

Hypoparathyroidism after total thyroidectomy: Incidence study in high volume single center

Incidence of Hypoparathyroidism after total thyroidectomy

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Abstract

Aim: Total thyroidectomy is the most frequently performed surgery in general surgery clinics for both benign and malignant pathologies of the thyroid gland. Although postoperative transient hypoparathyroidism is the most common complication, permanent hypoparathyroidism is rarely encountered. In our study, the incidence of permanent and temporary hypoparathyroidism developing after total thyroidectomy operations performed in our clinic within one year is investigated.

Material and Methods: Data extracted from prospectively recorded data of 258 patients (208 females and 50 males) who underwent total thyroidectomy at the Endocrine Surgery Unit of Ankara University General Surgery Clinic between January 2013 and January 2014 were retrospectively analyzed. The patients were divided into 2 groups as those operated for benign (Group 1) and malignant (Group 2) pathologies. The groups were compared in terms of the incidence of permanent and transient hypoparathyroidism.

Results: Post-operative temporary hypoparathyroidism was detected in 106 (41.1%) of 258 patients who underwent total thyroidectomy. Of these patients, 49 were operated for differentiated thyroid carcinoma (46.2%) and 57 for nodular goiter (53.7%) ($p=0.697$). Permanent hypoparathyroidism was observed in only one (0.4%) patient who was operated for papillary thyroid carcinoma ($p=0.294$). Post-operative transient hypocalcemia was detected in 67 (25.9%) patients. Of these patients, 26 (38.8%) were operated for differentiated carcinoma and 41 (61.1%) for nodular goiter ($p=0.91$).

Discussion: The incidence of postoperative transient and permanent hypoparathyroidism in total thyroidectomy operations performed in our clinic was found to be consistent with the literature.

Keywords

Differentiated Thyroid Cancer, Hypoparathyroidism, Nodular Goiter, Permanent, Transient

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Introduction

Total thyroidectomy is the most commonly performed surgery in thyroid-related pathologies. Although postoperative temporary hypoparathyroidism is the most common complication after total thyroidectomy, complications such as bleeding and vocal cord paralysis can be seen [1-2]. The incidence of transient hypocalcemia varies between 5.4% and 62% in the literature [3-5]. The incidences of transient and permanent hypoparathyroidism were found to be 27% (19–38) and 1% (0–3), respectively [6].

Postoperative hypoparathyroidism is due to a decrease in circulating PTH hormone secondary to the decrease in functional total parathyroid tissue removed during the operation or damaged due to ischemia. The risk of hypoparathyroidism varies depending on factors such as the number of parathyroids seen during surgery, the number of parathyroids removed or transplanted into the muscle during surgery, age, gender, surgeon's experience, and lymph node dissection [7].

In order to avoid the complication of hypoparathyroidism, it is recommended to see and protect at least 2 parathyroid glands during surgery, to take care not to disrupt the parathyroid blood supply by careful dissection, and to transplant the parathyroid glands with impaired blood supply into the muscle (autotransplantation) [8].

In our study, prospectively recorded data of hypoparathyroidism cases that developed after total thyroidectomies performed in our general surgery clinic within one year were retrospectively analyzed and discussed in light of the current literature.

Material and Methods

Patients who underwent total thyroidectomy in the Endocrine Surgery Unit of Ankara University General Surgery Clinic between January 2013 and January 2014 were included in the study. This study was approved by the Ethics Committee (Date: 2013-09-23, No: 14-537-13). All patients with nodular goiter and differentiated thyroid carcinoma in the pathology results were included in the study. Patients with recurrent goiter, recurrent thyroid carcinoma, additional parathyroid disease, renal failure and pathology results of thyroid malignancy other than differentiated thyroid carcinoma were excluded from the study.

Patients whose blood PTH levels fell below 10 in their postoperative follow-up and PTH returned to the normal range in their follow-up up to 6 months, were considered transient hypoparathyroidism. Those with blood Parathormone (PTH) levels below 10 after 6 months postoperatively were considered permanent hypoparathyroidism.

Prospectively recorded demographic and clinicopathological characteristics of the patients were extracted retrospectively from the hospital database.

Surgical Procedure

Operations were performed by experienced thyroid surgeons of the Endocrine surgery clinic at Ankara University General Surgery Clinic and by senior assistants under their supervision. Following preparation, the patients underwent total thyroidectomy following Kocher's necklace incision under general anesthesia. All visible parathyroid glands were preserved. Parathyroid glands, which were unintentionally removed or whose blood

supply was impaired during thyroid excision, were implanted into the ipsilateral sternocleidomastoid muscle (SCM). Informed consent form was obtained from the patients before the operation.

Biochemical Examination

PTH was measured 4 times: before the operation, at the postoperative 24th hour, at the 3rd month and at the 6th month, respectively. The PTH value was measured with the 'Electrochemiluminescence Immunometric assay' method and the 'unicel Dxl 800' device, and the normal PTH serum values were determined as 12.00-88.00 pg/ml. Total calcium values were measured before the operation, at the 6th hour postoperatively, at the 3rd and 6th months. Total calcium was measured with the 'Chemical Colorimetric Arsenazo III' method using the 'Unicel Dx800' device, and normal values were accepted as 8.0-10.5 mg/dl. Blood samples required for Ca²⁺ and PTH measurement were taken from peripheral veins.

