A clinical pathway for the postoperative management of hypocalcemia after pediatric thyroidectomy reduces blood draws.

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Abbreviations: PTC, papillary thyroid cancer; PTH, parathyroid hormone; MEN2a, Multiple Endocrine Neoplasia type 2a; PTEN, Phosphatase and tensin homolog; MNG, multinodular goiter; IRB, Institutional Review Board; iPTH, intact parathyroid hormone.

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ABSTRACT:

OBJECTIVES: Postoperative calcium management is challenging following pediatric thyroidectomy given potential limitations in self-reporting symptoms and compliance with phlebotomy. A protocol was created at our tertiary children's institution utilizing intraoperative parathyroid hormone (PTH) levels to guide electrolyte management during hospitalization. The objective of this study was to determine the effect of a new thyroidectomy postoperative management protocol on two primary outcomes: (1) the number of postoperative calcium blood draws and (2) the length of hospital stay.

STUDY DESIGN: Institutional review board approved retrospective study (2010-2016).

METHODS: Consecutive pediatric total thyroidectomy and completion thyroidectomy ± neck dissection cases from 1/1/2010 through 8/5/2016 at a single tertiary children's institution were retrospectively reviewed before and after initiation of a new management protocol. All cases after 2/1/2014 comprised the experimental group (post-protocol implementation). The pre-protocol control group consisted of cases prior to 2/1/2014. Multivariable linear and Poisson regression models were used to compare the control and experimental groups for outcome measure of number of calcium lab draws and hospital length of stay.

RESULTS: 53 patients were included (n=23, control group; n=30 experimental group). The median age was 15 years. 41 patients (77.4%) were female. Postoperative calcium draws decreased from a mean of 5.2 to 3.6 per day post-protocol implementation (Rate Ratio = 0.70, p

< 0.001), adjusting for covariates. The mean number of total inpatient calcium draws before protocol initiation was 13.3 (±13.20) compared to 7.2 (±4.25) in the post-protocol implementation group. Length of stay was 2.1 days in the control group and 1.8 days post-protocol implementation (p = 0.29). Patients who underwent concurrent neck dissection had a longer mean length of stay of 2.32 days compared to 1.66 days in those patients who did not undergo a neck dissection (p = 0.02). Hypocalcemia was also associated with a longer mean length of stay of 2.41 days compared to 1.60 days in patients who did not develop hypocalcemia (p<0.01).

CONCLUSIONS: The number of calcium blood draws was significantly reduced after introduction of a standardized protocol based on intraoperative PTH levels. The hospital length of stay did not change. Adoption of a standardized postoperative protocol based on intraoperative PTH levels may reduce the number of blood draws in children undergoing thyroidectomy.

KEY WORDS: PTC, papillary thyroid cancer; PTH, parathyroid hormone, postoperative hypocalcemia, pediatric thyroidectomy, hospital length of stay

LEVEL OF EVIDENCE: 2c

Introduction

Management of pediatric thyroid disorders, particularly those requiring total thyroidectomy with or without neck dissection presents a unique set of challenges. Children diagnosed with a thyroid nodule carry a greater risk of malignancy compared to adults (22% vs. 14%) [1] and the incidence of pediatric thyroid cancer is increasing [2]. With a female to male ratio of 4-5:1, thyroid cancer is the second most common cancer among pediatric females [1, 3].

In 2015, the American Thyroid Association (ATA) published management guidelines for children with thyroid nodules and differentiated thyroid cancer [4]. Children with papillary thyroid cancer (PTC) are more likely to have regional lymph node involvement, extrathyroidal extension, and pulmonary metastasis. Surgical resection and radioactive iodine therapy have often produced favorable outcomes within this patient population [1]. The 2015 ATA pediatric thyroid guidelines recommend a total thyroidectomy for all sized PTC lesions; this is in contrast to the recommendation of a lobectomy for adult patients with certain low risk lesions [5]. This is based on data showing an increased incidence of bilateral and multifocal disease as well as an increased risk for recurrence and subsequent second surgical procedures when less than a near total thyroidectomy is performed in children. The guidelines also recommend surgical removal of hyperfunctioning nodules in children [4].

The ATA guidelines do not describe the postoperative management of pediatric thyroidectomy patients. There is a paucity of literature describing calcium management specifically in the pediatric population. In the adult thyroidectomy literature, multiple reports have demonstrated utility of an immediate postoperative PTH level in the subsequent electrolyte management, although management remains varied from institution to institution [6, 7].

