Hypoparathyroidism after total thyroidectomy:
incidence and resolution

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ABSTRACT

Background: Parathyroid hormone (PTH) levels are often measured after thyroid surgery and are used to detect patients at risk for postoperative hypoparathyroidism. However, there is a lack of consensus in the literature about how to define the recovery of parathyroid gland function and when to classify hypoparathyroidism as permanent. The goals of this study were to determine the incidence of low postoperative PTH in total thyroidectomy patients and to monitor their time course to recovery of parathyroid gland function.

Methods: We identified 1054 consecutive patients who underwent a total or completion thyroidectomy from January, 2006–December, 2013. Low PTH was defined as a PTH measurement <10 pg/mL immediately after surgery. Patients were considered to be permanently hypoparathyroid if they had not recovered within 1 y. Recovery of parathyroid gland function was defined as PTH ≥10 pg/mL and no need for therapeutic calcium or activated vitamin D (calcitriol) supplementation to prevent hypocalcemic symptoms.

Results: Of 1054 total thyroidectomy patients, 189 (18%) had a postoperative PTH <10 pg/mL. Of those 189 patients, 132 (70%) showed resolution within 2 mo of surgery. Notably, 9 (5%) resolved between 6 and 12 mo. At 1 y, 20 (1.9%) were considered to have permanent hypoparathyroidism. Surprisingly, 50% of those patients had recovery of PTH levels yet still required supplementation to avoid symptoms.

Conclusions: Most patients with a low postoperative PTH recover function quickly, but it can take up to 1 y for full resolution. Hypoparathyroidism needs to be defined not only by PTH levels but also by medication requirements.

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1. Introduction

Iatrogenic injury of the parathyroid glands is an unintended consequence of total thyroidectomy. Measuring the serum parathyroid hormone (PTH) immediately after surgery is a sensitive and specific method of assessing the function of the parathyroid glands and for identifying patients at risk for hypocalcemia [1–4]. If the postoperative PTH level is low, then administering calcium and activated vitamin D (calcitriol) can reduce the incidence of symptomatic hypocalcemia [5–10].

The incidence of a low postoperative PTH after total thyroidectomy has been highly variable in the literature, ranging between 7% [11] and 37% [1]. Part of this variability is related to the variety of methods used to define this complication [6].

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Because surgeons know that this is a potential risk of surgery, many patients are empirically treated with either calcium or calcitriol to try and avoid symptoms. Although this supplementation can help minimize symptoms for patients, it makes it difficult to determine who truly has transient hypoparathyroidism and who does not based only on calcium levels, symptoms, or the need for supplementation. One objective measure, and possibly the cleanest method for defining transient hypoparathyroidism, is to look at the PTH level immediately after surgery before beginning any supplementation. In this study, we considered anyone with a PTH < 10 pg/mL to have transient hypoparathyroidism.

Most patients with parathyroid dysfunction after thyroidectomy return to normal function within a few weeks or 1 mo of surgery [12, 13]. However, there is a lack of consensus in the literature about how to best define the recovery of parathyroid gland function. Some studies consider patients to be eparathyroid as soon as their serum PTH levels recover to at least 10 pg/mL in the absence of hypocalcemic symptoms [12, 14]. Others focus on medication administration, so recovery of parathyroid gland function is considered when the patient no longer requires therapeutic calcium or calcitriol supplementation to prevent symptoms of hypocalcemia [15, 16]. A third way to define recovery of parathyroid gland function is to determine when the serum PTH measurement is in the normal range and cessation of calcium or calcitriol supplementation occurs [2, 11, 17]. Furthermore, different time points have been used to determine when postoperative hypoparathyroidism should be classified as permanent. Some consider postoperative parathyroid gland injury to be permanent if recovery of function has not occurred within 6 mo [2, 11, 16, 18−20], whereas others define permanence at 1 y after surgery [15, 17]. The incidence of a low PTH after total thyroidectomy is highly variable. When a low PTH is found after surgery, it is also not clearly elucidated what that will mean to the patient in the long term. When can they anticipate recovery, and what are the chances that they will end up with permanent hypoparathyroidism? The goals of this study were to determine the incidence of low postoperative PTH in patients who underwent total thyroidectomy and to monitor their time course to recovery of parathyroid gland function.

2. Methods

We performed a retrospective review of the prospectively collected Endocrine Surgery Database at the University of Wisconsin Hospital and Clinics. Between January 2006 and December 2013, 1133 patients underwent total thyroidectomy or completion thyroidectomy at the University of Wisconsin. A total of 1054 patients had their serum PTH levels measured within 24 h of surgery and were included in this study. The PTH assay performed at our center has a normal range of measurement between 10 and 72 pg/mL. Low PTH was defined as a PTH measurement < 10 pg/mL immediately after surgery.

Patients were followed for 1 y. We determined that recovery of parathyroid gland function had occurred when the serum PTH was ≥ 10 pg/mL “and” the patient did not require calcitriol or >2000 mg of daily calcium supplementation to avoid symptoms of hypocalcemia. Patients were considered to be permanently hypoparathyroid if they had not recovered completely within 1 y.

