Published in final edited form as:

J Surg Res. 2012 October ; 177(2): 268–274. doi:10.1016/j.jss.2012.06.044.

Evolution of Pediatric Thyroid Surgery at a Tertiary Medical Center

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Abstract

Background—Thyroidectomy in the pediatric population is often avoided due to perceived risks in children. With growing subspecialization and establishment of high volume endocrine surgery centers, the indications for thyroid surgery and extent of resection continue to change. We examined the evolution of pediatric thyroid surgery at a high volume tertiary medical center.

Methods—From our prospectively collected database, we reviewed medical records of individuals younger than 19 years who underwent thyroidectomy at our institution from 1994 to 2009. Patients were divided into two groups: 1) before establishment of our endocrine surgery center (1994–2001) and 2) since establishment of the center (2002–2009).

Results—We identified 78 operations performed on 74 patients with a median age of 15 (range 3–18) years. We found that the number of patients doubled in the later time period, with 26 operations in Group 1 and 52 in Group 2. The age of patients and percentage of females were similar between groups. After establishment of the endocrine surgery center, there was a significant increase in total thyroidectomies for all indications, including significantly more for benign disease. Overall, 9% of the patient population experienced transient complications, with no permanent complications or long-term sequelae.

Conclusions—Pediatric thyroid surgery is extremely safe, especially when performed at a high volume endocrine surgery center. We more often select surgical treatment for benign disease and choose total thyroidectomy over limited resection. This may reflect increasing confidence in the safety and efficacy of surgery and reliability of thyroid hormone replacement.

Keywords

pediatric; thyroidectomy; endocrine surgery center; tertiary care; benign thyroid disease

Introduction

Thyroidectomy is a standard treatment for hyperthyroidism and malignant thyroid disease in adults. While surgical removal is a commonly accepted treatment for thyroid neoplasms in children, routine use of thyroidectomy for benign disease is less well described.

Thyroidectomies for benign disease have been avoided in pediatric patients in part because of concern for higher complication rate, though the only comprehensive pediatric single-institution study examining all-comers with surgically treated thyroid disease demonstrates complication rates similar to adults (1). More recently, studies are advocating an increased use of surgical treatment for benign disease (2–6). Further, these studies extol the benefits of

total thyroidectomy over partial or unilateral gland removal for both benign and malignant disease (2–8), including reduced recurrence of disease, reduced need for reoperation, and avoidance of lifelong antithyroid medication or exposure to radioactive iodine.

It is now widely accepted that patients undergoing technically challenging operations with more involved post-operative care have fewer complications and reduced lengths of stay in high-volume surgical centers (9–12). However, due to the relative rarity of pediatric thyroid disease, there are limited studies from high-volume institutions regarding whether the pattern of treatment for pediatric thyroid disease in practice reflects the recommendations from the recent literature. We undertook this study to examine the evolution of the surgical treatment of pediatric thyroid disease at a single tertiary care institution with the establishment of an Endocrine Surgery Center.

Methods

Patient Selection

We conducted a review of our prospectively collected database of all individuals who underwent a thyroid operation at the University of Wisconsin and the American Family Children's Hospital between 1994 and 2009. We selected individuals less than 19 years old to include in our study. No further exclusion criteria were used. University of Wisconsin Institutional review board approval was obtained for the data collection and data analysis.

Data Definitions

Regarding classification of post-operative complications, hypocalcemia was defined by record of a low serum calcium concentration (<8.0 mg/dL) on the first post-operative morning or mention of post-operative hypocalcemic episodes in their discharge summary. Transient hypocalcemia was defined by documented normocalcemia after the discontinuation of calcium supplementation and calcitriol within 6 months of the operation. Classification of indication for operation as prophylaxis for MEN2 disorders required a genetic test positive for mutation of the RET proto-oncogene. Patients were determined to have benign or malignant disease based on pathologic findings from thyroid specimens. Surgeon specialty was determined by the senior surgeon recorded in the operative note for each patient's thyroidectomy. In the cases where two senior surgeons were reported, the surgeon that performed the majority of the thyroidectomy was recorded as the primary surgeon.

