

Original Article: Prevalence of Hypocalcemia Following Thyroidectomy

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ABSTRACT

Introduction: Another rare surgical cause of voice change after thyroidectomy is cervical muscle injury. Causes of failure may include pulmonary edema, edema, or airway obstruction. The aim of this study was to determine the frequency of unplanned parathyroidectomy, unplanned parathyroidectomy, postoperative hypocalcemia and the risk of unplanned parathyroidectomy in patients undergoing thyroid surgery in our clinic. **Material and Methods:** Comparison of postoperative Ca value with age, gender, preoperative Ca value, dominant nodule diameter on ultrasonography (USG), type of surgery (total/lobectomy), and histopathological findings of thyroidectomy material (malignant/benign, with or without incident parathyroidectomy) is closed. Blood calcium levels below 8 mg/dL, measured after the first 24 hours after surgery, are indicative of postoperative hypocalcemia. **Results:** There was no relationship between nodule diameter and hypocalcemia. When patients were divided into malignant and benign groups, there was no significant difference between these groups in terms of performance after hypocalcemia. When patients were divided into groups with and without incident parathyroidectomy, there was no significant difference in postoperative hypocalcemia between these groups. **Conclusion:** In our study, female gender, age <28.5 years, low preoperative Ca value and total thyroidectomy were considered to be associated with hypocalcemia. Although there is no association between parathyroidectomy and postoperative hypocalcemia, this problem can be avoided by careful removal and imaging of the thyroid gland, especially in patients including patients with malignant thyroidectomy and total thyroidectomy.

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Introduction

Cancer surgery has a similar history. Albucasis may have started in AD 952 when he recorded the experience of getting a large goiter. Although similar methods have been published before, their results were not Validated [1-3]. Since then, the medical field has experienced ups and downs as its supporters and opponents have changed at different times. At one point in history, thyroid surgery was considered a dangerous operation, and as a result, surgeons might fear doing anything. Mayo applied unilateral or bilateral pole ligation before partial thyroidectomy in patients with severe thyrotoxicosis [4-6]. Dunhill recommends a second lobectomy for thyrotoxic patients who do not respond to primary surgery. The origin of Graves' disease was not understood until 1886, when PJ Moebius suggested that the cause was a malfunction of the thyroid gland itself. However, from a surgical standpoint, it doesn't make much of a difference. The goals of thyroid surgery remain unchanged: removal of the entire abnormal thyroid gland and any invasive tumors, preservation of parathyroid function, and maintenance or improvement of voice and swallowing. Decreased quality of life (QOL) after thyroid surgery is common and may include ongoing medication need [7], anti-thyroid medication, radiological/medical examinations, temporary and permanent hypoparathyroidism, postoperative temporary or persistent hoarseness, and difficulty swallowing. Voice disorders describe at least temporary in up to 80% of patients after thyroid surgery, but prevention, evaluation, and management are incomplete. After surgery, about 1 in 10 patients will have temporary nerve damage and 1 in 25 people will have long-term voice problems [8]. Although transient hoarseness is rarely seen in any surgery involving anesthesia, the possibility of laryngeal nerve injury in thyroid surgery

should be monitored more closely when hoarseness occurs following such surgeries [9]. The most common site of injury is one or both nerve roots (RLS) near the thyroid gland, the main nerve that controls the movement of the vocal cord (VF). Another important nerve to worry about is the bilateral laryngeal nerve (SLN), which is usually less directly affected during thyroid surgery, damage affects its ability to change voice and reduce predictable sounds. Another rare surgical cause of voice change after thyroidectomy is cervical muscle injury Causes of failure may include pulmonary edema, edema, or airway obstruction [10-12].

The aim of this study was to determine the frequency of unplanned parathyroidectomy, unplanned parathyroidectomy, postoperative hypocalcemia and the risk of unplanned parathyroidectomy in patients undergoing thyroid surgery in our clinic [13-15].

Material and Methods

Study Design: This study was conducted by retrospectively examining the records of patients who underwent thyroid surgery in a tertiary hospital between January 2018 and December 2020.