Transient hypocalcemia is believed to be caused by transient disruption of the blood supply to the parathyroid glands or removal of one or more glands. Hypocalcemia is the most common complication after thyroidectomy surgery and is often the cause of prolonged hospital stay and significant morbidity [8]. The largest series of pediatric thyroidectomy patients demonstrate transient hypocalcemia rates ranging from 13% to 47% and permanent hypocalcemia rates of 0.9% to 8% [8-11]. Pediatric patients with temporary or permanent hypoparathyroidism have more than twice as many laboratory assessments during the first postoperative year compared to patients with normal postoperative parathyroid function [11].

Freire *et al.* evaluated the diagnostic accuracy of intraoperative PTH to predict the risk of post thyroidectomy hypocalcemia in children in a prospective longitudinal cohort study [10]. In this study, normocalcemic patients had a 2.5 day average duration of hospitalization while the length of stay for hypocalcemic patients was 7 days ($p<0.5$). This study suggested a 5 minute postoperative PTH of 16 pg/mL predicted hypocalcemia with a sensitivity of 80%, specificity of 100%, and positive predictive value (PPV) of 100%.

Postoperative hypocalcemia surveillance and management is challenging following pediatric thyroidectomy because symptoms may not be self-reported and phlebotomy may be more challenging in a child. While mild symptoms of hypocalcemia can range from perioral and peripheral paresthesias, severe symptoms can include life threatening tetany and convulsions. Our institutional postoperative thyroidectomy management was highly variable between providers including surgeons, endocrinologists, and hospitalists. Specific variability included the frequency and type of calcium monitoring (ionized calcium, total serum calcium, or both), parathyroid hormone monitoring, and the use of intravenous or oral calcium supplements. Thus, a standardized protocol for postoperative management of total or completion thyroidectomy patients was developed and implemented by a multi-disciplinary team beginning in February 2014. The new protocol included an intraoperative PTH level to help standardize electrolyte management during the hospitalization.

The objective of this study was to determine the effect of a new pediatric thyroidectomy postoperative electrolyte management protocol on two primary outcomes: (1) number of postoperative calcium blood draws and (2) length of hospital stay.

Methods

Study Sample

Institutional Review Board approval at Seattle Children's Hospital was obtained. Consecutive total thyroidectomy (and completion thyroidectomy) cases with or without neck dissection from 1/1/2010 through 8/5/2016 were queried by CPT code using an institutional database. Patients $\geq$ 21 years and those who received primary thyroid lobectomy were excluded. Cases after 2/1/2014 were managed by the protocol (post-protocol implementation group). Cases prior to 2/1/2014 made up the control group. Data was collected by chart abstraction.

Protocol Design

A protocol for postoperative management of total or completion pediatric thyroidectomy patients was developed through local expert opinion (otolaryngology, endocrinology, and pediatric hospitalist) and extensive literature review within standard framework as determined by Seattle Children's Hospital Department of Clinical Standard Work. This protocol **(Figure 1)** was locally published and implemented beginning in February 2014. The protocol utilizes intraoperative intact parathyroid hormone levels (iPTH) collected 25 minutes (approximately five half-lives) after thyroid gland removal for stratification of patients to either high (iPTH of less than or equal to 16 pg/mL) or low risk (greater than 16 pg/mL) -for postoperative hypocalcemia. This cutoff was selected based on the prospective longitudinal cohort study by Freire *et al* [10]. Intact PTH levels were analyzed using a chemiluminescent immunoassay on the Vitros 3600 platform. Patients deemed to be at high risk for hypocalcemia were immediately started on standard dosing of calcium carbonate and calcitriol for empiric treatment of hypocalcemia. Initial postoperative calcium monitoring frequency was determined by the level of risk for hypocalcemia. All patients had immediate serum total calcium levels drawn if they had signs or symptoms of hypocalcemia (**Figure 1**). Biochemical hypocalcemia levels were defined by the laboratory as total serum calcium values < 8.7 mg/dL.

Statistical Analysis

Descriptive statistics were calculated for all demographic and outcome variables. Multivariable linear and Poisson regression models were used to compare pre and post protocol length of stay and number of calcium draws, controlling for type of surgical procedure, patient age, and hypocalcemia post-surgery. Hypocalcemia and the presence of a neck dissection were specifically accounted for in the regression model as those factors may independently increase length of stay and number of calcium draws. Intraoperative PTH hormone levels were used to classify patients into high risk (PTH ≤ 16) and low risk (PTH > 16) categories. Wilcoxon Rank Sum tests were used to compare length of stay and number of calcium draws between the risk categories. Chi-square, Fisher's Exact, and Wilcoxon rank sums tests were used to assess patient characteristic differences between the pre and the post-protocol groups. Significance testing was done at the $\alpha = 0.05$ level. SAS 9.4 (SAS Institute Inc., Cary, NC, USA) was used for analyses.

