Original Research

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

OTO Open
2021, Vol. 5(4) 1–6
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DOI: 10.1177/2473974X211059070
http://oto-open.org
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Rate of Incidental Parathyroidectomy in a Pediatric Population

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Abstract

Objective. Incidental parathyroidectomy is a relatively common occurrence in thyroid surgery, which may lead to hypoparathyroidism and postoperative hypocalcemia, but it is not well studied in children. The objectives of this study were to determine the rate of incidental parathyroidectomy, identify potential risk factors, and investigate postoperative complications in children undergoing thyroidectomy.

Study Design. Retrospective cohort study.

Setting. Patients who underwent thyroidectomy over a 10-year period at a tertiary children's hospital.

Methods. Pathology reports were reviewed to determine incidental parathyroid gland tissue. Additional data collected included patient demographics, type of procedure, underlying thyroid pathology, as well as immediate and long-term postoperative clinical outcomes.

Results. Of 209 patients, 65 (31%) had incidental parathyroidectomy. Several variables were associated with incidental parathyroidectomy on univariable analysis. However, in the final multivariable model, only thyroidectomy with lymph node dissection was associated with increased odds of having incidental parathyroidectomy (odds ratio, 3.3; $P = .04$; 95% CI, 1.1-9.8). After a median follow up of 1 year, a significantly higher percentage of patients with incidental parathyroidectomy had evidence of long-term hypoparathyroidism (9/62 [15%] vs 3/144 [2%], $P = .001$).

Conclusion. Incidental parathyroidectomy was relatively common in our pediatric thyroidectomy population, which may be a result of several anatomic, clinical, and surgeon-related factors. Close attention to parathyroid preservation with meticulous surgical technique is the most practical method of preventing long-term hypoparathyroidism and hypocalcemia.

Keywords

child, thyroidectomy, parathyroidectomy, neck dissection, hypocalcemia, hypoparathyroidism

Received September 30, 2021; accepted October 20, 2021.

Thyroidectomy is a common operation with conservative estimates of about 150,000 thyroid procedures done each year in the United States.[1] This is part of a global trend toward increased diagnosis and treatment of thyroid disease over the past several years.[2] Consequently, much attention and research have been given to thyroidectomy outcomes, complications, and various related factors. Pediatric thyroidectomy, however, remains a small subset of total thyroidectomies performed, since pediatric thyroid cancer is rare and elective pediatric thyroidectomy for nodules or Graves' disease is even less common. Multiple studies have demonstrated that pediatric thyroid disease differs from the greater adult population in many ways that influence decision making and treatment, such as presenting with more advanced disease in thyroid cancers.[1,3] Thyroidectomy in young children is often accompanied with worsened outcomes, such as higher complication rates and longer hospital stays.[4] Additionally, complications may have longer-lasting and burdensome consequences in children when compared with adults. In response to these challenges, there has been increasing attention on pediatric-specific research, high-volume pediatric thyroidectomy centers, and optimizing outcomes.[5,6]

Incidental parathyroidectomy (IPE) is a relatively common but underrecognized complication in thyroidectomy. While most studies report on rates of hypocalcemia or hypoparathyroidism, which can result from several factors, preventing IPE

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This project was presented as a poster at the 2021 Annual Meeting of the Triological Society; April 9, 2021; New Orleans, Louisiana.

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and preserving parathyroid tissue in situ surgically is the most practical measure to prevent harm from the surgical perspective. IPE contributes to transient hypoparathyroidism and postoperative hypocalcemia and is typically a necessary feature of permanent hypoparathyroidism.[7] Transient and permanent hypoparathyroidism may manifest with hypocalcemia symptoms, including life-threatening hypocalcemia in the form of tetany and cardiac arrhythmias, as well as osteoporosis and decreased quality of life related to lifelong supplementation with permanent hypoparathyroidism.[8] IPE rates vary widely in the adult literature and are not well described in children.[9] The objective of this study was to examine the rate of IPE and to identify risk factors and complications in children undergoing thyroidectomy.

Materials and Methods

Study Design, Ethics, Setting, and Participants

A retrospective cohort study was conducted of patients who underwent thyroidectomy (lobectomy or total thyroidectomy, with or without neck dissections) at a tertiary care children's hospital between January 2010 and October 2020. Study approval was obtained from the institutional review board at Children's Hospital Los Angeles, and consent was waived due to the retrospective nature of the study. Patients were excluded if no pathology report was available or they were ≥19 years of age.

