# HEALTH SCIENCES **MEDICINE**

## Risk factors for hypocalcemia and correlation between thyroid volume and incidental parathyroidectomy after total thyroidectomy: single center experience

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**Cite this article as**: Sivgin H, Bostan MS. Risk factors for hypocalcemia and correlation between thyroid volume and incidental parathyroidectomy after total thyroidectomy: single center experience. J Health Sci Med 2023; 6(2): 421-427.

## ABSTRACT

**Aim**: We aimed to investigate correlation between the effects of age, sex, disease, pathologic diagnosis, parathyroid autotransplantation, presence of parathyroid in the pathology specimen and clinicopathological variables and thyroid volume, postoperative hypocalcemia after bilateral total thyroidectomy.

**Material and Method**: A retrospective study planned in tertiary university hospital on patients undergone bilateral total thyroidectomy and neck dissection when necessary surgery for thyroid pathologies. Minimum calcium values in the postoperative period were recorded as transient or permanent hypocalcemia. The cases were statistically analyzed for the relationship between the volume of the thyroid gland removed and hypocalcemia. The effects of sex, pathological diagnosis, preoperative hyperthyroidism, anatomical retrosternal extension, number of parathyroid glands seen and preserved intraoperatively, parathyroid gland autoimplantation, parathyroid gland removal in the pathological specimen, nerve monitoring, bilateral total thyroidectomy and central and lateral neck dissection were analyzed for postoperative hypocalcemia.

**Results**: Totally 763 patients were included in the study. The mean age of the patients was 50.6 years (SD:12.8) and the sex of 575 (75.4%) patients was female. Hypocalcemia was more common in women than in men (31% vs 17%; p<0.001). Patients who underwent incidental parathyroidectomy (IPT) (yes, 43% vs no, 25%; p<0.001) and parathyroid autotransplantation (yes, 82% vs no, 27%; p=0.001) had statistically significantly higher rates of hypocalcemia. In the univariate analysis, it was determined from the available data that an increase in thyroid volume had a statistically significant effect on hypocalcemia, albeit at a low level [OR:1.002 (95%CI:1-1.004]. In the multivariate logistic regression model, the independent variables associated with postoperative hypocalcemia were female sex [OR: 2.33 (95%CI: 1.49-3.62)], thyroid volume [OR: 1.003 (95%CI:1-1.005)], IPT [OR:2.29 (95%CI:1.48-3.54)] and parathyroid autotransplantation [OR:1.999 (95%CI:2.1-47.5)]. While the effect of increased thyroid volume on hypocalcemia was very low, being female and incidental parathyroidectomy increased hypocalcemia 2.3 fold and parathyroid autotransplantation increased hypocalcemia 10-fold.

**Conclusion**: Incidental parathyroidectomy is a remarkable association, which determines the complication of postoperative hypocalcemia, and the presence of parathyroid tissue in the pathology specimen in cases with small thyroid volume.

Keywords: Hypocalcemia, thyroidectomy, thyroid volume, incidental parathyroidectomy

## INTRODUCTION

Thyroid surgery is one of the most common surgical interventions performed today. Bilateral total thyroidectomy is the surgical procedure accepted by surgeons as the gold standard for thyroid cancer, suspected cancer, or bilateral benign conditions, and is now safely performed (1). Hypocalcemia is most commonly seen in surgery after bilateral thyroidectomy and requires temporary or permanent treatment (1,2). In different series, the incidence of transient hypocalcemia is reported to be 0.3-49%, and the incidence of permanent hypocalcemia is 0-13%. Hypocalcemia can be asymptomatic or cause a wide range of symptoms ranging from mild symptoms to life-threatening clinical findings. (2) In cases of hyperthyroidism and graves, post-surgical hypocalcemia is defined as hemodilution secondary to stress, increased urinary calcium excretion, hungry bone syndrome, osteodystrophy, and autoimmune fibrosis, while in severe hypocalcemia cases, hypoparathyroidism

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secondary to surgical trauma, devascularization, and iatrogenic parathyroidectomies are indicated. (3,4) Many studies have evaluated factors that may be risk for hypocalcemia after total thyroidectomy and various factors that may predict hypocalcemia in the preoperative period. (4) Predicting whether hypocalcemia will develop and starting treatment early is critical to reducing the length of hospital stay. In this study, the relationship between hypocalcemia, which is one of the complications encountered after thyroidectomy surgery, and the thyroid gland size of the patients was statistically analyzed to determine whether thyroid volume is an influential factor in the occurrence of hypocalcemia. Apart from this main objective, the effects of age, sex, disease, pathologic diagnosis, parathyroid autotransplantation, presence of parathyroid in the pathology specimen, and hormonal activity of the thyroid gland on thyroid volume were also analyzed.