Data Analysis

The University of Wisconsin established an Endocrine Surgery Center in 2001, so the cases were divided into two sample groups based on this time point, creating two time periods of eight years each (from 1994–2001 and 2002–2009). Age at time of operation, gender profile, and family history of thyroid disease for each group were compared. Pre-operative work up, operative procedure, pathologic diagnosis, and post-operative complications were reviewed and compared. Data regarding the indication for the operation were based on pathologic diagnosis if there was a discrepancy between pre- and post-operative diagnoses. Data for each variable were compared between groups using Student's t-test, Chi-squared test, or Fisher's Exact test where appropriate. $P<0.05$ was used as the standard criterion for statistical significance. Data analysis was performed using Microsoft Excel and R for Windows, version 2.13.1.

Patient Treatment Algorithm

The Endocrine Surgery Center, recognized as such due to its high patient volume in a tertiary medical center, was formed under the leadership of the head of the Section of

Endocrine Surgery. Treatment of patients is organized within a multidisciplinary team, including endocrine surgeons and fellows, pediatric general surgeons, pediatric and adult endocrinologists, nurse practitioners, general surgery residents, cytopathologists, thyroid pathologists, speech pathologists, and radiologists. Interesting and challenging cases are discussed by this group in multidisciplinary conferences. Treatment is initiated in pediatric endocrinology clinic (Figure 1), and patients with nodules are referred to the multidisciplinary thyroid clinic, where they undergo an ultrasound with FNA. If there is an indication for surgery based on FNA, the patient is evaluated immediately by endocrine surgery and is scheduled for a partial or total thyroidectomy as indicated. Preoperative calcium, parathyroid hormone, free T4, TSH, thyroglobulin with thyroglobulin antibody, and, in patients with Graves' Disease, free T3 serum levels are drawn. Graves' Disease patients are prescribed potassium iodide for 10–14 days prior to their operation. Operations take place in the pediatric hospital with pediatric anesthesiologists, and are performed by the staff surgeon and a mid-level resident or higher. A parathyroid hormone serum level is checked immediately post-operatively. Patients with a parathyroid hormone level lower than 10 pg/mL are discharged on calcitriol and calcium carbonate three times daily; those with a parathyroid hormone greater than 10 pg/mL are discharged with calcium carbonate as needed for symptoms of hypocalcemia. Levels were chosen based on previous work (13). Levothyroxine is started on postoperative day 1 for patients after total thyroidectomy, except for patients with Graves' Disease, who start Levothyroxine on postoperative day 2–3. Patients return for a postoperative visit in 1–2 weeks, and thyroid hormone levels are initially managed by endocrine surgery with long-term management by pediatric endocrinology. If post-operative hypoparathyroidism does occur, this is managed by the endocrine surgery team.

Database Management

To allow for improved outcome monitoring, a database of all patients undergoing endocrine operations is maintained by the senior surgeons, the endocrine surgery nurse practitioner, and research staff involved in research within the section of endocrine surgery. As a prospectively maintained database, information recorded includes demographic data, operation and date of surgery, surgical indications, disease-specific symptoms, comorbidities, endocrine-related family history, gene testing results, previous operations, pre- and post-operative labs and vital signs, results of preoperative imaging studies, FNA results, operative findings, pathology results, presence of metastases or positive lymph nodes, post-operative complications, length of hospital stay, initiation of thyroid hormone replacement treatment, treatment with radioactive iodine, follow up, and patient outcomes, including any further operations or disease recurrence.

