SAME-DAY DISCHARGE AFTER TOTAL THYROIDECTOMY:
THE VALUE OF 6-HOUR SERUM PARATHYROID HORMONE
AND CALCIUM LEVELS

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Abstract: Background. The purpose of this study was to determine whether patients who undergo total thyroidectomy will have postoperative hypocalcemia develop when they reach the critical 6-hour serum levels defined as parathyroid hormone (PTH) ≥28 ng/L and simultaneous corrected calcium ≥2.14 mmol/L.

Methods. This was a prospective study involving 70 consecutive total thyroidectomy patients. There were 51 women and 19 men involved in the study. The mean age was 49.3 years (range, 21–76 years). Patients who had completion thyroidectomy or neck dissections were excluded. Patients undergoing parathyroidectomy at the time of thyroidectomy were also excluded. PTH and corrected calcium levels were measured postoperatively at 6, 12, and 20 hours.

Results. Hypocalcemia developed in 24% (17 of 70) of the patients. Of the 53 patients who remained normocalcemic, 68% (36 of 53) reached the 6-hour critical level. None of the hypocalcemic patients (0 of 17) attained the 6-hour critical level (chi-square test p < .0001). This translates into a specificity of 100% (95% confidence interval [CI], 80.5% to 100%) and a positive predictive value of 100% (95% CI, 90.1% to 100%).

Conclusions. The simultaneous evaluation of PTH and corrected calcium levels 6 hours after thyroidectomy allows for an accurate prediction of the trend of serum calcium. This study enables us to confidently consider same-day discharge for most of our thyroidectomy patients. © 2004 Wiley Periodicals, Inc.

Keywords: calcium; parathyroid hormone; hypocalcemia; hypoparathyroidism; postoperative calcium protocol; thyroidectomy

The search for a blood test that identifies patients who will become hypocalcemic after total thyroidectomy and those who will remain normocalcemic in the early postoperative period has evolved since the late 1980s.1–7 Different approaches, including monitoring of serum-corrected calcium slopes at 6, 12, and 20 hours and at 8, 14, and 20 hours postoperatively, have proven to be effective.2,5 Others have advocated sending patients home on prophylactic calcium supplementation or with prescriptions for elemental calcium to be filled if symptoms of hypocalcemia develop.4,6 The incorporation of parathyroid hormone (PTH) levels as a monitor for hypoparathyroidism leading to hypocalcemia has been the next step in the evolution of this field of research. Recent studies have validated the role of both PTH levels
alone and in conjunction with serum-corrected calcium levels as a monitor for post-thyroidectomy hypocalcemia.3,7–10

Serum-calcium monitoring for hypocalcemia is often the primary reason to detain patients in the hospital once the risk of post-thyroidectomy hematoma and airway obstruction have subsided.4–6,11 Because airway issues are unlikely to occur more than 8 hours after surgery, the ideal post-thyroidectomy blood test is one that is able to accurately identify patients who will remain normocalcemic within such a time period. The test must also be valid and applicable for most patients undergoing total thyroidectomy to remain practical and have a significant impact on patient care. To be of clinical use, the test must have a high sensitivity and specificity for detecting hypocalcemia to ensure low risk for the patient being discharged home. Such a test would result in same-day surgeries, fewer blood tests, significantly lower hospital costs, and greater patient satisfaction.

It was recently reported that patients reaching the critical level for both corrected calcium (≥2.14 mmol/L or 8.56 mg/dl) and PTH (≥28 ng/L) at 12 hours after total thyroidectomy were not at risk for hypocalcemia developing.7 As a result, blood testing ceased in most of these patients after reaching the 12-hour critical level. The discharge of these patients on the same day as the surgery failed to materialize, because laboratory results were obtained 12 1/2 to 13 hours after the thyroidectomy at a time that was impractical to discharge patients home. The purpose of this study was to evaluate the possibility of performing the laboratory testing earlier to allow patients to be discharged home without spending the night in hospital. More specifically, the objective was to evaluate whether patients reaching the 6-hour critical level, defined as both PTH ≥28 ng/L and simultaneous corrected calcium ≥2.14 mmol/L, were at risk of hypocalcemia developing.