## MATERIAL AND METHOD

Tokat University Clinical Gaziosmanpaşa Researches Ethics Committee approval was received (Date:20.10.2022, Decision No:22-KAEK-215). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The data of the patients who underwent BTT and neck dissection when necessary, in the General Surgery Department of Tokat Gaziosmanpaşa University Faculty of Medicine between January 2010 and October 2022, and whose information was obtained, were evaluated retrospectively. Minimum calcium values in the postoperative period were recorded. Patients with abnormal preoperative serum PTH and calcium values, patients younger than 18 years of age, patients with hypocalcemia clinic as a result of the previous thyroidectomy, and patients with parathyroid adenoma were excluded from the study. A serum calcium level below 8 mg/dL was defined as hypocalcemia, recovery of hypocalcemia for less than 6 months was defined as transient hypocalcemia, and use of calcium and active vitamin D due to persistent hypocalcemia was defined as permanent hypocalcemia. The volume of the thyroid gland removed during the operation was calculated separately for each lobe using the standard ellipsoid formula (Miccoli formula: width x height x length x  $\pi$  / 6). The cases were statistically analyzed for the relationship between the volume of the thyroid gland removed and hypocalcemia. The effects of sex, pathological diagnosis, preoperative hyperthyroidism, anatomical retrosternal extension, number of parathyroid glands seen and preserved intraoperatively, parathyroid gland autoimplantation, parathyroid gland removal in the pathological specimen, nerve

monitoring, BTT and central and lateral neck dissection on the development of hypocalcemia were evaluated. In statistical evaluation, Chi-square and Fisher's exact test were used for pairwise comparison of groups, and nominal regression analysis was used for multivariate evaluation. p<0.05 was considered significant.

## Statistical Evaluation of Data

SPSS (Statistical Package for the Social Sciences) version 25.0 (IBM Corp., Armonk, NY, USA) program was used for statistical analysis. Whether the scores obtained from each continuous variable were normally distributed was analyzed by descriptive, graphical and statistical methods. The Kolmogorov-Smirnov test was used to test the normality of the scores obtained from a continuous variable by statistical method. While evaluating The relationship between two continuous variables was analyzed by Pearson correlation test. Univariate and multivariate logistic regression modeling was used to measure the effect of independent variables on the dependent variable. In addition, ROC analysis was used for the most appropriate thyroid volume discrimination to predict the presence of incidental parathyroidectomy. Results were evaluated at 95% confidence interval and significance was evaluated at p<0.05.

## RESULTS

## **Patient Characteristics**

Totally 763 patients were included in the study. The mean age of the patients was 50.6 years (SD:12.8) and the sex of 575 (75.4%) patients was female. BTT was performed in 737 patients (96.6%) and completion thyroidectomy in 26 patients (3.4%). Postoperative hypocalcemia was seen in 210 (27.5%) patients, 158 (20.7%) transient, and 52 (6.8%) permanent. Hypocalcemia was symptomatic in 106 (13.9%) and asymptomatic in 104 (13.6%) patients. Histopathologically, 231 (30.3%) patients were malignant and 532 (69.7%) were benign. Of the malignant patients, 214 (93%) were papillary carcinoma, 8 (4.4%) follicular carcinoma, 3 (1.3%) anaplastic carcinoma, 3 (1.3%) medullary carcinoma, and 3 (1.3%) mixed type carcinoma. Histopathologic examination revealed that 110 (14.4%) patients had IPT. There was one parathyroid gland in 90 (11.8%), two in 18 (2.4%), and three in 3 (0.3%) patients who underwent IPT. The mean postoperative Ca-Min. level was 8.29 mg/dl (SD: 0.68), median thyroid volume was 59 (Range: 3.5-627), and 106 (13.9%) patients received IV replacement therapy postoperatively. Patient demographic and clinicopathologic characteristics are detailed in Table 1.