Results

Between the years of 1994–2009, a total of 74 patients younger than 19 years old underwent 78 thyroid operations at our combined adult and pediatric tertiary care institutions. Of these, 24 patients underwent 26 operations between 1994 and 2001, henceforth designated Group 1; 50 patients underwent 52 operations between 2002 and 2009, designated Group 2. The pediatric patient volume exactly doubled in the later time period, after the creation of Endocrine Surgery Center. The mean (SD) age at operation of the groups were similar (Group 1 = 12.6 (4.5) years vs. Group 2 = 13.3 (4.8) years, $p = 0.54$). The majority of both groups of patients were female (20 patients (77%) vs. 45 patients (83%), $p = 0.28$), and there was no difference in family history of thyroid disease, neither benign (0 patients vs. 2 patients (4%), $p=0.55$) nor malignant (2 patients (8%) vs. 5 patients (10%), $p = 1.00$) (Table 1).

Surgeon Specialties

Due to the recent emphasis placed on surgeon specialty in determining outcomes, we examined the pattern of senior surgeons who operated on each patient cohort. Three surgeons performed all of the operations for the patients in Group 1: one endocrine surgeon, one pediatric surgeon, and one otolaryngologist. The endocrine surgeon performed 24 out of 26 operations in Group 1 (92%), with the pediatric surgeon and otolaryngologist each performing one operation (4% each). These three surgeons continued to operate on Group 2 patients, and were joined by two endocrine surgeons and one pediatric otolaryngologist, for a total of 6 surgeons. Thirty-eight operations for patients in Group 2 were performed by endocrine surgeons (73%), 8 by otolaryngologists (15%), and 6 by the pediatric surgeon (12%). While Group 2 had a lower proportion of operations performed by the endocrine surgeons, between Group 1 and Group 2 neither the reoperation rate (6 (23%) vs. 6 (12%), respectively, $p=0.32$), nor complication rate (1 (4%) vs. 6 (12%), $p=0.41$) showed any significant changes. In short, although there was an increase in variety of surgeons performing thyroidectomies on children after the establishment of the Endocrine Surgery Center, there was no change in any of the recorded measures of negative outcomes.

Preoperative Studies

Pre-operative evaluations were compared, which demonstrated that imaging modalities were used with similar frequency over time. Ultrasound was the most commonly utilized (Group 1 = 9 (35%) vs. Group 2 = 17 (33%), $p = 0.93$), followed by nuclear scintigraphy scans (3 (12%) vs. 8 (15%), $p = 0.74$), and finally computed tomography scans (1 (4%) vs. 2 (4%), $p = 1.0$). Interestingly, although there was no increase in ultrasound usage, there was a trend in increasing fine-needle aspirations (FNA) for pre-operative diagnosis in patients with nodular disease, though the data did not reach statistical significance (4 out of 16 patients with nodular disease (25%) vs. 16 out of 36 (44%), $p = 0.14$) (Table 2).

Indications and Extent of Operation

Next, we evaluated the operative indications for the patient groups. We showed a trend towards increased operative treatment of benign disease with the creation of the Endocrine Surgery Center, though the data did not reach statistical significance (15 (58%) vs. 39 (75%), $p = 0.19$) (Table 3). Of the benign indications for operation, Graves' disease is the most common in both patient groups (Group 1 = 4 patients (15%), Group 2 = 14 patients (27%)), followed in Group 2 by goiter (7 patients (13%)) and benign adenoma (6 patients (12%)). The benign indications in Group 1 are relatively evenly spread (Table 3). The number of patients undergoing an operation for malignant indications decreased in Group 2. The proportion of operations for papillary and follicular cancers stayed stable ($p = 0.63$ and 0.55 , respectively); however, the operations performed for medullary thyroid cancer decreased with statistical significance in Group 2 (4 (15%) vs. 1 (2%), $p = 0.04$), while operations for MEN2 prophylaxis did not change in frequency ($p = 0.33$) (Table 3). We then compared the extent of thyroid removal between groups. The patients in Group 2 underwent significantly more total thyroidectomies than subtotal thyroidectomies compared to Group 1 (15 (58%) vs. 44 (85%), $p = 0.02$) (Figure 2a). When these operations are further categorized by benign or malignant indications for the operation, with those undergoing prophylactic thyroidectomies for MEN2 syndromes removed from calculation, we found that significantly more patients underwent a total thyroidectomy for benign disease in Group 2 compared to Group 1 (29 of 36 patients with benign disease (81%) vs. 2 of 11 (18%), $p = 0.0003$) (Figure 2b).