Power Calculation

A sample size of 50 produces greater than 80% power to detect a difference in length of stay of 0.5 days with a standard deviation between 0.2 and 0.6 between the control and experimental groups.

Results

Sixty-seven cases resulted from CPT query. Fourteen were excluded by procedure type (primary thyroid lobectomy), leaving a total of 53 patients that met inclusion criteria (see **Table 1** for demographics). Patient age ranged from 4 to 21 years, with a median age of 15 years. The majority of patients were female (77.4%). There were 30 patients managed in the pre-protocol implementation period and 23 in the post-protocol implementation period.

The most common diagnosis was papillary thyroid cancer (PTC) in 34 cases (64.2%). Out of these 34 cases of PTC, 18 (52.9%) had metastatic disease involving the central or lateral neck. Of the patients with PTC, 5 (14.7%) were incidental findings in the context of Graves' disease and/or multinodular goiter, 4 (11.8%) had follicular variant PTC and 1 (2.9%) had diffusely infiltrating PTC. There were 7 (13.2%) cases of Graves' disease, 5 (9.4%) cases each of C-cell hyperplasia (4 with MEN2a and 1 with PTEN syndrome), follicular adenoma, and multinodular goiter (1 of which had toxic multinodular goiter), 3 (5.7%) cases of follicular carcinoma, and 1 (1.9%) case of large B-cell lymphoma.

A total of 46 (86.8%) of patients underwent a total thyroidectomy, with 22 (47.8%) also undergoing a concurrent neck dissection (ipsilateral, bilateral, or central neck dissections were grouped together). There were 7 (13.2%) patients who underwent a completion thyroidectomy, with only 1 (14.3%) undergoing a concurrent central neck dissection.

The unadjusted mean number of total calcium draws was 13.3 (±13.20) in the pre-protocol implementation group compared to 7.2 (±4.25) after protocol initiation. When controlling for type of surgical procedure, patient age, and postoperative hypocalcemia, the number of calcium draws decreased from a mean of 5.2 per day in the pre-protocol implementation period to 3.6 per day in the post-protocol implementation period (Rate Ratio = 0.70, $p < 0.001$). Patient age was not associated with the number of calcium draws after accounting for other factors. Patients who underwent a procedure with neck dissection had a slightly higher rate of calcium draws compared to patients who received a procedure without neck dissection (Rate Ratio = 1.19, $p = 0.07$); however, this finding was not statistically significant. There was a higher rate of calcium draws for patients who developed hypocalcemia (both asymptomatic and symptomatic) compared to those who did not develop hypocalcemia (Rate Ratio = 1.23, $p = 0.03$) **(Table 2)**.

There were 31 (58.5%) patients that developed hypocalcemia post-operatively, 4 (12.9%) of which were symptomatic. 17 out of the 23 patients who underwent neck dissection (73.9%) also had transient hypocalcemia while only 12 out of the 30 patients that did not have a neck dissection (40%) had hypocalcemia.

The unadjusted mean length of stay after protocol initiation was 2.0 (±1.24) compared to 2.4 (±1.62) in the control group. When controlling for type of surgical procedure, patient age, and postoperative hypocalcemia, the mean length of stay decreased from 2.10 days in the pre-protocol implementation period to 1.84 days in the post-protocol implementation period (p = 0.29) **(Table 3).** Patients who underwent a neck dissection stayed in the hospital for a mean of 2.32 days compared to 1.66 days in those patients who did not receive a neck dissection as part of their procedure (p = 0.02). The presence or absence of a neck drain was not included in the multivariate analysis for the hospital length of stay. Hypocalcemia was also associated with a longer length of stay, with a mean of 2.41 days compared to 1.60 days in patients who did not develop hypocalcemia (p<0.01). Older patients overall had a lower length of stay (**Table 3**).

There were 9 patients that had a PTH ≤16 and were classified into a high risk group and 14 patients that were placed in a low risk group (PTH > 16). The high risk group received a median of 3.94 draws more than the lower risk group (p < 0.01). Median length of stay did not significantly differ between the two groups (p = 0.14) (**Table 4**).

Discussion

A protocol was developed for postoperative management of pediatric thyroidectomy patients through multidisciplinary collaboration of pediatric otolaryngologists, surgical hospitalists and endocrinologists. The goal of this work was to evaluate the effect of the protocol on patient outcomes. The number of calcium blood draws was significantly reduced by the protocol without increasing the hospital length of stay in this challenging group of patients. An observation by the authors was the enthusiasm with which the protocol was adopted by all care providers. It provided clarity to the multiple physicians caring for the patient, but also the lab technicians, the nurses in the operating room and on the ward, and it helped establish accurate expectations for the patient and family.