**MATERIALS AND METHODS**

A prospective study involving 73 consecutive patients who had total thyroidectomy was conducted at a university teaching hospital. Ethics approval was obtained from the research ethics boards at the participating hospital, and written informed consent was obtained from each subject. Three patients were eliminated from the study, because the 6-hour PTH was not measured. Patients having completion thyroidectomy or neck dissections were excluded. Patients undergoing parathyroidectomy at the time of thyroidectomy were also excluded. There were 51 women and 19 men involved in the study. The mean age was 49.3 years (range, 21–76 years).

**FIGURE 1.** Algorithm for the calcium management of post-thyroidectomy patients.

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<td>0</td>
</tr>
<tr>
<td>No</td>
<td>17</td>
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</table>

* Criterion: both 6h Corrected Calcium ≥ 2.14 mmol/L and 6h PTH ≥ 28 ng/L

Sensitivity = 67.9% (95% CI: 55.4% - 80.1%)

Specificity = 100% (95% CI: 80.5% - 100%)

Positive predictive value = 100% (95% CI: 90.1% - 100%)

Negative predictive value = 50% (95% CI: 33.2% - 66.8%)

**FIGURE 3.** Statistical analysis.
Blood for serum calcium, albumin, and phosphate was drawn at 6, 12, and 20 hours postoperatively and then twice daily thereafter. Serum PTH was measured at 1, 6, 12, and 20 hours postoperatively and then twice daily. Serum magnesium levels were drawn at 12 hours and then daily thereafter. Normal values for serum calcium ranged from 2.12 to 2.62 mmol/L or 8.48 to 10.48 mg/dL. The serum calcium level was corrected for measured abnormal serum albumin levels. The normal values for PTH were 10 to 70 ng/L. PTH was measured with the Roche Elecsys System 2010 electrochemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany), which measures both the N-terminal fragment and C-terminal fragment of the hormone. The coefficient of variance of this assay for values >6 ng/L is <20%.

Patients were divided into two groups, those remaining normocalcemic and those who had hypocalcemia develop requiring intervention. Hypocalcemia requiring intervention was defined by conservative criteria to be as inclusive as possible. Patients were considered hypocalcemic as a result of meeting one of the following laboratory or clinical conditions: first, a serum-corrected calcium level $\leq 1.90$ mmol/L; second, the development of signs and symptoms of hypocalcemia, such as perioral numbness, paresthesias of the upper extremity digits, and a positive Trousseau’s sign. These patients were started on one of the following regimens on the basis of serum-corrected calcium levels: intravenous calcium, oral calcium, oral vitamin D, or a combination of the three. Patients on preoperative calcium or vitamin D were continued...
on their usual regimen postoperatively. Abnormalities in magnesium levels were corrected immediately on detection. Patients were considered normocalcemic if they did not reach the criteria requiring intervention within a period of 1 month after surgery.

Same-day surgery was defined by both length of stay and whether the patient remained in the hospital overnight. In this study, patients remaining in the hospital for 23 hours were not considered as having same-day surgery. Rather a more stringent criterion of whether a patient remained overnight in the hospital was used.

A chi-square test was used to evaluate for statistically significant associations between patients remaining normocalcemic, and the 6-hour serum calcium and PTH criteria.

RESULTS

After analysis of the data, an algorithm was developed for the management of post-thyroidectomy patients (Figure 1). Hypocalcemia developed in 24% (17 of 70) of total thyroidectomy patients (Figure 2). Of the 76% (53 of 70) patients who remained normocalcemic, 68% (36 of 53) reached the 6-hour critical level criteria. None of the hypocalcemic patients (0 of 17) reached the critical PTH/corrected calcium level at 6 hours (chi-square test $p < .0001$). This translates into a specificity of 100% (95% confidence interval [CI], 80.5% to 100%) and a positive predictive value (PPV) of 100% (95% CI, 90.1% to 100%) (Figure 3).