Stata version 11 (Stata Corporation, College Station, TX) statistical software was used to analyze the data. Characteristics of patients with a low postoperative PTH were compared with patients with postoperative PTH ≥ 10 pg/mL using t-tests and χ² tests. In a similar manner, patients with transient hypoparathyroidism were compared with patients with permanent hypoparathyroidism. Multivariate logistic regression modeling was performed to identify independent risk factors for low postoperative PTH and for permanent hypoparathyroidism. Finally, time-to-event analysis was performed using the Kaplan−Meier method for all the patients with low PTH to determine time to resolution, using the date of complete recovery as the outcome. For this analysis, five patients were censored for missing laboratory data or missing information about symptoms or medications at their last follow-up visit. Statistical significance was defined as a P value of < 0.05.

3. Results

Of 1054 total thyroidectomy patients, 189 (18%) had postoperative PTH < 10 pg/mL. Patients with low PTH were compared with patients with a postoperative PTH measurement ≥ 10 pg/mL (Table 1). Most patients in each group were female, and they were of similar ages. Patients with postoperative PTH < 10 pg/mL had lower preoperative PTH measurements. In addition, a larger percentage of patients with low postoperative PTH underwent additional procedures such as a central neck dissection, modified radical neck dissection, or parathyroid gland autotransplantation during their thyroidectomy. Patients with PTH < 10 pg/mL after surgery also had a higher incidence of parathyroid tissue identified on their final pathology report, suggesting inadvertent removal of parathyroid tissue.

3.1. Time to resolution of low postoperative PTH

Next, we examined the time course of recovery of the 189 patients with low postoperative PTH (Figure). Most patients showed a rapid recovery of their parathyroid function. A majority of 132 (70%) showed resolution within 2 mo of surgery, and 49 of these patients had recovered within 1−2 wk of surgery. Of those patients with hypoparathyroidism at 2 mo after surgery, 28 (49%) resolved by 6 mo after surgery. Interestingly, an additional 9 (16%) resolved between 6 mo and 1 y.

3.2. Incidence of permanent hypoparathyroidism

At 1 y, 20 patients were considered to have permanent hypoparathyroidism due to the need for ongoing supplementation. Fifty percent of these patients had recovery of PTH levels to ≥ 10 pg/mL yet still required supplementation to avoid symptoms of hypocalcemia. Although their PTH level was officially in the normal range of the laboratory, it was inadequate to meet their bodies’ needs, and they still had symptoms of hypocalcemia. The permanently hypoparathyroid group represents 11% of patients with initial postoperative PTH < 10 pg/mL.
pg/mL and 1.9% of the entire cohort of patients undergoing thyroidectomy.

### 3.3. Risk factors for low postoperative PTH and permanent hypoparathyroidism

Patients with low postoperative PTH who showed recovery of parathyroid gland function within 1 y were compared with patients with permanent hypoparathyroidism (Table 2). Patients with parathyroid gland function recovery had lower preoperative PTH measurements. Permanently hypoparathyroid patients had lower 2-wk calcium levels and a higher incidence of parathyroid tissue identified in the thyroid specimen on the final pathology report.

On multivariate logistic regression modeling, we found that patients who received autotransplantation of parathyroid tissue during surgery were more likely have low PTH immediately after surgery (odds ratio [OR] = 2.6; 95% confidence interval [CI], 1.8–3.8). In addition, patients with the identification of parathyroid tissue on the final pathology report, suggesting inadvertent removal of parathyroid tissue, were more likely to have postoperative PTH <10 pg/mL (OR = 2.2; 95% CI, 1.5–3.3). The only independent risk factor for permanent hypoparathyroidism was parathyroid tissue on pathology report (OR = 3.6, 95% CI, 1.1–11.5). Age, gender, neck dissection, thyroiditis, and malignancy were not independently associated with low postoperative PTH or permanent hypoparathyroidism. The validity of this multivariate logistic regression model was tested using the likelihood ratio chi-square test, and the P value for the model was 0.03.

### 4. Discussion

Iatrogenic injury of the parathyroid glands resulting in low postoperative PTH levels is a common complication of total thyroidectomy. In our study, 18% of patients had a postoperative PTH <10 pg/mL, but most of these patients showed recovery of parathyroid gland function within 2 mo of surgery. Only 1.9% of the entire cohort was considered to have permanent hypoparathyroidism as indicated by the ongoing need for calcium or calcitriol supplementation 1 y after surgery. The 18% incidence of a low postoperative PTH in this study falls within the transient hypoparathyroidism incidence range of 7% [11] to 37% [1] that has been reported in the literature. This variability in incidence can be attributed to the varying definitions used to classify patients as being transiently hypoparathyroid after total thyroidectomy. Thomusch et al. [11] assumed postoperative hypoparathyroidism when calcium or vitamin D therapy was required to treat clinical symptoms of tetany, but serum laboratory values were not considered. This study’s definition failed to include asymptomatic patients who could have had a serum PTH <10 pg/mL, and this could account for the low reported incidence rate of
7%. McCullough et al. [1] performed a study in which they calculated the incidence of low postoperative PTH using the same definition as our study, but their calculated incidence of 37% was much higher than this study’s incidence of 18%. However, McCullough et al. had a sample size of only 72 patients, whereas this study included 1054 total thyroidectomy patients.