Inclusion and Exclusion criteria: Those with pain recurrence and those with mid-neck surgery were excluded from the study.

Method: Comparison of postoperative Ca value with age, gender, preoperative Ca value, dominant nodule diameter on ultrasonography (USG), type of surgery (total/lobectomy), and histopathological findings of thyroidectomy material (malignant/benign, with or without incident parathyroidectomy) is closed. Blood calcium levels below 8 mg/dL, measured after the first 24 hours after surgery, are indicative of postoperative hypocalcemia. Hypocalcemia lasting longer than six months is considered

transient hypocalcemia, while hypocalcemia lasting longer than six months is considered permanent hypocalcemia. Vocal cord paralysis lasting less than six months is considered temporary, and vocal cord paralysis lasting longer than six months is considered permanent. Postoperative Ca values were correlated with age, gender, preoperative Ca values, large nodule diameter on USG, type of surgery (total/lobectomy), and histopathological examination of thyroidectomy products (malignant/benign, with or without thyroid gland problem). parathyroidectomy to identify hypocalcemia risk factors). In addition, according to the final pathological results, the patients were divided into two groups as with and without combined parathyroidectomy. Risk factors for event parathyroidectomy were determined.

Ethical Considerations: This study was carried out after being approved by the ethics committee of Tabriz University of Medical Sciences. All study participants signed the informed consent form. No fees were charged to the patients. All complications were resolved in the shortest possible time by the research team.

Data Analysis : All collected data were analyzed using the Statistical Package for the Social Sciences Software Version 20 (SPSS; IBM Corporation, Armonk, NY). Data are presented as mean, standard deviation, median, minimum and maximum, percentage and number. The

Shapiro-Wilk W test was performed when the sample size of the continuous variable was <50 ; When the value is >50 , the Kolmogorov-Smirnov test is performed. When the distribution between two independent groups was given, the independent sample t-test was used; Mann-Whitney U test was performed when there was no normal distribution. Pearson chi-square test is used when values > 5 in 2×2 comparisons of categorical variables; When the significance is between 3 and 5, the Yates test is performed. However, Fisher's exact test was performed when the expected value was <3 . In multivariate analysis, risk groups are shown with logistic regression analysis together with the probability of occurrence in the previous analysis. $P < 0.05$ was considered significant.

Results

Of the 55 patients, 25 were male and 30 were female. On USG, the diameter of the central nodule is 2.9 cm (range 0.5 - 10.5 cm). Total thyroidectomy was performed in 29 patients, 20 of which were thyroid lobectomy. Postoperative transient hypocalcemia occurred in 31 patients (31.01%) and there was no risk of hypocalcemia in the follow-up. 15 patients (1.7%) regular music, 4 patients (0.46%). Postoperative bleeding was observed in two patients (2%). Twelve of them were repeated and bleeding was controlled. Six patients were discharged. There was no postoperative mortality(Figure 1).

