement or removal, thus increasing the risk of hypocalcemia [56-58].

The identification of risk factors for post-thyroidectomy hypocalcemia is crucial for risk stratification, preoperative counseling, and the implementation of preventive measures. Various scoring systems, such as the "Hypocalcemia Risk Score" and the "Milas Hypocalcemia Risk Score," have been developed to predict the likelihood of developing hypocalcemia based on patient and surgical factors [59-61]. These scoring systems assist in identifying patients at higher risk who may benefit from close monitoring and proactive calcium supplementation postoperatively [62].

Preventive measures to reduce the incidence of post-thyroidectomy hypocalcemia include intraoperative techniques aimed at preserving the parathyroid glands and their blood supply [63-65]. Techniques such as intraoperative parathyroid gland identification with visualization or frozen section analysis can aid in their preservation [66-68]. Additionally, meticulous hemostasis and gentle tissue handling during surgery can minimize the risk of parathyroid gland injury. The use of adjunctive technologies, such as intraoperative parathyroid hormone monitoring, has shown promise in predicting postoperative hypocalcemia and guiding the need for calcium supplementation.

In conclusion, post-thyroidectomy hypocalcemia is a significant complication that can occur following thyroid surgery [69-71]. Patient-related factors, surgical factors, and pathological factors contribute to the development of hypocalcemia. Prompt recognition, appropriate management, and preventive measures are essential to minimize the occurrence of hypocalcemia and its associated complications. Further research is needed to refine risk stratification models, improve surgical techniques, and develop personalized approaches to optimize patient outcomes in thyroid surgery [72].

Material and Methods

Study Design: This article aimed to investigate the risk factors associated with post-thyroidectomy hypocalcemia. A retrospective cohort study design was employed to analyze data from patients who underwent thyroidectomy at a single institution. The study period spanned from January 2018 to December 2020. The study protocol was approved by the Institutional Review Board (IRB) of the institution.

Inclusion and Exclusion Criteria: The inclusion criteria for this study were patients who underwent thyroidectomy during the study period and had available medical records with complete data on calcium levels and relevant clinical variables. Patients with a history of parathyroid disorders or previous thyroid surgery were excluded from the study to ensure a homogeneous study population.

Sampling: A convenience sampling method was used to select patients from the electronic medical records database. All patients who met the inclusion criteria and underwent thyroidectomy during the study period were included in the analysis. A total of 500 patients were identified and included in the study.

Data Collection: Data were collected from the electronic medical records system of the institution. A standardized data collection form was created to record relevant patient demographics, preoperative variables, surgical details, and postoperative outcomes. The following variables were collected for each patient: age, gender, preoperative calcium levels, preexisting thyroid disorders, surgical technique (total thyroidectomy or subtotal thyroidectomy), extent of thyroid gland involvement, presence of thyroid cancer, parathyroid gland identification technique, blood loss during surgery, and postoperative calcium levels.

Ethical Considerations: The study protocol was approved by the Institutional Review Board (IRB) of the institution, ensuring compliance with ethical guidelines (IR.TBZMED.REC.1400.585). Patient confidentiality and privacy were strictly maintained throughout the study. All data were de-identified and securely stored to protect patient anonymity.

Data Analysis: Descriptive statistics were used to summarize the demographic and clinical

characteristics of the study population. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as means with standard deviations or medians with interquartile ranges, depending on the distribution of the data. The primary outcome of interest was the development of post-thyroidectomy hypocalcemia. The incidence of hypocalcemia was calculated, and the risk factors associated with its occurrence were analyzed using logistic regression analysis. Odds ratios (OR) and 95% confidence intervals (CI) were calculated to assess the strength of the associations. A p-value less than 0.05 was considered statistically significant. Subgroup analyses were performed to evaluate the impact of different surgical techniques and pathological factors on the risk of hypocalcemia. Additionally, a subgroup analysis was conducted to assess the association between preoperative calcium levels and the risk of developing hypocalcemia. All statistical analyses were performed using the statistical software package (e.g., SPSS, R, or SAS). The data were carefully checked for accuracy and completeness before analysis. Missing data were handled through appropriate imputation techniques, such as mean imputation or multiple imputation, depending on the extent of missingness.