| Table 1. Patient characteristics         |              |
|--|--------------|
| Variables (N=763)                        | n(%)         |
| Age, mean (sd)                           | 50.6 (12.8)  |
| Male                                     | 188 (24.6)   |
| Female                                   | 575 (75.4)   |
| Malign                                   | 231 (30.3)   |
| Benign                                   | 532 (69.7)   |
| Thyroid volume, median (range)           | 59 (3.5-627) |
| Incidental parathyroidectomy             | 110 (14.4)   |
| Total Thyroidectomy                      | 737 (96.6)   |
| Completion Thyroidectomy                 | 26 (3.4)     |
| Parathyroid autotransplantation          | 11 (1.4)     |
| Lymph node dissection                    | 23 (3.0)     |
| Thyroiditis                              | 208 (27.3)   |
| Retrosternal goitre                      | 102 (13.4)   |
| Previous thyroid surgery                 | 19 (2.5)     |
| Preoperative hyperthyroid                | 242 (31.7)   |
| Postoperative Ca-Min. (mg/dl), mean (sd) | 8.29 (0.68)  |
| Hypocalcemia                             | 210 (27.5)   |
| Symptomatic                              | 106 (13.9)   |
| Asymptomatic                             | 104 (13.6)   |
| Transient                                | 158 (20.7)   |
| Permanent                                | 52 (6.8)     |
| IV Ca supplementation                    | 106 (13.9)   |
| Calsitriol                               | 52 (6.8)     |
| sd:standard deviation                    |              |

## Factors Related to Postoperative Hypocalcemia Univariate Analysis Results

Hypocalcemia was more common in women than in men (31% vs 17%; p<0.001). Patients who underwent IPT (yes, 43% vs no, 25%; p<0.001) and parathyroid

autotransplantation (yes, 82% vs no, 27%; p=0.001) had statistically significantly higher rates of hypocalcemia. In the univariate analysis, it was determined from the available data that an increase in thyroid volume had a statistically significant effect on hypocalcemia, albeit at a low level [OR:1.002(95%CI:1-1.004]. Although not statistically significant, postoperative hypocalcemia was higher in patients with a preoperative diagnosis of hyperthyroidism (yes, 32% vs no, 26%; p=0.071). There was no statistically significant difference in the incidence of hypocalcemia according to age and other clinicopathologic features (p>0.05) (**Table 2**).

## Multivariate Regression Analysis Results

Multivariate logistic regression analysis using the enter method was performed, including variables (sex, thyroid volume, IPT, parathyroid autotransplantation, and preoperative hyperthyroidism) that were significantly statistically (p<0.05) or nearly significantly (p<0.10) associated with hypocalcemia in univariate analyses. According to the results of the regression analysis, the coefficient of determination of the model was R2(Nagelkerke)=0.10. Accordingly, it was found that 10% of the variance in the dependent variable was explained by the independent variables. Since the p-value in the model (F=51.78, p<0.001) is smaller than the value, it is determined that the model is significant at 95% confidence level. The correct classification probability of the model was obtained as 74%. The model predicted hypocalcemia 74% correctly with the variables used. According to the multiple logistic regression model, the independent variables associated with postoperative