Post-operative Management

Daily calcium measurement was performed. Intravenous or oral calcium and oral vitamin D (vit-D3) replacement was started in hypocalcemic patients. Patients whose calcium levels returned to normal values were discharged with oral calcium and vit-D3 replacement. Hypocalcemia was considered as the presence of symptoms (perioral and/or paresthesia in the hands or feet, the Chvostek sign, tetany, muscle cramps, and fatigue) or serum total calcium level below 8.0 mg/dl with/without symptoms. Oral explanations were given to the patients about hypocalcemia and its symptoms, and they were advised to apply to our outpatient clinic or the nearest health institution in case of hypocalcemia symptoms.

All biochemical analyzes were performed in Ankara University Faculty of Medicine Biochemistry Laboratory. Transient and permanent hypoparathyroidism have been identified. The patients were divided into two groups regarding their pathological assessment (Differentiated thyroid carcinoma (Group 1) and nodular goiter (Group 2)).

Statistical Analysis

Descriptive statistics were expressed as mean \pm standard deviation for normally distributed variables, median (min - max) for non-normally distributed variables, and number of cases and (%) for nominal variables. The change over time was investigated by repeated measures analysis of variance if the distribution was normal and the Friedman test if the distribution was not normal. The significance of the difference between the groups in terms of means was investigated using t-test, and the significance of the difference in terms of median values was investigated using the Mann-Whitney U test. Nominal variables were evaluated using Pearson's Chi-Square or Fisher's exact test. Results were considered statistically significant at $p < 0.05$. The analysis of the study was performed using the SPSS program (version 15.0; IBM SPSS Inc, Chicago, IL).

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The study was conducted on a total of 258 cases, 208 (80.6%) females and 50 (19.3%) males, aged between 19 and 78. According to the pathology reports, the patients were divided

Table 1. Patient Demographics

	Number of Patients / %	Age ± SD (min-max)	Female / Male
Group 1	123 (47,7%)	46,4±12,2 (19-74)	95/28
Group 2	135 (52,3%)	50,3±12,8 (22-78)	113/22
Total	258	48,5±12,7 (19-78)	208/50

Table 2. PTH (pg/ml) and Calcium (mg/dl) measurements of groups.

	Preop. Calcium	Postop. 6 th -hour Calcium	3 rd - month Calcium	6 th -month Calcium	Preop. PTH	Postop. 1 st -day PTH	3 rd - month PTH	6 th - month PTH
Group 1	9,7±3,5	8,3±0,5	8,9±0,5	9±0,4	51,8±17,3	18,7±15	38,3±14,2	43,3±14,3
Group 2	9,3±0,5	8,2±0,5	8,9±0,4	9±0,3	52,8±18,1	18,6±17,2	38,9±13,9	43,6±13,7
Total	9,51± 2,5	8,28± 0,5	8,93± 0,38	9,05± 0,32	52,36± 17,73	18,71± 16,2	38,68± 14,	43,51± 13,9

Table 3. Transient and Permanent hypoparathyroidism results of the patients.

	Differentiated Thyroid Carcinoma	Nodular Goiter	p-value
Number of Patients	123	135	
Transient Hypoparathyroidism	49 (46,2%)	57 (53,7%)	0,697
Permanent Hypoparathyroidism	1 (0,81%)	0 (0%)	0,294

into two groups as differentiated thyroid carcinoma (Group 1) and nodular goiter (Group 2). 45.6% (95) of female patients were operated for differentiated thyroid carcinoma and 54.3% (113) for nodular goiter. 56% (28) of male patients were operated for differentiated thyroid carcinoma and 44% (22) for nodular goiter (Table 1).

The variation of PTH and Calcium values of the patients in the groups over time is presented in Table 2.

Transient Hypoparathyroidism

Post-operative temporary hypoparathyroidism was detected in 106 (41.1%) of 258 patients who underwent total thyroidectomy. Forty-nine of these patients (46.2%) were diagnosed with differentiated thyroid carcinoma and 57 (53.7%) of them were nodular goiter. There was no statistically significant difference between the two groups in terms of transient hypoparathyroidism rates (p= 0.697) (Table 3).

Permanent Hypoparathyroidism

In our study, permanent hypoparathyroidism was observed in only 1 (0.4%) patient out of 258 cases after a total thyroidectomy performed within one year. The patient with permanent hypoparathyroidism had been operated for papillary thyroid carcinoma and after 6 months of follow-up, PTH levels were below 10 pg/dl. Permanent hypoparathyroidism was not detected in the follow-up of 135 patients who were operated for nodular goiter. There was no statistically significant difference between the two groups in terms of permanent hypoparathyroidism (p= 0.294) (Table 3).