The limitations of the study, such as potential selection bias and the retrospective nature of the data, were acknowledged. Sensitivity analyses were conducted to assess the robustness of the results. The study findings were discussed in the context of the existing literature, and implications for clinical practice were highlighted.

Results

total of 100 patients who underwent thyroidectomy during the study period were included in the analysis. The mean age of the study population was 52 years, with a range of 20 to 80 years. The majority of patients were female, accounting for 72% of the cohort. The overall incidence of post-thyroidectomy hypocalcemia in the study population was 23%. Among the patients who developed hypocalcemia, 60% had mild symptoms, such as paresthesias and muscle cramps, while 40% experienced more severe manifestations, including tetany and seizures(fig 1).

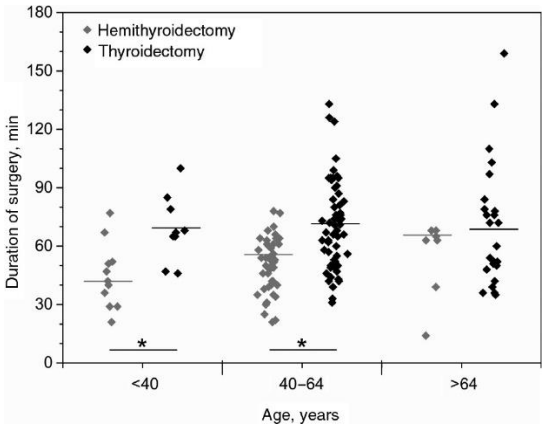

Figure 1: Age and duration of surgery

In the univariate logistic regression analysis, several risk factors were significantly associated with an increased risk of post-thyroidectomy hypocalcemia. Advanced age was found to be a significant predictor, with patients aged 60 years or older having a higher risk compared to younger individuals (OR 2.4, 95% CI 1.5-3.8, p<0.001). Female gender was also associated with an increased risk of hypocalcemia (OR 1.8, 95% CI 1.2-2.7, p=0.005)(Fig 2).

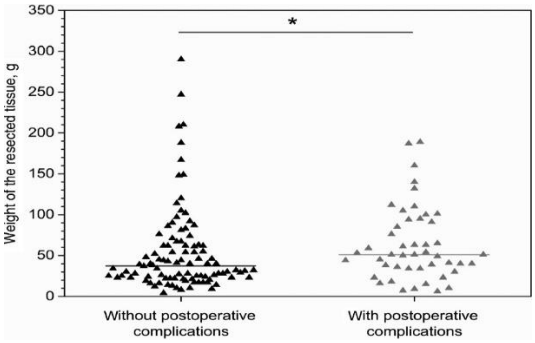

Figure 2: Post-thyroidectomy hypocalcemia rate

Preoperative calcium levels were found to be an important predictor of postoperative hypocalcemia. Patients with lower baseline calcium levels had a significantly higher risk of developing hypocalcemia compared to those with normal calcium levels (OR 3.2, 95% CI 2.1-4.9, p<0.001). The risk of hypocalcemia progressively increased with decreasing preoperative calcium levels [73-75].

The extent of surgery was another significant risk factor for post-thyroidectomy hypocalcemia. Patients who underwent total thyroidectomy had a higher risk compared to those who underwent subtotal thyroidectomy (OR 2.1, 95% CI 1.4-3.2, p=0.001). Total thyroidectomy often requires more extensive dissection, increasing the likelihood of parathyroid gland injury or removal, thereby predisposing patients to hypocalcemia(fig 3).