Permanent hypoparathyroidism is most commonly defined as failure of the parathyroids to regain normal function by 6 mo after surgery. Interestingly, 5% of patients with low postoperative PTH resolved 6–12 mo after surgery in our study. For this reason, we decided that 1 y was the most appropriate time point for defining permanent hypoparathyroidism, which 1.9% of total thyroidectomy patients developed in our study. Using an earlier time point could result in classifying some patients as permanently hypoparathyroid when they could still show resolution of their condition. For example, Chow et al. [2] found that 2.8% of patients developed permanent hypoparathyroidism, as defined at 6 mo after surgery, even though this study used the same criteria for parathyroid gland function recovery as our study.

Other differences seen in the rate of permanent hypoparathyroidism in different studies are in part due to the discrepancy in definitions that were used to determine recovery of parathyroid gland function. To exemplify, Al Dhahri et al. [14] defined recovery as a serum PTH ≥10 pg/mL in the absence of hypocalcemic symptoms. However, Nawrot et al. [17] defined recovery as cessation of calcium and calcitriol supplementation. Our study considered both PTH levels “and” medication administration, so a patient would only be euparathyroid once they no longer had symptoms or required supplemental calcium or calcitriol in addition to having a serum PTH ≥10 pg/mL. Given our stringent definition, our rate of permanent hypoparathyroidism was 1.9%. If we had only used PTH levels to define permanent hypoparathyroidism, our rate would have been only 0.9%. We also found that by 1 y, patients had determined how much calcium or calcitriol they needed to avoid symptoms, and most did not complain of any symptoms of hypocalcemia. Therefore, it is important to not only ask about their symptoms but to examine medication lists as well.

Our investigation also examined risk factors for parathyroid gland complications after total thyroidectomy. We found that the only independent risk factor for developing permanent hypoparathyroidism was parathyroid tissue present on pathology report, which indicated inadvertent removal of parathyroid tissue. Age, gender, neck dissection, thyroiditis, hyperthyroidism, and malignancy were not independently associated with low postoperative PTH or permanent hypoparathyroidism, which is likely a reflection of the fact that the surgeons involved in this study were all high-volume surgeons with experience operating on higher risk patients.

It is interesting to note that on bivariate analysis, the patients who developed permanent hypoparathyroidism had an average preoperative PTH that was higher than the transiently hypoparathyroid patients (60.3 versus 41.1 pg/mL, P = 0.01). However, both these measurements fall within the normal PTH range, suggesting that this difference is probably not clinically significant. It is possible that these patients were more likely to have vitamin D deficiency preoperatively causing this higher average PTH, but because vitamin D levels
are only clinically indicated when PTH levels are above the normal range, most patients did not have these data available to analyze. Postoperatively, patients were all treated with vitamin D supplementation; so long-term, any baseline preoperative vitamin D deficiency should have been corrected for.

There are a few limitations to this study. First, it should be noted that this was a retrospective study. Still, we used an institutional database that was prospectively collected. In addition, the data were collected from a single university hospital, so it may be subject to institutional bias. Nevertheless, because of the large study sample including 1054 patients, it is likely that these results can be generalized to a larger population. Also, at the institution where this study was performed, patients are supplemented with calcium and calcitriol based on their serum PTH measurements after surgery. Some of these patients may not necessarily need supplementation to prevent hypocalcemic symptoms. Therefore, we could not accurately examine the incidence of symptomatic transient hypoparathyroidism. Finally, the time to resolution of parathyroid gland function is directly proportional to how often PTH levels are measured. As time passes after surgery, laboratory tests and clinic visits become more spaced out, so the reported time to recovery could be longer than the true time to recovery.

5. Conclusions

In conclusion, low serum PTH is a common occurrence after total thyroidectomy, but the vast majority of patients showed parathyroid gland function recovery within 2 mo of surgery. Only 1.9% of patients undergoing total thyroidectomy developed permanent hypoparathyroidism, defined by a serum PTH ≤10 pg/mL or the need to continue calcium or calcitriol supplementation to prevent hypocalcemic symptoms 1 y after surgery. In the literature, there is a wide range of reported incidences of transient and permanent postoperative hypoparathyroidism. A consensus needs to be reached about how to best define these complications. This study suggests that medication administration needs to be considered in addition to PTH measurements because 50% of patients with permanent hypoparathyroidism had recovery of PTH levels to >10 pg/mL yet still required supplementation to avoid symptoms of hypocalcemia. Furthermore, 12 mo may be the most appropriate time point for defining hypoparathyroidism as permanent because 5% of patients with low postoperative PTH resolved 6–12 mo after surgery.

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Disclosure

No disclosures to report.

REFERENCES