|                                 | Category   | n   | n (%)      | Hypocalcemia       |          |                     |          |
|---------------------------------|------------|-----|------------|--------------------|----------|---------------------|----------|
| Variables (N=763)               |            |     |            | Univariate         |          | Multivariate        |          |
|                                 |            |     |            | OR (95% CI)        | р        | OR (95% CI)         | р        |
| Age, mean(sd)                   | <50        | 333 | 97 (29.1)  | 1.15 (0.84-1.59)   | 0.382    | NA                  |          |
|                                 | ≥50        | 430 | 113 (26.3) | 1                  |          | NA                  |          |
| Sex                             | Female     | 575 | 179 (31.1) | 2.29 (1.5-3.5)     | < 0.001* | 2.33 (1.49-3.62)    | < 0.001* |
|                                 | Male       | 188 | 31 (16.5)  | 1                  |          | 1                   |          |
| Thyroid pathology               | Malign     | 231 | 63 (27.3)  | 0.98 (0.7-1.39)    | 0.919    | NA                  |          |
|                                 | Benign     | 532 | 147 (27.6) | 1                  |          | NA                  |          |
| Thyroid volume                  | All        | 763 | NA         | 1.002 (1-1.004)    | 0.036*   | 1.003 (1.001-1.005) | 0.001*   |
| Incidental parathyroidectomy    |            | 110 | 47 (42.7)  | 2.24 (1.48-3.4)    | < 0.001* | 2.29 (1.48-3.54)    | < 0.001* |
| Thyroid surgery type            | Total      | 737 | 205 (27.8) | 1.62 (0.6-4.35)    | 0.340    | NA                  |          |
| 7 0 7 71                        | Completion | 26  | 5 (19.2)   | 1                  |          | NA                  |          |
| Parathyroid autotransplantation |            | 11  | 9 (81.8)   | 12.34 (2.64-57.58) | 0.001*   | 9.99 (2.1-47.5)     | 0.004*   |
| Lymph node dissection           |            | 23  | 8 (34.8)   | 1.42 (0.59-3.4)    | 0.431    | NA                  |          |
| Thyroiditis                     |            | 208 | 66 (31.7)  | 1.33 (0.94-1.88)   | 0.112    | NA                  |          |
| Retrosternal goitre             |            | 102 | 29 (28.4)  | 1.05 (0.66-1.67)   | 0.825    | NA                  |          |
| Previous thyroid surgery        |            | 19  | 4 (21.1)   | 0.7 (0.23-2.12)    | 0.525    | NA                  |          |
| Preoperative hyperthyroid       |            | 208 | 77 (31.8)  | 1.36 (0.97-1.9)    | 0.071    | 1.27 (0.88-1.83)    | 0.207    |

hypocalcemia were female sex [OR: 2.33(95%CI: 1.49-3.62)], thyroid volume [OR: 1.003(95%CI:1-1.005)], IPT [OR:2.29(95%CI:1.48-3.54)] and parathyroid autotransplantation [OR:1.999(95%CI:2.1-47.5)]. While the effect of increased thyroid volume on hypocalcemia was very low, being female and IPT increased hypocalcemia 2.3-fold and parathyroid autotransplantation increased hypocalcemia 10-fold (**Table 2**).

### **Relationship Between Continuous Variables**

There was a positive correlation between thyroid volume and age (r=0.170; p=<0.001) and a weak negative correlation between postoperative Ca minimum level (r=-0.088; p=0.015) and the number of parathyroid glands removed (r=-0.114; p=0.002) (**Table 3**).

| Table 3. Relationship between continuous variables |        |                   |  |  |  |
|--|--------|-------------------|--|--|--|
| Variables  | Age    | Thyroid<br>volume |  |  |  |
| Thyroid volume                                     | 0.170* |                   |  |  |  |
| Postoperative CaMin                                | 0.004  | -0.088**          |  |  |  |
| Incidental number of parathyroid glands            | 0.004  | -0.114**          |  |  |  |
| *:p<0.001, **:p<0.05, Pearson Correlation          |        |                   |  |  |  |

## **ROC Analysis Result**

The cut-off value for thyroid volume in determining the risk of IPT was 70 and the AUC value was 61%. For the thyroid volume cut-off value of 70, sensitivity 0.75 (95%CI: 0.66-0.84), specificity 0.45 (95%CI: 0.35-0.55), PPV 0.19 (95%CI: 0.11-0.27), NPV 0.92 (95%CI: 0.87-0.97) and accuracy 0.49 (95%CI: 0.39-0.59) were calculated (**Table 4**). Univariate analysis revealed that the only variable associated with IPT was thyroid volume. The IPT rate was higher in patients with a thyroid volume below 70 (19% vs 8%). When thyroid volume of 70 and above was accepted as reference, thyroid volume below 70 was 2.5 (95%CI: 1.59-3.99) times more associated with IPT (p<0.001).