Post-protocol implementation, patients were stratified into high and low risk groups based on intraoperative PTH values. Early identification and management of the high risk population was an important part of the protocol. Patients in the high risk group inherently had more frequent calcium draws on the protocol compared to those in the low risk group. Interestingly, patients managed on the risk stratified postoperative calcium supplementation regimen initiated by the protocol had a similar length of stay in both groups. This suggests that patients that are at higher risk for postoperative hypocalcemia are being appropriately managed on the protocol.

One retrospective study on adults suggests transient hypocalcemia occurred in 1.5% of patients that underwent a completion thyroidectomy and 12.5% of patients that underwent a total thyroidectomy. There may be a significantly lower risk for hypocalcemia following a completion thyroidectomy compared to a total thyroidectomy [12]. Future studies should be performed in a larger pediatric cohort to determine whether patients undergoing completion thyroidectomy are equally at risk for developing postoperative hypocalcemia as those undergoing total thyroidectomy.

Risk stratification based on intraoperative PTH allowed the provider to educate patients about the immediate postoperative inpatient management of hypocalcemia. It was also important that patients and their families were educated regarding the risk of hypocalcemia appropriately upon discharge. Morris *et al.* looked into long-term follow-up on pediatric patients undergoing thyroidectomy and concluded that more than 40% of pediatric patients were unable to fully adhere to postoperative medication regimens [11]. They concluded that it is imperative to educate families about the postoperative expectations including anticipated medications and precise dosing information, the hazards of medication nonadherence, and anticipated laboratory testing and clinic visit frequency [11].

In this study, transient hypocalcemia developed in 58.5% of patients and symptomatic hypocalcemia developed in 12.9% of patients. In comparison, the Freire *et al.* pediatric thyroidectomy prospective longitudinal cohort study demonstrated similar transient hypocalcemia rates of 47% and symptomatic hypocalcemia rates of 15% [10]. In contrast, adult literature suggests transient hypocalcemia rates of 1.5-52% of cases [12-14]. This variability may be secondary to differences in defining hypocalcemia. The difference may also be secondary to variances in susceptibilities in pediatric population or due to differences in operations on the pediatric population. Over half of the patients with PTC in this study, had metastatic disease to the neck and nearly half of all pediatric patients undergoing a total thyroidectomy also underwent a neck dissection. It must be noted that referral patterns changed as time elapsed and more pediatric patients were operated at our institution for benign disease in the post-protocol implementation group than in the pre-protocol implementation group.

This study suggests that pediatric patients undergoing thyroidectomy with neck dissection may have a higher rate of hypocalcemia. This supports the results of a multivariate analysis that shows that central and bilateral lymph node dissection and the presence of malignancy are independent predictors of postoperative hypocalcemia in the pediatric population [8]. The high rate of transient hypocalcemia in the pediatric population underscores the importance of postoperative electrolyte management in this population.

Patients who underwent a procedure with neck dissection had a higher rate of calcium draws compared to patients who received a procedure without neck dissection however; this finding was not statistically significant. There was a higher rate of calcium draws for patients who developed hypocalcemia (both asymptomatic and symptomatic) compared to those who did not develop hypocalcemia. Patients who underwent a neck dissection and those with hypocalcemia remained hospitalized for a longer period.

It is important to note that after the initiation of the protocol, the decrease in length of stay did not reach statistical significance. This study was a retrospective review and limitations of this study include reliance on electronic medical record to obtain data regarding length of hospital stay. A further limitation of this project was that it did not include a review of the rate of incidental parathyroid gland removal in the two groups. The study did however account for biochemical hypocalcemia in the multivariable regression model. Other factors may have influenced length of stay that differed during the pre- and post-implementation time periods. These include differences in how individual surgeons managed postoperative patients, along with the involvement of hospitalists in managing the patients, and differences in endocrinology recommendations. Future studies should focus on compliance with the protocol in addition to the feasibility of modifications to the protocol to further reduce blood draws.

Hypocalcemia after thyroidectomy can add to the cost of the hospital stay by delaying discharge. Ultimately the goal of future research is to determine the most cost effective protocol for the management of postoperative hypocalcemia. One prospective study on the role of intraoperative rapid PTH monitoring for predicting thyroidectomy-related hypocalcemia suggests the cost of the assay is $280 per patient, while the cost of an overnight stay approaches $3000 however a formal cost-effectiveness survey needs to be performed [7]. Future studies should be performed in a larger pediatric cohort to determine the cost-effectiveness of this protocol.