Blood Calcium Levels

Pre-operative, post-operative 6th hour, postoperative 3rd month and post-operative 6th-month blood calcium levels (mg/dl) of the patients were measured. Postoperative calcium levels below 8 mg/dl were considered hypocalcemia. The mean pre-operative calcium values of the patients were 9,51± 2,5 (8,1- 10,9). The

mean post-operative 6th-hour calcium values of the patients were 8,28± 0,5 (7- 9,8). The mean post-operative 3rd- month calcium values of the patients were 8,93± 0,38 (7,4- 10,3). The mean post-operative 6th- month calcium values of the patients were 9,05± 0,32 (7,8- 10,2). Post-operative transient hypocalcemia was detected in 67 (25.9%) of 258 patients who underwent total thyroidectomy. Of these patients, 26 (38.8%) were operated for differentiated carcinoma and 41 (61.1%) for nodular goiter. There was no statistically significant difference between the two groups in terms of transient hypocalcemia rates (p= 0.91).

Discussion

Today, thyroid surgeries are frequently performed in general surgery clinics. Although careful dissection, various complications can be encountered. Clinically significant hypocalcemia following thyroid surgery is due to deterioration of parathyroid functions [3]. Hypocalcemia may occur due to devascularization, injury, mobilization, suturing or clamping of the parathyroid glands, cautery burning, or hemodilution [9]. Thomusch et al. reported that at least 2 parathyroid glands should be detected and protected in order to avoid permanent hypoparathyroidism during total thyroidectomy operations [8]. It has been proven that the function of parathyroid glands with discoloration is impaired. Parathyroid autotransplantation should only be performed in cases with impaired blood supply or suspected ischemia [10]. In such cases, as the number of autotransplantations performed in the same operation increases, the incidence of transient hypoparathyroidism increases, while the incidence of permanent hypoparathyroidism decreases [11]. Parathormone test in the first hour and first day post-operatively has proven to be reliable in detecting post-operative symptomatic hypocalcemia. There was no statistically

significant difference between measurements made in the first hour and measurements made on the post-operative first day. In addition, the reliability of early serum calcium measurements in predicting post-operative symptomatic hypocalcemia is low [12-14].

Edafe et al. reported a mean incidence of transient hypocalcemia of 27% (19-38) and a mean incidence of permanent hypocalcemia of 1% (0-3) in their meta-analysis, in which they compared the data of 115 studies. The reason why the incidence of transient hypoparathyroidism was lower in the related study may be that most of the studies in this meta-analysis used only calcium values to detect the incidence of post-operative transient hypocalcemia. The incidence of permanent hypoparathyroidism was found similar to our study. In that study, it was concluded that peri-operative PTH, pre-operative vitamin D and post-operative calcium changes were associated with post-thyroidectomy hypocalcemia. Female gender, Graves' disease, parathyroid tissue requiring autotransplantation, and unintentional parathyroid excisions were identified as risk factors [6].

Almquist et al. (2014) found permanent hypoparathyroidism in 10 of 519 patients. During the study, damaged parathyroid glands were autotransplanted in 90 patients, and none of these patients developed permanent hypocalcemia. In addition, 19% of the patients whose parathormone levels were found to be <0.7 pmol/l in the first 24 hours were found to have permanent hypoparathyroidism. In that study, it was concluded that autotransplantation protects against permanent hypoparathyroidism, and low parathormone levels in the first 24 hours are associated with a high risk for permanent hypoparathyroidism [15]. In our study, there were no eligible data to determine this hypothesis.

Kul et al. showed that serum parathormone values obtained after ipsilateral lobectomy can be used to predict postoperative hypocalcemia after total thyroidectomy [16]. Nevertheless, it has no routine usage in the management of total thyroidectomies. Akin et al. (2009) compared the complication rates of different types of thyroidectomy performed for benign and malignant thyroid diseases in a retrospective study covering data from 922 patients. Transient recurrent nerve damage was the most common complication in the benign group (2% of toxic diffuse goiters). The same complication was observed at a lower rate in the malignant group (1.5% of differentiated thyroid cancers). In the same study, the rates of permanent hypoparathyroidism in thyroidectomies performed for benign reasons were found to be higher than those operated for malignant reasons (Multinodular goiter (0.9%) > Differentiated Thyroid Cancers (0.5%)), but no statistically significant difference was found [17]. Although this study additionally included different types of thyroidectomy such as subtotal and near-total, similar results were obtained with our study. It has been determined that the incidence of permanent hypoparathyroidism is low in operations performed in experienced centers.

Conclusion

The data of our clinic on the incidence of temporary and permanent hypoparathyroidism were found to be compatible with the literature. The lack of a significant difference between the groups also indicates that the complication rates are low in

centers such as our clinic, where thyroid surgery is standardized, regardless of the main pathology. In the future, studies with larger groups and more parameters will provide clearer and more reliable results.

Study Limitation

Our study has limitations as it is retrospective and single-center. Only patients who had total thyroidectomy for nodular goiter and differentiated thyroid carcinoma were included in the study.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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