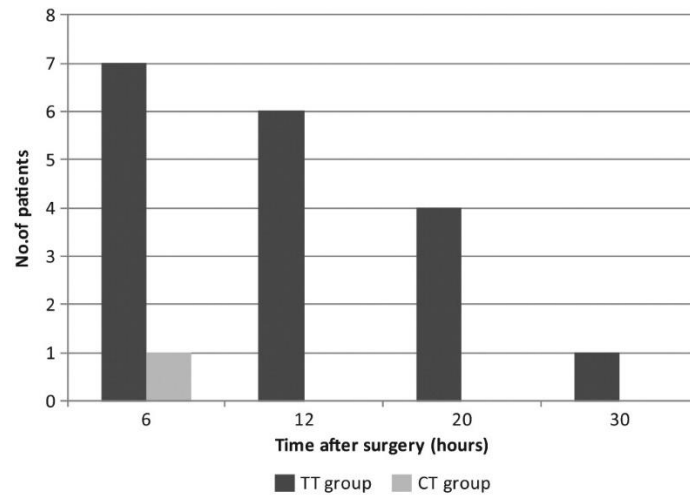


Figure 1: Characters in participants

According to the postoperative histopathological results, there were 33 (35.5%) patients in the malignant group and 24 (64.5%) patients in the benign group. Histopathological malignancy type: 26 cases of papillary carcinoma, 2 cases of alveolar carcinoma, 1 case of follicular carcinoma, 5 cases of medullary carcinoma, 5 cases of anaplastic carcinoma. 5 (9%) Histopathological examination was performed in 2% of the patients, while histopathological examination was not performed in 31 (90.8%) patients. Six patients who incidentally underwent parathyroidectomy had two functioning parathyroid glands, and 12

patients who incidentally underwent parathyroidectomy had only one. Parathyroidectomy complication was performed in five patients (6.2%).

When the male and female groups were compared, it was found that the incidence of hypocalcemia was higher in women than in men, and the difference was significant ($p=0.003$). Evaluation of postoperative hypocalcemia according to age showed a significant difference ($p=0.016$) in the group with hypocalcemia below the mean. According to the ROC analysis; It has been shown that there is a risk of hypocalcemia under 28 years of age (Figure 2 and Figure 3).

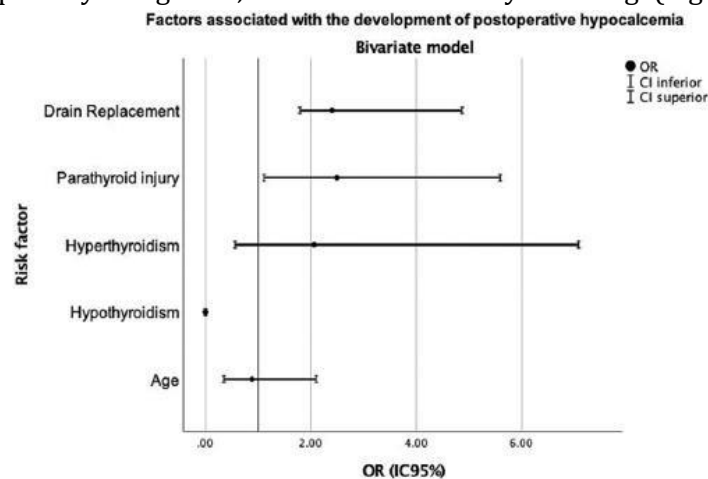


Figure 2: Hypocalcemia risk Factor after thyroidectomy

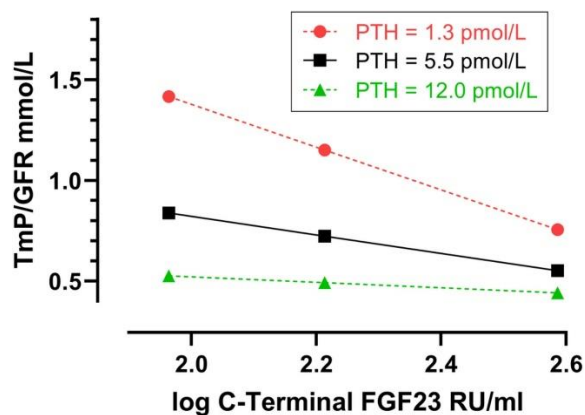


Figure 3: ROC results in thyroidectomy

5 years with 90% sensitivity. Evaluation of hypocalcemia according to preoperative Ca values showed that the change in hypocalcemia was less in the group with high preoperative Ca values, and this difference was significant

($p=0.000$). According to the type of surgery, the incidence of transient hypocalcemia was higher in the total thyroidectomy group than in the lobectomy group, and the difference was significant ($p=0.006$) (Figure 4).