| Table 4. ROC curve analysis results  |                      |  |  |
|--|----------------------|--|--|
|  | Thyroid volume       |  |  |
| Incidental parathyroidectomy   |                      |  |  |
| Cut-off  | 70                   |  |  |
| AUC (95% CI)   | 0.614 (0.558-0.671)* |  |  |
| Sensitivity (95% CI)   | 0.75 (0.66-0.84)     |  |  |
| Specificity (95% CI)   | 0.45 (0.35-0.55)     |  |  |
| PPV (95% CI)   | 0.19 (0.11-0.27)     |  |  |
| NPV (95% CI)   | 0.92 (0.87-0.97)     |  |  |
| Accuracy (95% CI)  | 0.49 (0.39-0.59)     |  |  |
| *:p<0.001, PPV:<br>positive predictive value, NPV=negative predictive value, AUC: are<br>a under the curve |                      |  |  |

| Table 5. Risk factors for incidental parathyroidectomy                |     |            |                              |          |  |  |
|---|-----|------------|------------------------------|----------|--|--|
| Variables(N=763)  | n   | (0/)       | Incidental parathyroidectomy |          |  |  |
| Category  |     | n(%)       | Univariate                   |          |  |  |
|   |     |            | OR(95%CI)                    | р        |  |  |
| Age   |     |            |                              |          |  |  |
| <50   | 333 | 42 (12.6)  | 1                            |          |  |  |
| ≥50   | 430 | 68 (15.8)  | 1.3 (0.86-1.97)              | 0.213    |  |  |
| Sex   |     |            |                              |          |  |  |
| Male  | 188 | 22 (11.7)  | 1                            |          |  |  |
| Female  | 575 | 88 (15.3)  | 1.36 (0.83-2.25)             | 0.224    |  |  |
| Thyroid pathology   |     |            |                              |          |  |  |
| Malign  | 231 | 36 (15.6)  | 1.14 (0.74-1.76)             | 0.545    |  |  |
| Benign  | 532 | 74 (13.9)  | 1                            |          |  |  |
| Thyroid surgery type  |     |            |                              |          |  |  |
| Total   | 737 | 104 (14.1) | 0.55 (0.22-1.4)              | 0.207    |  |  |
| Completion  | 26  | 6 (23.1)   | 1                            |          |  |  |
| Previous thyroid surgery  |     |            |                              |          |  |  |
| Yes   | 19  | 2 (10.5)   | 1                            |          |  |  |
| No  | 744 | 108 (14.5) | 1.44 (0.33-6.34)             | 0.627    |  |  |
| Preoperative hyperthyroid   |     |            |                              |          |  |  |
| Yes   | 208 | 30 (14.4)  | 0.999 (0.64-1.57)            | 0.998    |  |  |
| Thyroid volume (cn  | n³) |            |                              |          |  |  |
| <70   | 442 | 83 (18.8)  | 2.52 (1.59-3.99)             | < 0.001* |  |  |
| ≥70   | 321 | 27 (8.4)   | 1                            |          |  |  |
| *:p<0.05, OR: Odds ratio, CI: Confidence interval, 1: Reference value |     |            |                              |          |  |  |

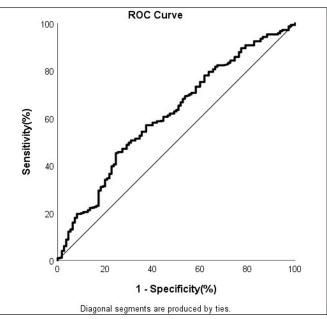


Figure 1. ROC curve of Incidental parathyroidectomy

## DISCUSSION

Postoperative hypocalcemia was observed in 210 (27.5%) patients, 158 (20.7%) transient and 52 (6.8%) permanent. Hypocalcemia was symptomatic in 106 (13.9%) patients and asymptomatic in 104 (13.6%) patients. In the univariate analyzes of 12 variables evaluated on hypocalcemia in our study, it was seen that the variables that were statistically significant or close to significance were sex, thyroid volume, IPT, parathyroid

autotransplantation, and preoperative hyperthyroidism. According to the multivariate logistic regression model; the independent variables associated with postoperative hypocalcemia were found to be female sex, thyroid volume, IPT and parathyroid autotransplantation. While the effect of thyroid volume increase on hypocalcemia is very low; It was determined that being female and performing IPT increased hypocalcemia 2.3 times, and performing parathyroid autotransplantation increased hypocalcemia 10 times. However, age, recurrence, neck dissection, presence of thyroiditis, thyroid pathology and retrosternal extension, which were reported as risk factors for hypocalcemia in some studies, were not found to be significant risk factors in our study.