Postoperative calcium management is challenging following pediatric thyroidectomy because symptoms are less self-reported and blood draws need to be kept to a minimum. This protocol was initially developed because postoperative management was highly variable at our institution, however, the simplicity of the protocol can easily be replicated at other institutions which may have similar variability in postoperative management between providers. This protocol also supplements the extreme paucity of pediatric literature for postoperative thyroidectomy care. This is the only study to our knowledge to describe a comprehensive protocol for the management of postoperative hypocalcemia in the pediatric thyroidectomy population. This protocol has significantly decreased the number of calcium draws in children undergoing thyroidectomy at our institution.

Conclusion

Adoption of a standardized postoperative protocol based on intraoperative PTH levels may reduce the number of blood draws in children undergoing thyroidectomy. In the adult population, advocates of outpatient surgery have demonstrated the safety of protocols that supplement all patients with calcium and vitamin D without obtaining laboratory tests [15, 16]. In our proposed pediatric protocol, postoperative calcium supplementation is weight based. Future research looking into the feasibility of adopting outpatient based protocols is necessary in the pediatric population especially in older children with similar dosage requirements as current adult protocols.

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References

1. Hogan, A.R., et al., *Pediatric thyroid carcinoma: incidence and outcomes in 1753 patients.* J Surg Res, 2009. 156(1): p. 167-72.
2. Gupta, A., et al., *A standardized assessment of thyroid nodules in children confirms higher cancer prevalence than in adults.* J Clin Endocrinol Metab, 2013. 98(8): p. 3238-45.
3. Wu, X.C., et al., *Cancer incidence in adolescents and young adults in the United States, 1992-1997.* J Adolesc Health, 2003. 32(6): p. 405-15.
4. Francis, G.L., et al., *Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer.* Thyroid, 2015. 25(7): p. 716-59.
5. Haugen, B.R., *2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: What is new and what has changed?* Cancer, 2017. 123(3): p. 372-381.
6. Grodski, S. and J. Serpell, *Evidence for the role of perioperative PTH measurement after total thyroidectomy as a predictor of hypocalcemia.* World J Surg, 2008. 32(7): p. 1367-73.
7. Higgins, K.M., et al., *The role of intraoperative rapid parathyroid hormone monitoring for predicting thyroidectomy-related hypocalcemia.* Arch Otolaryngol Head Neck Surg, 2004. 130(1): p. 63-7.
8. Chen, Y., et al., *Pediatric thyroidectomy in a high volume thyroid surgery center: Risk factors for postoperative hypocalcemia.* J Pediatr Surg, 2015. 50(8): p. 1316-9.
9. Kundel, A., et al., *Pediatric endocrine surgery: a 20-year experience at the Mayo Clinic.* J Clin Endocrinol Metab, 2014. 99(2): p. 399-406.
10. Freire, A.V., et al., *Predicting hypocalcemia after thyroidectomy in children.* Surgery, 2014. 156(1): p. 130-6.
11. Morris, L.F., et al., *Long-term follow-up data may help manage patient and parent expectations for pediatric patients undergoing thyroidectomy.* Surgery, 2012. 152(6): p. 1165-71.
12. Merchavy, S., et al., *Comparison of the incidence of postoperative hypocalcemia following total thyroidectomy vs completion thyroidectomy.* Otolaryngol Head Neck Surg, 2015. 152(1): p. 53-6.
13. Noureldine, S.I., et al., *Early predictors of hypocalcemia after total thyroidectomy: an analysis of 304 patients using a short-stay monitoring protocol.* JAMA Otolaryngol Head Neck Surg, 2014. 140(11): p. 1006-13.
14. Pattou, F., et al., *Hypocalcemia following thyroid surgery: incidence and prediction of outcome.* World J Surg, 1998. 22(7): p. 718-24.
15. Terris, D.J., et al., *Outpatient thyroid surgery is safe and desirable.* Otolaryngol Head Neck Surg, 2007. 136(4): p. 556-9.
16. Grubey, J.S., et al., *Outpatient thyroidectomy is safe in the elderly and super-elderly.* Laryngoscope, 2017.

Table 1. Demographic characteristics of patients that underwent thyroid surgery between January 2010 and August 2016.

Table 2. Adjusted rate ratios and 95% confidence intervals for the association between calcium draws and protocol implementation using a multivariable Poisson regression.[1]

Table 3. Adjusted model-based estimates for mean length of stay, using a multivariable linear regression.[1]

Table 4. Unadjusted comparison of sample distributions between PTH risk groups using Wilcoxon Rank Sums Test.

Table 1. Demographic characteristics of patients that underwent thyroid surgery between January 2010 and August 2016.

