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## A postoperative parathyroid hormone-based algorithm to reduce symptomatic hypocalcemia following completion/total thyroidectomy: A retrospective analysis of 591 patients ☆

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### ABSTRACT

**Background:** An institutional protocol for selective calcium/calcitriol supplementation after completion/total thyroidectomy was established based on the 4-hour postoperative parathyroid hormone level. The aim of this study was to evaluate the outcomes of this protocol 5 years after implementation.

**Methods:** All patients who underwent completion/total thyroidectomy from January 2012 to December 2016 were reviewed. Predictors of a 4-hour parathyroid hormone level <10 pg/mL and symptomatic hypocalcemia were assessed.

**Results:** Of 591 patients, 448 (76%) had a 4-hour parathyroid hormone  $\geq 10$ , 72 (12%) had a 4-hour parathyroid hormone of 5–10, and 71 (12%) had a 4-hour parathyroid hormone <5. Hypocalcemic symptoms were infrequent (30/448, 7%) if the 4-hour parathyroid hormone was  $\geq 10$ ; 56% (40/71) of those with a 4-hour parathyroid hormone <5 reported symptoms. With 4-hour parathyroid hormone of 5–10, symptoms were reported in 32 of 72 (44%) patients; supplementation at discharge included calcium ( $n=55$ , 76%), calcium and calcitriol ( $n=12$ , 17%), or none ( $n=5$ , 7%). Ten patients subsequently received calcitriol for persistent symptoms. On multivariate analysis, predictors of 4-hour parathyroid hormone <10 included incidental parathyroidectomy, malignancy, and thyroiditis; predictors of hypocalcemic symptoms included age <55 and 4-hour parathyroid hormone <10.

**Conclusion:** After completion/total thyroidectomy, patients with a 4-hour parathyroid hormone  $\geq 10$  can be safely discharged without routine supplementation. The addition of calcitriol to calcium supplementation should be strongly considered for patients with a 4-hour parathyroid hormone of 5–10.

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### Introduction

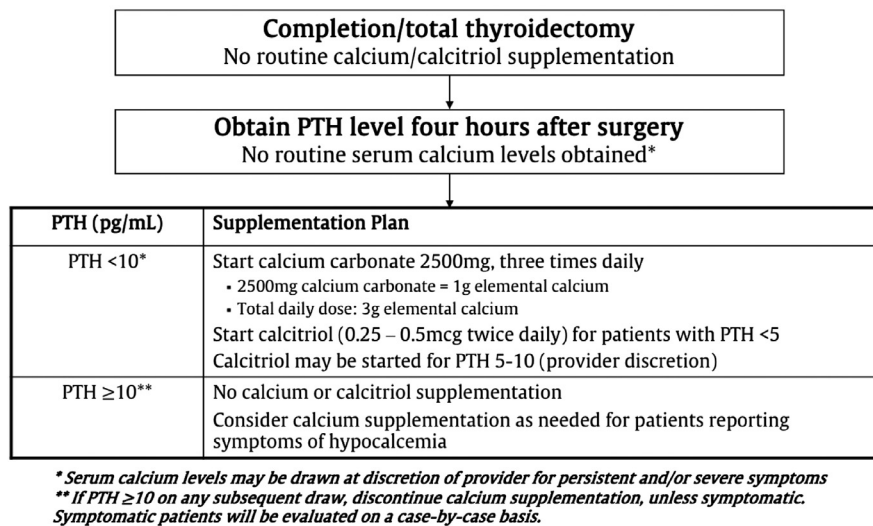
Hypocalcemia is the most common complication following completion/total thyroidectomy, and transient hypocalcemia has been reported in 10% to 40% of patients.<sup>1–6</sup> Postoperative hypocalcemia results from hypoparathyroidism caused by unintentional resection, manipulation, or devascularization of the parathyroid glands. Post-thyroidectomy hypocalcemia is typically transient; however, in up to 10% of patients, hypoparathyroidism may be permanent, defined as lasting longer than 6 months.<sup>1–3,6,7</sup>

The optimal algorithm for management of postoperative calcium supplementation to prevent symptomatic hypocalcemia has been debated, because the nadir for serum calcium may occur 48–72 hours postoperatively and the majority of patients are discharged the same day or within the first 24 hours of surgery.<sup>8</sup> Some authors have advocated for routine calcium supplementation for all patients given the risks of hypocalcemia and the relatively low cost of oral calcium supplements.<sup>9–11</sup> However, routine supplementation is likely not necessary for most patients, and may lead to oversupplementation resulting in hypercalcemia and the associated costs of potentially unnecessary laboratory testing and follow-up visits.<sup>4,12</sup> Studies have examined the use of serum calcium and/or parathyroid hormone (PTH) levels to identify patients most at risk for hypocalcemia to guide selective use of calcium supplementation, and postoperative PTH levels have been reported to be an accurate predictor of postoperative hypocalcemia.<sup>1–6,13–17</sup>

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**Fig 1.** Institutional protocol for selective calcium and calcitriol supplementation following completion/total thyroidectomy.