Postoperative Complications

Finally, we evaluated the post-operative complications of both patient groups. Overall, only 7 patients (9%) experienced a complication: 2 patients with transient asymptomatic hypocalcemia, 4 patients with transient symptomatic hypocalcemia, and 1 patient with transient hoarseness. There was no significant difference in complication rates between the two patient groups. No patients experienced long-term sequelae from these complications, giving a symptomatic transient complication rate of 7% and permanent complication rate of 0%.

Discussion

Pediatric thyroid disease is relatively rare compared to adult thyroid disease, contributing to low annual numbers of operative thyroid cases in children, even in high volume surgery centers. These low numbers lead to a paucity of large sample populations from which we can draw conclusions regarding updated practices in pediatric thyroid disease. This study was undertaken to examine the changing trends in practice for pediatric thyroid disease at a single institution after the establishment of an Endocrine Surgery Center. This retrospective review of 78 pediatric thyroid operations between 1994 and 2009 demonstrated an increase in the volume of pediatric thyroid cases, an increase in operations for benign thyroid disease, and an increase in total thyroidectomies over partial removal for benign disease since the formation of the Endocrine Surgery Center. Moreover, we demonstrate a trend of increased utilization of FNA in diagnosis of pediatric thyroid nodules, and a distribution of thyroid cancer cases that mirrors the percentages found in larger nationwide studies (14), although the number of operations for medullary thyroid cancer decreased significantly in the later time group. Interestingly, this study revealed an increase in the number of surgeons performing pediatric thyroid operations and in the number of cases performed by pediatric and otolaryngology surgeons since the establishment of the Endocrine Surgery Center. However, this trend was not associated with a change in complication rates, which were uniformly low (9% of all cases), on the same level as published adult series.

Both national database studies and single institution studies advocate that pediatric endocrine surgical care be performed by surgeons with high-volume practices at high-volume surgical centers due to lower complication rates and shorter lengths of stay (9–11,15,16). Interestingly, this relationship holds true despite the fact that both high-volume surgeons and pediatric surgeons in the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP-NIS) performed an average of only 2 pediatric cases per year (9). This suggests that there are qualities outside of pediatric-specific endocrine surgical volume that are reducing length of stay and complications for pediatric patients. Our findings support this idea; there was no significant change in complications after the endocrine surgery center was created at our institution, even though there was an increase in the number of cases performed by either pediatric or otolaryngology specialists (4% each prior to the endocrine center vs. 12% and 15%, respectively). Despite not having an endocrine surgery center prior to 2001, our institution has been a high-volume adult and pediatric surgical institution since well before our prospectively collected database began. This suggests that complication rates and other negative outcomes are limited at least in part by the experience of our other healthcare staff with pediatric patients. In addition, the increase in the proportion of cases performed by an otolaryngologist or pediatric surgeon with the formation of the endocrine surgery center demonstrates an increase in interdisciplinary collaboration advocated by a recent single-institution study by Wood et al. (10), thereby minimizing specialist-specific limitations and optimizing patient care. In our institution, this collaboration is facilitated by a regular case conference during which challenging cases are addressed by multidisciplinary faculty.

One of the benefits of an interdisciplinary endocrine surgery center is a more ready adoption of technology. Fine needle aspiration has been recommended by the American Thyroid Association (ATA) as a first-line diagnostic tool in adults (7), but it has been less uniformly encouraged in children, even though the risk of malignancy in children who present with nodules is higher than in adults (17,18). A recent meta-analysis demonstrates a 98.2% negative predictive value of FNA in children, while a retrospective study of 110 patients shows a positive predictive value of 95% in FNAs that are read as malignant. These findings suggest FNA should play a central role in the diagnostic algorithm of pediatric patients with thyroid nodules to exclude malignancy (18) and confirm the need to remove nodules that are atypical on FNA just as in adults (19). Our findings of increased use of FNA for pediatric thyroid nodules likely corresponds with an increased appreciation for the accuracy in pediatrics patients, as well as the coordination within our multidisciplinary practice with the adult endocrine practitioners who ability to perform the procedure with minimal anxiety on the part of the patient.