	Pre-Protocol *N (%)*	*Post-Protocol* *N (%)*	*Overall* *N (%)*	*P-Value*
Age, median (IQR)	16.0 (4.0)	14.0 (5.0)	15.0 (5.0)	0.18*
Sex				0.60†
Female	24 (80.0)	17 (73.9)	41 (77.4)	
Male	6 (20.0)	6 (26.1)	12 (22.6)	
Race				0.36‡
White or Caucasian	15 (50.0)	8 (34.8)	23 (43.4)	
Other	7 (23.3)	7 (30.4)	14 (26.4)	
Patient Refused	5 (16.7)	1 (4.3)	6 (11.3)	
Asian	1 (3.3)	3 (13.0)	4 (7.5)	
More Than 1 Race	1 (3.3)	2 (8.7)	3 (5.7)	
Native Hawaiian and Other Pacific Islander	1 (3.3)	1 (4.3)	2 (3.8)	
Black or African American	0 (0.0)	1 (4.3)	1 (1.9)	
Ethnicity				0.38†
Non-Hispanic/Other/Refused	24 (80.0)	16 (69.6)	40 (75.5)	
Hispanic	6 (20.0)	7 (30.4)	13 (24.5)	
Diagnosis [1]				0.04‡
Papillary Thyroid Cancer	22 (73.3)	12 (52.2)	34 (64.2)	
With Metastases	10	8	18	
Incidental Finding	2	3	5	
Graves' Disease	1 (3.3)	6 (26.1)	7 (13.2)	
C-Cell Hyperplasia	3 (10.0)	2 (8.7)	5 (9.4)	
Follicular Adenoma	3 (10.0)	2 (8.7)	5 (9.4)	
Multinodular Goiter	2 (6.7)	3 (13.0)	5 (9.4)	
Follicular Carcinoma	3 (10.0)	0 (0.0)	3 (5.7)	
Large B-Cell Lymphoma	0 (0.0)	1 (4.3)	1 (1.9)	
Surgical Procedure				0.38†
Total Thyroid	24 (80.0)	22 (95.7)	46 (86.8)	
With Neck Dissection	14	7	21	
Completion	6 (20.0)	1 (4.3)	7 (13.2)	
With Neck Dissection	1	0	1	
Hypocalcemia	19 (63.3)	12 (52.2)	31 (58.5)	0.41†
Symptomatic Hypocalcemia	2	2	4	

[1] Patient can have more than 1 diagnosis; percentage sum will be > 100. †Chi-Square Test. ‡Fisher's Exact Test. *Wilcoxon Rank Sum Test.

Table 2. Adjusted rate ratios and 95% confidence intervals for the association between calcium draws and protocol implementation using a multivariable Poisson regression.[1]

Predictor	*Rate Ratio (Number of Calcium Draws/Day)*	*95% CI*	*p-value*
Protocol			
Post-Protocol	0.70	0.58, 0.84	< 0.001
Pre-Protocol (Reference)	---	---	---
Procedure			
With Neck Dissection	1.19	0.99, 1.43	0.07
Without Neck Dissection (Reference)	---	---	---
Hypocalcemia			
Yes	1.23	1.02, 1.48	0.03
None (Reference)	---	---	---

[1] Analysis also adjusted for age.

Table 3. Adjusted model-based estimates for mean length of stay, using a multivariable linear regression.[1]