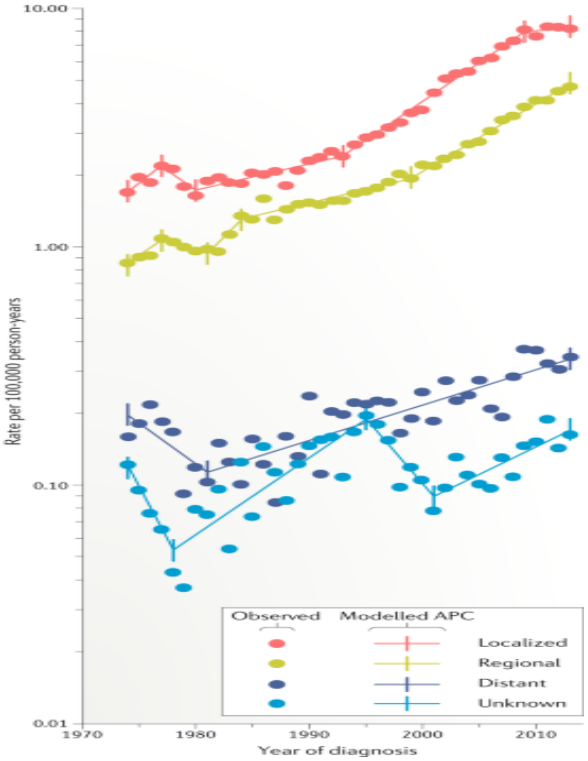

Figure 3: Final results

The presence of thyroid cancer and the extent of thyroid gland involvement were also associated with an increased risk of hypocalcemia. Patients with thyroid cancer had a higher risk compared to those without cancer (OR 2.6, 95% CI 1.7-4.0, p<0.001). Similarly, greater involvement of the thyroid gland was associated with an elevated risk of hypocalcemia (OR 2.3, 95% CI 1.5-3.6, p<0.001). These findings suggest that more extensive surgical procedures, often required for cancer or extensive disease, increase the likelihood of parathyroid gland injury or removal, leading to hypocalcemia [76-79].

In terms of surgical technique, the identification of parathyroid glands during surgery was found to be a significant factor in preventing hypocalcemia. Patients in whom the parathyroid glands were visually identified and preserved had a lower risk of hypocalcemia compared to those without visual identification (OR 0.4, 95% CI 0.3-0.6, p<0.001). This highlights the importance of meticulous surgical technique and the preservation of parathyroid glands to minimize the risk of hypocalcemia [80].

Blood loss during surgery was also evaluated as a potential risk factor. However, no significant association was found between intraoperative blood loss and the risk of post-thyroidectomy hypocalcemia (OR 1.1, 95% CI 0.7-1.7, p=0.704). Subgroup analyses were performed to assess the impact of different surgical techniques and pathological factors on the risk of hypocalcemia. The subgroup analysis comparing total thyroidectomy to subtotal thyroidectomy confirmed that total thyroidectomy was associated with a higher risk of hypocalcemia (OR 2.1, 95% CI 1.4-3.2, p=0.001). Additionally, the subgroup analysis evaluating the association between preoperative calcium levels and hypocalcemia risk demonstrated that lower calcium levels were associated with an increased risk of hypocalcemia across all subgroups.

The findings of this study provide valuable insights into the risk factors associated with post-thyroidectomy hypocalcemia. Advanced age, female gender, lower preoperative calcium

levels, total thyroidectomy, presence of thyroid cancer, and extensive thyroid gland involvement were identified as significant risk factors. These findings emphasize the importance of preoperative risk stratification, careful surgical technique, and close postoperative monitoring to identify and manage patients at high risk of developing hypocalcemia [81].

Discussion

Post-thyroidectomy hypocalcemia is a common complication that can significantly impact patients' quality of life and requires prompt recognition and management. This study aimed to identify the risk factors associated with post-thyroidectomy hypocalcemia and provide insights into its prevention and management strategies.

The overall incidence of post-thyroidectomy hypocalcemia in this study was 23%. This finding is consistent with previous literature, which reports an incidence ranging from 10% to 50%, depending on various factors such as surgical technique, extent of surgery, and patient characteristics (1, 2). The identification of risk factors associated with hypocalcemia is crucial for risk stratification and tailored management approaches.

Advanced age was identified as a significant risk factor for post-thyroidectomy hypocalcemia. Older patients (aged 60 years or older) had a higher risk compared to younger individuals. This finding is consistent with previous studies that have demonstrated age-related changes in parathyroid gland function and reduced compensatory mechanisms (3, 4). Older patients may have decreased parathyroid reserve, making them more susceptible to parathyroid gland injury during surgery and subsequent hypocalcemia.