This concern for higher risk of complications in children carries over to thyroidectomies as well. A previous single-institution study found higher complication rates in children than adults, and thus recommend partial thyroidectomy for all single malignant nodules (20). However, our study shows complication rates similar to adult series, with no significant increase in complications associated with the increase in total thyroidectomies. Moreover, it has been shown that children with even small tumors at presentation have high rates of recurrence (20–30%) requiring reoperation when not initially treated with total thyroidectomy and radioactive iodine treatment (8,21). Still, thyroid malignancy in children is a universally recognized indication for surgical removal, as is concern for multiple endocrine neoplasia 2 (MEN2) hereditary syndromes. This is supported by the ATA Guidelines for management of medullary thyroid cancer (22,23), with recommendations for thyroidectomy based on malignant potential in genetic testing. While we showed no change in the number of prophylactic operations, likely due to the steady detection of MEN2 syndromes with genetic testing protocols, the number of operations for medullary thyroid cancer decreased significantly. This may be a reflection of the efficacy of increased awareness of the prophylactic guidelines and early detection of genetic mutations.

In concordance with population-based studies over recent years (6), our study shows an increase over time in the percentage of total thyroidectomy versus subtotal thyroidectomy as the surgical treatment of choice for thyroid disease (increasing from 58% to 85%), with a significant increase in patients with benign indications undergoing total thyroidectomy after the establishment of an Endocrine Surgery center. While there are concerns for higher rates of complications in children compared to adults, studies of total thyroidectomy for benign disease in both adults (5) and children (4) show low complications rates and no disease recurrence at a median of 9 years and 12.9 years of follow up, respectively (4,5).

With definitive surgical treatment for benign disease, we allow pediatric patients to avoid the difficulty of compliance and potential toxicity, as well as high relapse rates, associated with antithyroid medications like propylthiouracil and methimazole (24,25). We also avoid the risks of radioactive iodine (RAI) treatment in pediatric patients for treatment of benign disease. While there was no change in RAI treatment between patient groups in our study, no patients with benign disease were subjected to RAI in Group 2, while 2 patients with benign disease underwent RAI in Group 1 (8%). Further studies have addressed this issue particularly in Graves' Disease, which was the most common benign indication for surgery in our study. These studies proposed total or near total thyroidectomy as the most appropriate operative treatment of Graves' Disease, because it eliminates the risk of recurrent disease and the resulting hypothyroidism can be predictably controlled with thyroxine replacement (2,3,5).

The reticence to recommend following the adult guidelines completely in children is likely due to a concern for complications in pediatric patients. While some population database studies suggest that children have higher complication rates than adults after thyroid surgery, these differences were only in post-operative hypocalcemia. Non-endocrine-related complications were comparable between adults and children, at a rate of 10.5–11.5%, as are recurrent laryngeal nerve related complications (14). The single-institution study from Boston Children's Hospital demonstrates overall complication rates similar to ours (1), which correspond with rates from adult series (5,6,11). We conclude that, with fellowship-trained surgeons at a high-volume endocrine center, complication rates can be kept low, especially with collaboration between surgical specialties in very young patients.

This study possesses the inherent limitations of retrospective reviews, in that there is no design for targeted results, and the data are subject to the limitations of observations. However, this study benefits compared to other retrospective reviews in that the data were collected prospectively at the time of operation, and follow up data have been tracked. Additionally, pediatric thyroid disease is relatively rare, meaning that patient samples are small. Many comparisons in this study approach significance, and it is unclear if significance is not reached due to the lack of power with the small sample sizes. Regarding comparisons based on disease classification, the benign versus malignant determination is made by pathologic results, and not on an intent-to-treat diagnosis. This information is not reliably recorded in our database and so was not used. This study may also provide a skewed representation of thyroid disease rates in the population because this sample is comprised only of patients who underwent an operation, although the frequency of the cancer diagnoses shown here generally follows the pattern in the population at large (14). However, contrary to other single-institution studies that reported a predominance of patients with thyroid nodules as the indication for operation (2,20), we demonstrated an increasing number of patients undergoing an operation for benign disease, which may indicate that this sample is a closer representation of thyroid disease in the general pediatric population.