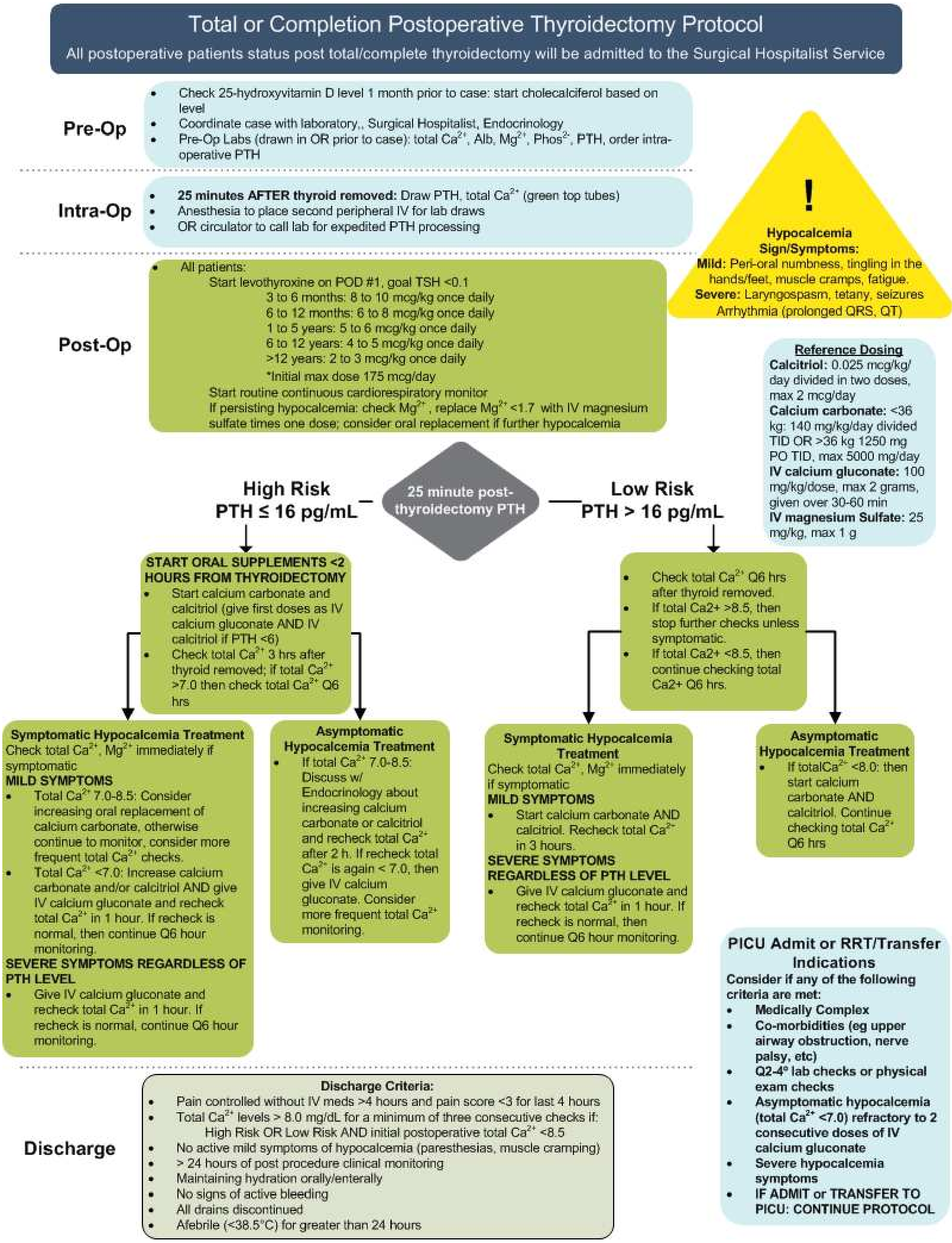
Predictor	*Estimated Mean Length of Stay (Days)*[2]	*95% CI*	*p-value*
Protocol			
Post-Protocol	1.84	1.51, 2.23	0.29
Pre-Protocol (Reference)	2.10	1.78, 2.48	---
Procedure			
With Neck Dissection	2.32	1.89, 2.85	0.02
Without Neck Dissection (Reference)	1.66	1.42, 1.95	---
Hypocalcemia			
Yes	2.41	2.02, 2.87	< 0.01
None (Reference)	1.60	1.33, 1.93	---

[1] Analysis also adjusted for age.
[2] Model was built on the log scale to approximate the normal distribution of length of stay. These estimates represent the exponentiated estimated model-based mean.

Table 4. Unadjusted comparison of sample distributions between PTH risk groups using Wilcoxon Rank Sums Test.

	Low Risk[1]	*High Risk*[2]	
	Median (IQR)	*Median (IQR)*	*p-value*
Length of Stay	1.26 (0.83)	2.08 (0.41)	0.14
Calcium Draws	5.50 (3.00)	9.44 (3.00)	< 0.01