In a study, it was stated that hypocalcemia is related to young age (5). In another study, when age and hypocalcemia status were compared, the risk of hypocalcemia was determined to be high in those younger or older than the age range of 45-84 (6). In our study, however, no significant difference was found between age and the development of postoperative hypocalcemia and hypoparathyroidism. Female sex has been identified as a risk factor for postoperative hypocalcemia in studies with large series (7-10). Our study was performed on 575 (75.4%) female and 188 (24.6%) male cases. The female sex ratio was higher in patients with postoperative hypocalcemia compared to the other group. Postoperative hypocalcemia was observed in 210 (27.5%) patients, 158 (20.7%) transient and 52 (6.8%) permanent. 179 patients with hypocalcemia were female and 31 patients were male. In our study, it was seen that female sex was a significant independent risk factor in postoperative hypocalcemia.

There are studies on the risk of developing postoperative hypocalcemia in patients who underwent BTT due to hyperthyroidism. In another study involving 2108 patients who had undergone thyroid surgery, the relationship between early hypocalcemia and thyrotoxicosis was examined and no difference was found between those with and without Graves' disease in terms of the development of hypocalcemia. (11) In another study involving 380 patients who underwent BTT, 203 patients were operated for Graves' disease, 56 patients were operated for non-Gravesian hyperthyroidism, and 521 patients were operated for other benign reasons, and permanent hypoparathyroidism was found to be significantly higher in Graves patients compared to other patients. Although it was not statistically significant patients with preoperative hyperthyroidism, in postoperative hypocalcemia was higher.

While there are studies showing that malignancy has an effect on postoperative hypocalcemia in patients undergoing thyroidectomy (12-13), there are also studies claiming the contraversial (11). In our study, the pathology results of 231 (30.3%) patients were malignant, while the results of 532 (69.7%) patients were benign. There was no significant relationship between benign and malignant findings of the patients and postoperative hypocalcemia.

In a meta-analysis of 1132 patients including five studies, patients who had only BTT and those who had neck dissection combined with BTT were compared, and it was observed that transient hypocalcemia was statistically increased in patients with neck dissection added to thyroidectomy. In another study, which included 1030 patients who underwent BTT, temporary hypocalcemia developed in 28.2% of patients, permanent hypocalcemia developed in 2.6% of patients, and the development of hypocalcemia in patients who underwent central neck dissection and lateral neck dissection was found to be statistically significant (14). In a multicentric study examining retrosternal extension in 19,662 patients, it was reported that patients with retrosternal extension were more likely to develop temporary and permanent hypocalcemia than those without (15). In our study, when the operation, neck dissection and retrosternal extension were examined, it was seen that only BTT was performed in 737 patients, completion thyroidectomy was performed in 26 patients, and lateral neck dissection was added in 23 patients. Retrosternal extension was observed in 102 of the patients included in our study, and postoperative hypocalcemia was observed in 29 (28.4%) of them. When evaluated in terms of postoperative hypocalcemia; No statistical correlation was found between the type of operation, whether neck dissection was performed, and the presence of retrosternal extension.

In the literature, the leading surgical risk factors for transient hypocalcemia are the presence of the parathyroid gland in the surgery related to the parathyroid gland, parathyroid gland autotransplantation and IPT. In a meta-analysis evaluating 4 studies, it was determined that the incidence of transient hypocalcemia was significantly higher in patients who had one or more parathyroid gland autotransplantation. In a study of 271 patients who underwent thyroidectomy, permanent hypocalcemia was observed only in patients who did not undergo autotransplantation. Permanent hypoparathyroidism was not observed in any patient with postoperative hypocalcemia after autotransplantation (10). In a study involving 194 patients who underwent thyroid surgery, it was argued that routine autotransplantation almost completely eliminated postoperative permanent hypoparathyroidism (16). In a retrospective study, while autotransplantation was associated with transient hypocalcemia in 1482 patients who underwent thyroidectomy, permanent hypocalcemia was not.