Data Collection and Management

We reviewed the medical records of eligible patients and extracted the following data points: demographic information (age as a continuous variable, sex, race, ethnicity, insurance type), medical history, perioperative information (surgical procedures performed, length of procedure, surgical complications), and postoperative information (final pathology, common quality indicators, and long-term clinical outcomes). In particular, careful examination of the pathology report and operative report was carried out. IPE was defined as the histologic report of parathyroid tissue on the final pathology report, when not documented in the corresponding operative note as being excised or sampled intentionally. Permanent hypoparathyroidism was initially determined by documented calcium or calcitriol use at last follow-up and then confirmed by additional chart review. Study data were collected and managed with REDCap electronic data capture tools hosted at the Keck School of Medicine, University of Southern California.[10,11]

Statistical Analyses

Patient characteristics, operative details, and disease-related data points were investigated via univariable analysis for any correlation with IPE. Mann-Whitney tests were used for continuous variables with skewed distributions and Fisher's exact or chi-square tests for categorical variables. Potential risk factors with a univariable P value $<.1$ were considered for inclusion in multivariable logistic regression. We used Akaike's information criterion model selection and clinical relevance to distinguish among a set of possible models describing the relationship between these variables of interest and IPE. Study data were analyzed with Stata 13.1 (StataCorp).

Results

Of the 209 patients who underwent thyroidectomy in the study period, 65 (31%) had IPE (**Table 1**). The mean number of parathyroid glands reported, when present, was 1.3. There were no significant differences between those with and without IPE with regard to their sex, race/ethnicity, insurance type, or preoperative diagnoses. Patients with IPE had a slightly lower median age than those without IPE (14.8 vs 15.3 years, P = .07). On univariable analysis, patients with thyroidectomies that included lymph node dissection (33/65 [51%] vs 34/144 [24%], $P < .001$) and those with longer surgery times (182 vs 154 minutes, P = .007) had increased rates of IPE. Regarding final pathology reports, those with a tumor malignancy (36/65 [55%] vs 55/144 [38%], P = .02) or lymph node metastases (28/65 [43%] vs 35/144 [24%], P = .006) were more likely to have IPE. An overall 188 patients had complete follow-up information with a median follow-up period of just over 1 year (13.7 months; range, 2.4 months–8.5 years). In this group, a significantly higher percentage of patients with IPE had evidence of long-term hypoparathyroidism (9/62 [15%] vs 3/126 [2%], P = .001). Those with IPE were also more likely to have other complications, such as an injury to the recurrent laryngeal nerve (P = .05), and were more likely to have advance disease requiring postoperative treatment with radioactive iodine (P = .02).

In selecting the final multivariable model assessing potential risk factors, lymph node dissection was highly correlated with malignancy; specifically, 90% of patients who underwent lymph node dissection also had malignancy. For this reason, the malignancy variable was omitted from the best-fitting multivariable model with the lowest Akaike's information criterion number. In this final model, patients who had a lymph node dissection had 3.3-times the odds of IPE as those who did not have a lymph node dissection (P = .04; 95% CI, 1.1-9.8; **Table 2**), and this was the only variable to remain statistically significant.

Discussion

To our knowledge, this is the largest series reporting on IPE in the pediatric population. Our findings suggest that the risk of IPE is higher in the pediatric population when compared with adults. This may partially be explained by increased rates of malignancy in pediatric thyroid surgery as well as more advanced presentation such as high lymph node burden. However, half of our cases of IPE were in patients who did not receive lymph node dissection, suggesting that other factors unique to pediatric thyroidectomy may increase the risk of IPE. Our observed experience, particularly in younger patients, is consistent with other reports of increased difficulty in pediatric surgery, such as smaller dimensions of anatomic structures, as well as higher degrees of variable anatomy, such as unregressed thymic tissue and intracapsular parathyroid (**Figure 1**).[12-14] Even at a high-volume pediatric thyroid center, thyroid surgery remains uncommon in very young

Table 1. Demographics and Perioperative and Follow-up Characteristics of Those With and Without Incidental Parathyroid Excision.[a]