1. PTH values ≤ 16 are considered low risk
2. PTH values > 16 are considered high risk


Total or Completion Postoperative Thyroidectomy Protocol
All postoperative patients status post total/complete thyroidectomy will be admitted to the Surgical Hospitalist Service
Pre-Op
• Check 25-hydroxyvitamin D level 1 month prior to case: start cholecalciferol based on level
• Coordinate case with laboratory,, Surgical Hospitalist, Endocrinology
• Pre-Op Labs (drawn in OR prior to case): total Ca2+, Alb, Mg2+, Phos2-, PTH, order intra-operative PTH
Intra-Op
• 25 minutes AFTER thyroid removed: Draw PTH, total Ca2+ (green top tubes)
• Anesthesia to place second peripheral IV for lab draws
• OR circulator to call lab for expedited PTH processing
Post-Op
• All patients:
Start levothyroxine on POD #1, goal TSH <0.1
3 to 6 months: 8 to 10 mcg/kg once daily
6 to 12 months: 6 to 8 mcg/kg once daily
1 to 5 years: 5 to 6 mcg/kg once daily
6 to 12 years: 4 to 5 mcg/kg once daily
>12 years: 2 to 3 mcg/kg once daily
*Initial max dose 175 mcg/day
Start routine continuous cardiorespiratory monitor
If persisting hypocalcemia: check Mg2+, replace Mg2+ <1.7 with IV magnesium sulfate times one dose; consider oral replacement if further hypocalcemia
!
Hypocalcemia Sign/Symptoms:
Mild: Peri-oral numbness, tingling in the hands/feet, muscle cramps, fatigue.
Severe: Laryngospasm, tetany, seizures Arrhythmia (prolonged QRS, QT)
Reference Dosing
Calcitriol: 0.025 mcg/kg/day divided in two doses, max 2 mcg/day
Calcium carbonate: <36 kg: 140 mg/kg/day divided TID OR >36 kg 1250 mg PO TID, max 5000 mg/day
IV calcium gluconate: 100 mg/kg/dose, max 2 grams, given over 30-60 min
IV magnesium Sulfate: 25 mg/kg, max 1 g
High Risk PTH ≤ 16 pg/mL
25 minute post-thyroidectomy PTH
Low Risk PTH > 16 pg/mL
START ORAL SUPPLEMENTS <2 HOURS FROM THYROIDECTOMY
• Start calcium carbonate and calcitriol (give first doses as IV calcium gluconate AND IV calcitriol if PTH <6)
• Check total Ca2+ 3 hrs after thyroid removed; if total Ca2+ >7.0 then check total Ca2+ Q6 hrs
• Check total Ca2+ Q6 hrs after thyroid removed.
• If total Ca2+ >8.5, then stop further checks unless symptomatic.
• If total Ca2+ <8.5, then continue checking total Ca2+ Q6 hrs.
Symptomatic Hypocalcemia Treatment
Check total Ca2+, Mg2+ immediately if symptomatic
MILD SYMPTOMS
• Total Ca2+ 7.0-8.5: Consider increasing oral replacement of calcium carbonate, otherwise continue to monitor, consider more frequent total Ca2+ checks.
• Total Ca2+ <7.0: Increase calcium carbonate and/or calcitriol AND give IV calcium gluconate and recheck total Ca2+ in 1 hour. If recheck is normal, then continue Q6 hour monitoring.
SEVERE SYMPTOMS REGARDLESS OF PTH LEVEL
• Give IV calcium gluconate and recheck total Ca2+ in 1 hour. If recheck is normal, continue Q6 hour monitoring.
Asymptomatic Hypocalcemia Treatment
• If total Ca2+ 7.0-8.5: Discuss w/ Endocrinology about increasing calcium carbonate or calcitriol and recheck total Ca2+ after 2 h. If recheck total Ca2+ is again < 7.0, then give IV calcium gluconate. Consider more frequent total Ca2+ monitoring.
Symptomatic Hypocalcemia Treatment
Check total Ca2+, Mg2+ immediately if symptomatic
MILD SYMPTOMS
• Start calcium carbonate AND calcitriol. Recheck total Ca2+ in 3 hours.
SEVERE SYMPTOMS REGARDLESS OF PTH LEVEL
• Give IV calcium gluconate and recheck total Ca2+ in 1 hour. If recheck is normal, then continue Q6 hour monitoring.
Asymptomatic Hypocalcemia Treatment
• If totalCa2+ <8.0: then start calcium carbonate AND calcitriol. Continue checking total Ca2+ Q6 hrs
PICU Admit or RRT/Transfer Indications
Consider if any of the following criteria are met:
• Medically Complex
• Co-morbidities (eg upper airway obstruction, nerve palsy, etc)
• Q2-4° lab checks or physical exam checks
• Asymptomatic hypocalcemia (total Ca2+ <7.0) refractory to 2 consecutive doses of IV calcium gluconate
• Severe hypocalcemia symptoms
• IF ADMIT or TRANSFER TO PICU: CONTINUE PROTOCOL
Discharge
Discharge Criteria:
• Pain controlled without IV meds >4 hours and pain score <3 for last 4 hours
• Total Ca2+ levels > 8.0 mg/dL for a minimum of three consecutive checks if: High Risk OR Low Risk AND initial postoperative total Ca2+ <8.5
• No active mild symptoms of hypocalcemia (paresthesias, muscle cramping)
• > 24 hours of post procedure clinical monitoring
• Maintaining hydration orally/enterally
• No signs of active bleeding
• All drains discontinued
• Afebrile (<38.5°C) for greater than 24 hours