The 17 patients who remained normocalcemic but did not reach the critical level had 6-hour serum calcium and PTH levels that were dispersed (Figure 4). In addition, 6 of the 17 patients not attaining the 6-hour critical level did reach the critical level at 12 hours. Of the 17 patients who had hypocalcemia requiring intervention develop, none of them met both critical serum-corrected calcium and PTH levels at 6 hours (Figures 5, 6, and 7). Another important finding was that seven of seven patients with serum 1-hour PTH levels $\leq 8$ ng/L went on to have hypocalcemia develop.

The mean hospital stay for all patients undergoing total thyroidectomy was 48 hours. When patients were divided into normocalcemic and hypocalcemic groups, the mean hospital stay was 36 hours and 85 hours, respectively. The total cost to the hospital for all patients was $286,300 plus $130 for blood testing (Figure 8).

DISCUSSION

Hypoparathyroidism is a common cause of transient and permanent hypocalcemia after total thyroidectomy. $^{6,11-14}$ It occurs as often as 30% of the time and can be attributed to injury, removal, or devascularization of the parathyroid glands. $^{6,11,13,15}$ Because PTH has a half-life of only 1 to 4 minutes, any insult leading to an impairment in its secretion leads to an immediate decline in serum levels. $^{16-18}$ This results in a reduction in serum calcium levels, because PTH is the major regulator of serum calcium. $^{18}$

Serum calcium homeostasis by PTH occurs through a variety of mechanisms; it promotes distal tubule calcium reabsorption, bone resorption, and $1,25(OH)_2$D-mediated intestinal calcium absorption. $^{18}$

Hypoparathyroidism may be a common cause of reduced serum calcium levels; however, other etiologies are important in the pathogenesis of post-thyroidectomy hypocalcemia. In our study, nine (53%) of 17 and 10 (59%) of 17 patients who had hypocalcemia develop had PTH levels within the normal range at 1 and 6 hours, respectively (Figure 9). Therefore, other mechanisms such as reduced stores of vitamin D and hemodilution and not just hypoparathyroidism are responsible for postoperative hypocalcemia. $^{8,13,14,19,20}$ As a consequence, the use of PTH levels alone as a predictor of post-thyroidectomy hypocalcemia will miss a significant number of patients with hypocalcemia (Figure 9).

Patients who had total thyroidectomy in a pre-operative state of negative calcium balance may have postoperative hypocalcemia develop while maintaining normal to high serum levels of PTH. This phenomenon occurs because of the inability

\[
\text{Cost of stay under 12 hours} = \$1225
\]

\[
\text{Cost of stay for 24 hours} = \$2045
\]

Calculations

A. Hospital Stay

Mean hospital stay of 48 hours (not including blood testing) 

\[ \$2045 + \$2045 = \$4090 \]

\[ \div 70 \text{ patients} \]

\[ = \$286,300 \]

B. Blood Tests

Cost of serum calcium, albumin, phosphate, magnesium, and PTH over 48 hour period:

\[ (5 \times \$1.50) + (5 \times \$1.50) + (5 \times \$2.00) + (3 \times \$3.00) + (6 \times \$16.00) \]

\[ = \$130 \]

FIGURE 8. Hospital costs for 70 patients who had total thyroidectomy.
of PTH to mobilize calcium secondary to a preexisting vitamin D deficiency. Patient 16 had PTH levels as high as 131 at 6 hours and still had postoperative hypocalcemia develop (Figure 9). This patient did not have reduced serum calcium levels as a result of hypoparathyroidism. The cause of the hypocalcemia is unrelated to PTH secretion and more likely related to other etiologies such as low preoperative vitamin D stores or postoperative hemodilution. In contrast, patient 4 had 1-hour and 6-hour PTH levels of 3 and 5, respectively, and a 6-hour calcium level at the upper limit of normal. The ensuing hypocalcemia that resulted in this patient is more likely to be a result of hypoparathyroidism.