	Incidental parathyroid excision		
	Yes (n = 65)	No (n = 144)	*P* value
Age, y, median (range)	14.8 (1-18.9)	15.3 (2.9-18.9)	.07[b]
Female	48 (74)	114 (79)	.4
Ethnicity			.6
Hispanic	28 (43)	57 (40)	
Non-Hispanic	37 (57)	87 (60)	
Public insurance	43 (66)	101 (70)	.6
Medical history			
Hyperthyroidism	9 (14)	32 (22)	.2
Hypothyroidism	6 (9)	6 (4)	.1
Procedure			<.001
Thyroidectomy + LND	33 (51)	34 (24)	
Thyroidectomy – LND	32 (49)	110 (76)	
Parathyroid reimplanted	7 (11)	8 (6)	.2
Length of surgery, min, median	182	154	.007[b]
Malignancy on pathology	36 (55)	55 (38)	.02
Any lymph node metastases	28 (43)	35 (24)	.006
No. of malignant lymph nodes, mean (SD)	10.2 (13.5)	5.5 (12.2)	.055
Any postoperative radioactive iodine	16 (29)	16 (13)	.02
Complications reported on follow-up			
Hypoparathyroidism	9 (15)	3 (2)	.001
Hoarseness	4 (6)	5 (4)	.4
Recurrent laryngeal nerve injury	5 (8)	3 (2)	.05
Scar revision	4 (6)	4 (3)	.2

Abbreviation: LND, lymph node dissection.
[a]Results are presented as No. (%) unless otherwise specified.
[b]Two-sample Wilcoxon rank-sum (Mann-Whitney) test.

Table 2. Final Multivariable Logistic Regression Showing Odds of Having an Incidental Parathyroid Excision.

	Odds ratio	*P* value	95% CI
Age	0.98	.8	0.86-1.1
Thyroidectomy with lymph node dissection	3.3	.04	1.1-9.8
History of hypothyroidism	3.0	.2	0.63-14.4
Length of surgery	1.0	.9	0.99-1.0
Any lymph node metastases	0.6	.4	0.19-1.9
No. of malignant lymph nodes	1.0	.3	0.98-1.1

patients, which may contribute to increased complication rates.

Much attention has been given to thyroidectomy outcomes, particularly to complications such as hematoma, laryngeal nerve injury, and hypocalcemia. Of these, hypocalcemia is the most common complication and is caused by hypoparathyroidism through surgical trauma, devascularization, or accidental removal of the parathyroid glands.[15] While transient hypocalcemia is common in total thyroidectomies even with meticulous technique, long-term or permanent hypoparathyroidism is rare and a result of loss of viable parathyroid tissue.[16] Previously published rates of postthyroidectomy hypoparathyroidism in children range from 1.5% to 25% and include reports of potential long-term sequelae, such as delayed childhood development, decreased bone health, and other negative impacts on quality of life, including reliance on supplementation.[17-19] While individual IPE has not been shown to be associated with permanent hypoparathyroidism given the redundancy of other parathyroid glands, IPE of multiple glands or in combination with other parathyroid injury is virtually a necessary condition.[7] We feel that the identification and preservation of parathyroid glands are the most

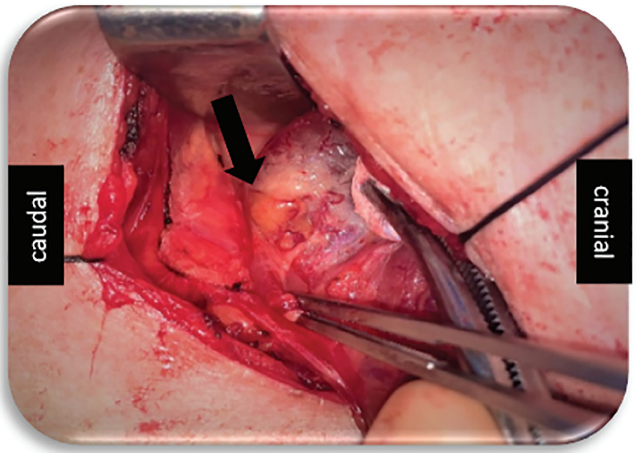

Figure 1. Intracapsular parathyroid gland on the inferior edge of the right thyroid gland (arrow), with capsule peeled back (DeBakey forceps).

important step in preventing IPE as well as preventing long-term hypoparathyroidism.