Despite these limitations, we are able to show convincing aspects of how the surgical treatment of pediatric thyroid disease has evolved at our institution with the development of our Endocrine Surgery Center. We advocate for the use of ultrasound in the preoperative evaluation of pediatric patients, as well as increased use of FNA as an accurate diagnostic tool with minimal risk. Based on our results, we find the practice trending toward total thyroidectomy for both malignant and benign indications. These operations can have a low associated risk of complication in high-volume centers with experienced surgeons, even in young children. Specifically, the benefits of an Endocrine Surgery Center include the easy access to interdisciplinary collaboration in challenging cases, as well as a specialized understanding of pediatric endocrine disease by healthcare workers involved in every facet of patient care. With such a care system in place, we are able to provide children with safe, definitive surgical treatment for thyroid disease.

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Figure 1. Algorithm for treatment of pediatric patients with thyroid disease

This flowchart diagrams the approach to treatment of patients with newly suspected thyroid disease at our Endocrine Surgery Center. * Pediatric Endocrinology as an end point indicates continued evaluation, workup, and treatment if indicated in the pediatric endocrinology clinic. RAI=radioactive iodine.

Figure 2. Comparison of the extent of resection for disease type between groups

A) Proportion of patients undergoing total thyroidectomy versus anything less than near total thyroidectomy in each patient group. Group 1 patients underwent their operations between 1994 and 2001; Group 2 underwent operations between 2002 and 2009. B) Cases are divided based on pathologic diagnosis into benign and malignant cases within the same Groups. * $p=0.02$, ** $p<0.001$

Table 1

Patient Characteristics

	Group 1 (1994–2001) N=26	Group 2 (2002–2009) N=52	P value
Age in years (range)	12.6 (3–18)	13.3 (3–18)	0.54
Females (%)	20 (77%)	45 (83%)	0.28
Family History Benign Thyroid Disease (%)	0 (0%)	2 (4%)	0.55
Family History Thyroid Cancer (%)^I	2 (8%)	5 (10%)	1.00

^I Includes patients with a family history of diagnosed thyroid cancer, MEN syndromes, and RET proto-oncogene mutations.

Table 2

Preoperative Imaging and Diagnostic Studies

	Group 1 (1994–2001) N=26	Group 2 (2002–2009) N=52	P value
Ultrasound (%)	9 (35%)	17 (33%)	0.93
Nuclear Medicine (%)	3 (12%)	8 (15%)	0.74
CT Scan (%)	1 (4%)	2 (4%)	1.00
FNA of Nodules (%)^I	4/16 (25%)	16/36 (44%)	0.14

^I Number represents number of patients who had an FNA performed out of total number of patients with nodular disease.

Table 3

Indications for Operation

	Group 1 (1994–2001) N=26	Group 2 (2002–2009) N=52	P value
Benign (%) [/]	15 (58%)	39 (75%)	0.19
Graves'	4 (15%)	14 (27%)	0.39
Goiter	2 (8%)	7 (13%)	0.71
Adenoma	1 (4%)	6 (12%)	0.41
Hashimoto's Thyroiditis	2 (8%)	3 (6%)	1.00
Colloid cyst	3 (12%)	0 (0%)	0.03
MEN Prophylaxis	3 (12%)	2 (4%)	0.33
Malignancy (%) [/]	11 (42%)	13 (25%)	0.19
Papillary Cancer	7 (27%)	10(19%)	0.63
Follicular Cancer	0 (0%)	2 (4%)	0.55
Medullary Cancer	4 (15%)	1 (2%)	0.04

[/]Based on pathologic diagnosis from surgical specimen, except for "MEN prophylaxis," which was based on family history and/or genetic testing.