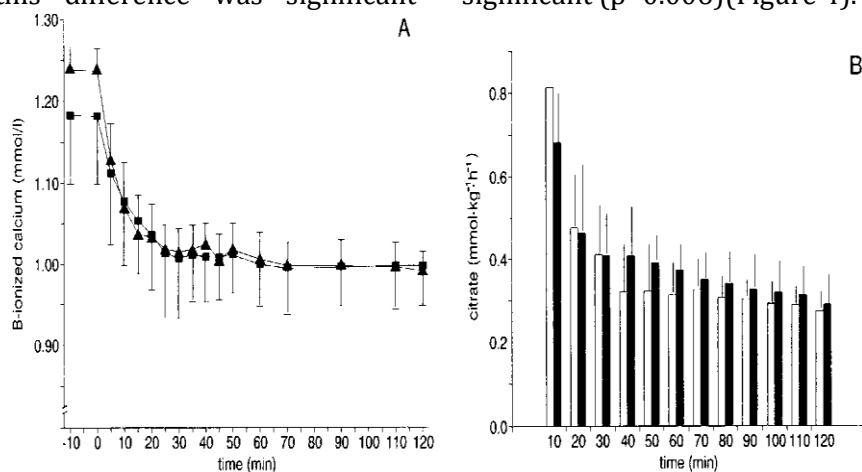


Figure 4: Hypocalcemia after 120 min after surgery

There was no relationship between nodule diameter and hypocalcemia. When patients were divided into malignant and benign groups, there was no significant difference between these groups in terms of performance after hypocalcemia. When patients were divided into groups with and without incident parathyroidectomy, there was no significant difference in postoperative hypocalcemia between these groups.

Regarding the risk of emergency parathyroidectomy, the rate of event parathyroidectomy was higher in the total

thyroidectomy group than in the lobectomy group ($p=0.037$). Parathyroidectomy complication rate was higher in the malignant group than in the benign group ($p=0.01$).

Discussion

The thyroid gland plays an important role in the endocrine system [16-18]. Cancer surgery is the most common endocrine surgery. The most common complication of thyroidectomy is hypocalcemia; Transient hypocalcemia occurs in 0.3% to 49% and permanent hypocalcemia is

reported in 0% to 13%. Many biochemical tests and compromises are made with hypocalcemia, which leads to a longer hospital stay. Hypocalcemia resolves spontaneously in many patients, but may remain if there is irreversible damage to the parathyroid gland. Because of this problem, the total cost of thyroidectomy also increases [19-21].

In our study, the incidence of postoperative transient hypocalcemia was found to be 31.01%. As can be seen, this rate is slightly higher than the meta-analysis in the literature (27%). Our rate of permanent hypocalcemia was lower than reported in the literature (1%). In terms of gender comparison, the incidence of hypocalcemia in women is higher than in men. In a meta-analysis of 10 studies and 3,443 patients, gender was reported as a risk factor for hypocalcemia. Based on our research and data, gender has been recognized as a risk factor for freedom [22-24]. Recent research on the size and location of the parathyroid glands in men and women may explain this [25].

In our study, when age was compared with hypocalcemia, the mean age was lower in the hypocalcemia group. In our study; It was determined that those under the age of 28.5 were at risk of developing hypocalcemia. According to our study, it was reported in the literature that the mean age of the group with hypocalcemia was higher than the group without hypocalcemia. Age was reported to be a risk factor for hypocalcemia in five studies and a meta-analysis involving 2,576 patients [26-28]. In our study, preoperative Ca values were lower in the patient group with postoperative hypocalcemia than in the patient group without postoperative hypocalcemia [29-31]. In a meta-analysis of 6 studies and 2,443 patients, no difference in baseline Ca values was reported in patients who developed diabetes hypocalcemia compared with those who did not [32]. In our study, the incidence of postoperative hypocalcemia was found to be higher in the

group that underwent total thyroidectomy compared to the group that underwent lobectomy. Studies in the literature have shown that total thyroidectomy is a risk factor for postoperative hypocalcemia [33-35]. This can be explained by the high probability of direct tumor or vascular injury during total thyroidectomy, since all four tumors are in the anatomical region [36].