However, there has been no consensus on the most appropriate timing or threshold PTH level that would predict symptomatic hypocalcemia and the need for postoperative supplementation.

In a prospective randomized study, we previously demonstrated that a PTH level drawn on the first postoperative day (POD1) was a highly specific predictor of clinically significant postoperative hypocalcemia and developed an institutional protocol for selective postoperative calcium and calcitriol supplementation based on these data.<sup>1</sup> We then validated our protocol and documented similar accuracy of a POD1 PTH level and a 4-hour postoperative PTH level <10 pg/mL in predicting an increased risk of symptomatic hypocalcemia.<sup>2</sup> The initial study was novel in its design as a prospective randomized trial, but both cohorts were relatively small (143 and 77 patients, respectively). Therefore, the aims of this study were to (1) evaluate the performance of our standardized calcium supplementation protocol in the treatment of patients who underwent completion/total thyroidectomy at risk for hypocalcemia in a large cohort, (2) further refine the protocol for patients with a 4-hour PTH <10 pg/mL, and (3) identify predictors of 4-hour PTH levels <10 pg/mL, the development of symptomatic hypocalcemia, and permanent hypoparathyroidism.

## Methods

This is a retrospective review of a single-institution prospectively maintained thyroid surgery database of all adult patients who underwent completion/total thyroidectomy from January 2012 to December 2016. This study was approved by the institutional review board at the Medical College of Wisconsin and is in compliance with HIPAA policies. Patients who underwent planned parathyroidectomy for a concurrent diagnosis of hyperparathyroidism at the time of thyroidectomy were excluded ( $n=96$ ). Prior to surgery, patients had serum calcium and 25-OH-vitamin D levels drawn, and vitamin D supplementation was recommended for the majority of patients with low preoperative levels (normal range: 32–100 ng/mL). Thyroidectomy was performed by 1 of 4 fellowship-trained endocrine surgeons. Devascularized parathyroid glands identified at the time of surgery were routinely autotransplanted in the sternocleidomastoid or sternohyoid muscle. The operative details for total thyroidectomy and parathyroid autotransplantation have been previously described.<sup>1</sup> A PTH level was obtained 4 hours postoperatively, and this level was used to guide calcium and calcitriol supplementation (Fig 1).

Following completion/total thyroidectomy, patients were routinely admitted for observation overnight; patients were assessed for symptoms of hypocalcemia, defined as perioral or acral paresthesias or muscle cramps in the extremities that improved with calcium supplementation. They were typically called within 24–48 hours after discharge by the surgical team to assess their recovery and to evaluate for symptoms of hypocalcemia. They were also re-counseled on symptom recognition and the use of calcium supplementation as needed until symptoms resolved. At the time of the first postoperative clinic visit (typically at 5–10 days), serum calcium and PTH levels were obtained for patients with a 4-hour PTH level <10 pg/mL and for those reporting persistent symptoms with a 4-hour PTH level ≥10 pg/mL. Routine postoperative labs were not obtained for asymptomatic patients with a 4-hour PTH ≥10 pg/mL. For those on supplementation, patients who remained asymptomatic and whose PTH levels improved (compared with the 4-hour PTH) were weaned from calcium and calcitriol supplementation according to our previously described protocol.<sup>1,2</sup>

Demographic and clinical data included age, sex, preoperative and postoperative laboratory values (serum calcium, 25-OH-vitamin D, and PTH), extent of surgery (completion vs. total thyroidectomy, performance of a central compartment neck dissection [CCND], and parathyroid autotransplantation), and final pathology (gland weight, histopathology, and presence of parathyroid tissue). A diagnosis of thyroid malignancy was made if a malignancy of any size was documented on final pathology. CCNDs were performed for prophylactic and therapeutic indications and included both unilateral and bilateral dissections.

Calcium with or without calcitriol supplementation at the time of discharge, as well as any changes to the supplementation regimen during the postoperative period, was recorded. Duration of calcium and calcitriol supplementation was evaluated to determine the rates of transient and permanent hypoparathyroidism. For the purposes of this study, transient hypoparathyroidism was defined as recovery of PTH level (≥10 pg/mL) or normal serum calcium levels in the absence of hypocalcemic symptoms and no calcium supplementation by 6 months postoperatively. Permanent hypoparathyroidism was defined as a PTH level <10 pg/mL associated with hypocalcemic symptoms and the need for ongoing calcium supplementation >1200 mg per day (the recommended daily intake of elemental calcium),<sup>18</sup> with or without calcitriol supplementation for ≥6 months postoperatively.

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