They also stated that the existence of a relationship between parathyroid autotransplantation and transient hypocalcemia was independent of thyroidectomy width and neck dissection. It was found that the increase in the number of autotransplanted glands also significantly increased the incidence of transient hypocalcemia (17,18). In our study, symptomatic transient hypocalcemia developed in 9 of 11 patients who underwent parathyroid autoimplantation, while it did not develop in 2 patients. The risk of developing hypocalcemia in autotransplanted patients was determined as 81.8%. It is noteworthy that there is a statistically significant increase in the incidence of hypocalcemia with parathyroid autotransplantation. In terms of postoperative hypocalcemia, it was observed that parathyroid autotransplantation increased the risk of hypocalcemia 10 times.

In our study, one of the independent factors effective for postoperative hypocalcemia was IPT. Although there are studies reporting that IPT has no effect on postoperative hypocalcemia, the rate of transient hypocalcemia was found to be higher in patients who underwent one or more IPT (19-22). In a meta-analysis of 1482 patients from four studies, the incidence of transient hypocalcemia was found to be higher in patients who underwent IPT. In the presence of IPT, the incidence of hypocalcemia increases from 25% to 42.7%. IPT rates in the literature vary between 5-29% (18-22). In our study, the number of patients who had IPT was 110, and the rate was 14.4%. Permanent hypocalcemia was observed in 47 of our 110 patients who had IPT. In terms of postoperative hypocalcemia, it was observed that IPT increased the risk 2.3 times. When the risk factors for IPT were evaluated, univariate analysis revealed no relationship with age, sex, histopathology, type of operation, and history of previous thyroid surgery. It was found that the only variable associated with IPT was thyroid volume. Thyroid volume was found to be less than 70 cm<sup>3</sup> in 83 of 110 patients with IPT. The rate of IPT was higher in patients with a thyroid volume less than  $70 \text{ cm}^3$  (18.8% vs 8.4%). When the thyroid volume of 70cm<sup>3</sup> and above is accepted as a reference; Thyroid volume less than 70 cm<sup>3</sup> was associated 2.5 times more with IPT. Thyroid dissection may be easier in large thyroid volume. Low thyroid volume, especially if there is a thyroiditis background, makes thyroid surgery and identification of parathyroid glands difficult due to adhesion to the surrounding tissues. In addition, anatomically the parathyroid location may be intrathyroidal. Depending on this situation, incidental parathyroidectomy can be performed during thyroidectomy. For this reason, we believe that low thyroid volume increases the risk of incidental parathyroidectomy and therefore postoperative hypocalcemia.

In the postoperative pathological examination, parathyroid tissue was not observed in pathology in 653 patients, while parathyroid tissue was observed in pathology in 110 patients. The presence of postoperative hypocalcemia was found to be high in patients with parathyroid tissue in pathology. In terms of postoperative hypocalcemia, it has been observed that the presence of incidental parathyroid tissue in pathology is negatively correlated with thyroid volume, and the incidence of parathyroid tissue in pathology increases as the volume size decreases.

In a study, it was found that the risk of postoperative hypocalcemia increases as the thyroid gland volume decreases (23). In another study, it was reported that the risk of hypocalcemia increased in those with a small thyroid volume and the risk of bleeding in those with a large thyroid volume (24). In our study, it was determined that the increase in thyroid volume had a statistically significant effect on hypocalcemia, albeit at a low level. There was a weak positive correlation between thyroid volume and age, postoperative minimum calcium level, and the number of incidentally removed parathyroid glands. As a result of the univariate analysis performed in our study, it was determined that the only variable associated with IPT was thyroid volume. In our study, where the cut-off value for thyroid volume was found to be 70 cm<sup>3</sup> in determining the risk of IPT, the rate of IPT was 2.5 times higher in patients with thyroid volume below 70 cm<sup>3</sup>.

One of the limitations of our study is that it is retrospective. Due to its retrospective nature, we realized that prophylactic calcium and vitamin d replacement in some patients led to limitations in clearly demonstrating hypocalcemia.

## CONCLUSION

In our study, we found a remarkable association of IPT, which determines the complication of postoperative hypocalcemia, and the presence of parathyroid tissue in the pathology specimen in cases with small thyroid volume. For this reason, we recommend that the parathyroid tissues and their blood supply be not affected as much as possible intraoperatively for postoperative hypocalcemia, especially in cases with small thyroid volume in the preoperative period..

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Tokat Gaziosmanpaşa University, Noninvasive Clinical Researches Ethics Committee (Date: 20.10.2022, Decision No: 22-KAEK-215)

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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