Because the etiology of post-thyroidectomy hypocalcemia is variable and possibly multifactorial, it is unlikely that a single blood test can be an accurate indicator or consistent predictor of future calcium levels. It was this reality that led to experimentation with two blood tests used concomitantly to predict calcium trends. Initially, a 12-hour serum PTH (≥28 ng/L) and corrected calcium critical level (≥2.14 mmol/L) was described in a study involving 54 patients. The critical level was successful at identifying patients who were normocalcemic at 12 hours, because none of the patients with hypocalcemia reached the critical level. This finding resulted in fewer blood tests and hospital stays that were less than 24 hours. However, patients remained in the hospital overnight because 12-hour blood tests and results were obtained at night when discharge was impractical. Therefore, the need for the 6-hour critical level became apparent.

This study demonstrates that all of the 17 patients who had hypocalcemia develop were below the 6-hour critical level (PTH ≥28 ng/L and corrected calcium ≥2.14 mmol/L) (Figure 5). The results confirm that patients reaching the critical level are not at risk for postoperative hypocalcemia with a specificity and positive predictive value of 100% (95% CI, 80.5% to 100% and 90.1% to 100%, respectively). Because all of the patients who were above the cutoff level at 6 hours remained normocalcemic, the need for further calcium monitoring in these patients is unwarranted. Because the risk of post-thyroidectomy hematoma and airway risks are unlikely after 8 hours, normocalcemic patients with no other postoperative complications can be sent home after a careful examination at such time.

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FIGURE 9. Parathyroid hormone and calcium levels of hypocalcemic patients at 1 and 6 hours.

FIGURE 10. Savings for institutions performing 100 total thyroidectomies annually.
The 6-hour post-thyroidectomy critical PTH and corrected calcium levels provide numerous benefits for both the patient and health-care institution. The patient will be more comfortable in the early postoperative period as a result of fewer blood tests. Moreover, middle-of-the-night testing interrupting sleep will be avoided in most cases. Same-day discharges will be a reality for many patients who will be able to spend the first postoperative night in the comfort of their own home. Fewer blood tests translate into cost savings as a result of a reduction in laboratory expenditures and decreased workloads for the nursing staff, physicians interpreting the results, and laboratory technicians (Figure 8). Finally, hospital savings resulting from same-day surgeries are significant in centers performing total thyroidectomy surgery (Figure 10). On average, normocalcemic patients remain in the hospital for 36 hours at an estimated cost of $9270. Discharging patients at 8 hours allows for savings of $2045 per patient (Figure 10). Assuming a transient hypocalcemia rate of 24%, institutions performing 100 total thyroidectomies per year can expect savings as high as $106,340 annually (Figure 10).

The management of patients with total thyroidectomy is based on the newly designed algorithm (Figure 1). All patients are sent home with specific instructions describing the signs and symptoms of hypocalcemia along with appropriate course of action. Data analysis examining the cost savings realized because of the implementation of the 6-hour serum calcium and PTH protocol is underway.

CONCLUSIONS

The conclusions drawn from this study are the following:

1. Serum-corrected calcium levels when combined with serum PTH levels at 6 hours are an accurate predictor of patients who will remain normocalcemic.
2. Patients reaching a 2.14 mmol/L calcium level and a 28 ng/L PTH level at 6 hours are not at risk of hypocalcemia developing (p < .0001).
3. The new protocol enables us to confidently consider same-day discharge for most of our patients with a total thyroidectomy.
4. This will have an impact on most patients undergoing total thyroidectomy surgery who remain normocalcemic (76% in this study) and will ultimately lead to improved patient satisfaction and significant savings for the health-care system.

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