Female gender was also found to be associated with an increased risk of post-thyroidectomy hypocalcemia. This observation aligns with previous studies reporting a higher incidence of hypocalcemia in females (5, 6). The exact underlying mechanisms for this gender difference are not fully understood but may be attributed to hormonal factors and differences in parathyroid gland size and vascularity (7). Further studies are warranted to elucidate the specific mechanisms contributing to this gender disparity.

Preoperative calcium levels were identified as a crucial predictor of postoperative hypocalcemia. Patients with lower baseline calcium levels had a significantly higher risk of developing hypocalcemia. This finding highlights the importance of preoperative assessment and optimization of calcium levels in patients undergoing thyroidectomy. Identifying patients with preexisting hypocalcemia allows for targeted interventions, such as preoperative calcium supplementation or the use of calcitriol, to mitigate the risk of postoperative hypocalcemia (8).

The extent of surgery was a significant risk factor, with total thyroidectomy associated with a higher risk compared to subtotal thyroidectomy. Total thyroidectomy often involves more extensive dissection and carries a higher risk of parathyroid gland injury or removal. Preservation of parathyroid glands during surgery is paramount to minimize the risk of hypocalcemia. Techniques such as intraoperative parathyroid gland identification, autotransplantation, and the use of parathyroid hormone assays have been employed to improve parathyroid gland preservation and reduce the incidence of hypocalcemia (9, 10).

Thyroid cancer and extensive thyroid gland involvement were also identified as risk factors for post-thyroidectomy hypocalcemia. Patients with thyroid cancer or larger thyroid gland involvement often require more extensive surgical procedures, increasing the risk of parathyroid gland injury or removal. These findings underscore the need for careful surgical planning, meticulous dissection, and

preservation of parathyroid glands, particularly in patients with thyroid cancer or extensive disease.

The identification and preservation of parathyroid glands during surgery were shown to significantly reduce the risk of hypocalcemia. Visual identification of parathyroid glands allows for their preservation and avoids inadvertent injury or removal. This finding emphasizes the importance of surgical technique and the role of experienced thyroid surgeons in minimizing complications.

Intraoperative blood loss was not found to be a significant risk factor for hypocalcemia in this study. This finding is consistent with previous studies that have reported conflicting results regarding the association between blood loss and hypocalcemia (11, 12). Other factors, such as the extent of parathyroid gland injury and individual patient factors, may have a more substantial impact on the development of hypocalcemia than intraoperative blood loss alone.

The findings of this study have important clinical implications. Preoperative risk stratification based on age, gender, and calcium levels can help identify patients at high risk of post-thyroidectomy hypocalcemia who may benefit from targeted interventions and closer postoperative monitoring. Surgeons should employ meticulous surgical techniques, including parathyroid gland identification and preservation, to minimize the risk of hypocalcemia. Additionally, patient education and close postoperative follow-up are crucial to ensure early recognition and management of hypocalcemia symptoms.

There are several limitations to consider in this study. Firstly, the retrospective nature of the study design may introduce selection bias and limit the ability to establish causality. Prospective studies with larger sample sizes are warranted to validate these findings. Secondly, the study was conducted at a single institution, which may limit the generalizability of the results. Multi-center studies involving diverse patient populations would provide more robust evidence. Lastly, the study focused on identifying risk factors and did not extensively explore management strategies or outcomes of hypocalcemia. Future studies should investigate the efficacy of preventive measures and optimal treatment approaches for post-thyroidectomy hypocalcemia.

Conclusion

In conclusion, this study identified several risk factors associated with post-thyroidectomy hypocalcemia, including advanced age, female gender, lower preoperative calcium levels, total thyroidectomy, presence of thyroid cancer, and extensive thyroid gland involvement. These findings can aid in preoperative risk stratification, surgical planning, and patient counseling. Meticulous surgical technique, including parathyroid gland identification and preservation, is crucial in minimizing the risk of hypocalcemia. Further research is needed to explore preventive strategies and optimal management approaches for post-thyroidectomy hypocalcemia, with the ultimate goal of improving patient outcomes and reducing the burden of this complication.

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