Rates of IPE are not often well reported, especially in the pediatric population, ranging widely in the adult literature from 2.3% to 29%.[7,20-23] Multiple patient-specific and surgical aspects have been considered risk factors for IPE in the adult literature, such as pathologic diagnoses and extent of surgery (eg, paratracheal dissection), as well as surgeon experience and volume.[24] Familiarity with the anatomy of parathyroid gland location and blood supply and recognition of parathyroid tissue are of great importance in avoiding IPE. Parathyroid glands arise from the endoderm of the third and fourth pharyngeal pouches as 2 pairs and come to rest in variable locations with respect to the thyroid gland, which descends from the midline thyroglossal tract. Intracapsular, intrathyroidal, and intrathymic locations are relatively common, which increases difficulty in locating and preserving these glands in thyroidectomy.[9,25] Additionally, while there are typically 4 glands, variable numbers of identifiable parathyroid glands have been reported.[26] When it comes to thyroidectomy for malignancy, there are increased levels of difficulty in preserving the parathyroid glands during paratracheal dissection due to the potentially similar appearance of lymph nodes, lymph node matting, and more extensive surgical dissection. Pediatric thyroidectomy commonly has many of the aforementioned conditions for increased difficulty in identifying parathyroid glands, with diminished surgical experience, more difficult and variable anatomy, and increased rates of lymphadenopathy.

We are limited from drawing concrete conclusions from the data based on the inherent limitations of our retrospective review, including the small number of patients with IPE, particularly those with long-term effects. There was the potential for misidentification of IPE, as we relied on surgeon documentation to "rule out" IPE in pathology reports. In some cases, it may be possible that a small sample of identified parathyroid was sent to confirm parathyroid and subsequently preserved but was not ultimately dictated in the operative report. Conversely, while generally our pathology specimens undergo meticulous sectioning techniques, especially in cases of malignancy, there may be some cases of IPE that were not seen or reported by pathology.

Several strategies to improve rates of IPE have been explored, such as including preoperative imaging for localization, in vivo imaging such as autofluorescence, or use of gamma probe.[27-29] For example, intraoperative autofluorescence allows surgeons to localize parathyroid gland tissue, as it selectively uptakes fluorescent dye as compared with surrounding thyroid tissue, thymic tissue, and nearby lymph nodes.[30] Kahramangil et al[31] reported that intraoperative autofluorescence imaging facilitated parathyroid gland identification in 27% to 67% of the time as compared with traditional localization by the surgeon and was more cost-effective than intraoperative frozen section examination. While individual studies in adult populations have noted some promise, most parathyroid localizing modalities are not used routinely. The safe and practical use in pediatric thyroidectomy of routine pre- or intraoperative parathyroid imaging is not yet studied. However, given the observed rates of pediatric IPE in our study, some of these technologies may deserve more interest. Improvements may be more immediately found in the shift of surgery toward high-volume centers, which have been well described as an effective strategy to improve the quality of outcomes in children and adults.[6,32] High-volume pediatric thyroid surgeons have been described as those who perform >30 cases per year.[33] Additionally, the American Thyroid Association has recommended that pediatric thyroid cancer be treated by high-volume surgeons in a multidisciplinary team, as is the case for all children in our institution.[3]

Greater attention and cognizance regarding rates of IPE in children, as highlighted by this study, may help encourage meticulous surgery and improved practices. We suggest identification and documentation of parathyroid glands, with care to preserve the vascular supply. Resection specimens should be examined for accidentally resected parathyroid tissue. When in doubt, intraoperative pathologic consultation should be done to confirm parathyroid tissue. Completely avulsed or devascularized glands should be used for autotransplantation. Finally, as pediatric thyroidectomy follows adult trends toward becoming an outpatient procedure, recognition of the risks of hypoparathyroidism should encourage use of rapid perioperative parathyroid hormone testing and appropriate replacement.

Conclusion

IPE was relatively common in our pediatric thyroidectomy series and may contribute to long-term hypoparathyroidism. IPE was associated with lymph node dissections, as well as increased rate of postoperative complications. Especially in these higher-risk populations of pediatric thyroidectomy, referral to high-volume centers should be considered.

Author Contributions

Grace Sahyouni, conceptualized and designed the study, collected data, drafted the initial manuscript, and reviewed and revised the manuscript; **Beth Osterbauer**, conceptualized and designed the study, collected data, carried out the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript; **Soyun Park**, conceptualized and designed the study, collected data, reviewed and revised the manuscript; **Connie Paik**, conceptualized and designed the study, collected data, reviewed and revised the manuscript; **Juliana Austin**, conceptualized and designed the study, collected data, reviewed and revised the manuscript; **Gabriel Gomez,** conceptualized and designed the study, collected data, reviewed and revised the manuscript; **Daniel Kwon**, conceptualized and designed the study, collected data, drafted the initial manuscript, and reviewed and revised the manuscript.

Disclosures

Competing interests: None.

Sponsorships: None.

Funding source: None.

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