In our study, no relationship was found between the nodule diameter measured by preoperative USG and postoperative hypocalcemia [37]. In our study, there was no difference between the two groups in the development of postoperative hypocalcemia when patients were divided into malignant and benign according to histopathological findings. Similar to our study, there are studies in the literature showing that malignancy is not a risk factor for hypocalcemia. Although the possibility of malignant nodules to involve the surrounding tissues and parathyroid glands in malignant patients increases the risk of parathyroid vascular and parenchymal injury, there is no significant difference in our method study [38-40].

In our study, in which we compared patients who had and had not undergone parathyroidectomy, there was no difference in hypocalcemia activity between the two groups. Similar to our study, although there are studies in the literature showing that parathyroidectomy status is not associated with postoperative hypocalcemia [41], there are also studies showing that parathyroidectomy status is associated with disease-related hypocalcemia. A meta-analysis including four studies and 1,482 patients reported that unplanned parathyroidectomy is a risk factor for postoperative hypocalcemia [42-44].

Hypoparathyroidism is a condition resulting from direct injury to the parathyroid gland, vascular devascularization, obstruction of venous drainage, and removal of the parathyroid gland [45-47]. Therefore, it may not be an

appropriate test to treat one or more parathyroid glands alone as a measure that does not determine the status of additional parathyroid glands and associated hypocalcemia. During thyroid surgery, it is important to protect the vascular structure of the parathyroid gland by connecting the thyroid artery closest to the thyroid capsule during the dissection of the gland [48-50]. The main limitation of this study is the retrospective design of the charts. However, it can be considered as a sufficient number for a single site consisting of 864 patients [51-53].

In our study, it was observed that the incidence of parathyroid tumors was higher in the malignancy group and in patients who underwent total thyroidectomy. Total thyroidectomy and malignancy are risk factors for event parathyroidectomy in meta-analyses and various studies in the literature. The presence of all four tumors in the anatomical region during total thyroidectomy may explain the increased risk of parathyroidectomy [54-56]. In the presence of malignant thyroid disease, total thyroidectomy surgery and invasion of the parathyroid gland or surrounding tissue from the malignant thyroid tissue will explain the possible outcome of parathyroidectomy [57].

There is debate about what precautions should be taken and when to predict postoperative persistent or persistent hypoparathyroidism. Some authors recommend starting and running the iPTH time monitor Asari et al. It has been shown that measuring iPTH levels 24 hours after total thyroidectomy and calcium levels the day after surgery predicts hypoparathyroidism with these measurements with high sensitivity, specificity, and good predictive value [58]. However, in another study, no significant correlation was found between the levels of 24 hours after PTH and the development of overt hypocalcemia. Another study supports the benefits of iPTH monitoring, but points out that

the high cost of monitoring is a major limitation for clinical use³.

More importantly, a decrease in blood calcium relative to the level before the first postoperative measurement (first morning after surgery) is indicative of subsequent hypocalcemia [59].

Therefore, we investigated the decrease in serum calcium (Δ) between the last assessment and the morning after surgery, and after examining the Δ distribution (Table III), we took 1.1 mg/dl (12% preoperatively) as the cut-off point. To predict hypocalcemia, the period in which calcium supplementation was initiated immediately if the decrease was ≥ 1.1 mg/dl was determined. An important part of this process is if the blood calcium level is in the range of 8, the patient is discharged immediately after removal (usually on the third day), 8-10,2 mg/dL.

Conclusion

In our study, female gender, age <28.5 years, low preoperative Ca value and total thyroidectomy were considered to be associated with hypocalcemia. Although there is no association between parathyroidectomy and postoperative hypocalcemia, this problem can be avoided by careful removal and imaging of the thyroid gland, especially in patients including patients with malignant thyroidectomy and total thyroidectomy. In conclusion, we propose here to evaluate the decrease in calcium levels after surgery compared to previous levels as a useful and simple indicator of hypocalcemia in all thyroidectomy patients. Using 1 mg/dl (12% of preoperative level) as a cut-off value to decide whether to start prophylactic calcium supplementation provides good results by allowing patients to be discharged on average approximately 2 days earlier.

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