Review Article

Thyroidectomy in children and adolescents: a systematic review

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Background: Thyroid surgery in pediatric population is not as common as that in adults, although they share the same indications, techniques and complications. This review aims to evaluate the surgical management of thyroid disease in patients under 18 years old.

Methods: We conducted a bibliographic search in the international literature. Data from the identified studies such as demographics, indication for surgery, type of procedure, complications and length of hospital stay were recorded. A retrospective review study of all patients under 18 years old who underwent thyroidectomy was performed.

Results: We included 37 retrospective studies and a total of 12,728 patients. Thyroidectomy was more common in female patients and the mean age was approximately 14 years old. The leading indication for surgery was benign thyroid pathology. Due to the surgical treatments' safety and effectiveness in young patients, total and subtotal thyroidectomy, whether for malignancies or benign diseases, is becoming more popular today. The most often occurring complication of pediatric thyroid surgery is hypoparathyroidism. Despite the high likelihood of recurrence of pediatric malignancies, overall survival rates of pediatric thyroid cancer are excellent.

Conclusions: Thyroidectomy performed by high-volume thyroid surgeons in children and adolescents is considered an efficient and safe method of treatment of thyroid disease.

Keywords: Pediatric thyroidectomy; thyroid surgery; thyroid disease; thyroid cancer (TC)

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Introduction

Pediatric thyroid disease includes either benign or malignant situations. The most frequent benign pathologies involve Graves' disease, toxic adenoma, congenital hyperthyroidism, thyroid nodules and goiter. Additionally, differentiated thyroid cancers (TCs) such as papillary, follicular and myeloid cancer are the most commonly malignancies in children. In case of medullary cancer, familial syndromes should be investigated (1,2).

For TC as well as for some benign thyroid disorders, total and subtotal thyroidectomy is the treatment option in pediatric patients, while prophylactic procedure is left for high-risk cancer development in the future. Since thyroid pathology favors malignancy in younger ages, lymph node dissection is common (3).

Endocrine surgery in patients under 18 years of age has similar philosophy as adult surgery concerning the surgical techniques. Major complications from thyroidectomy include recurrent laryngeal nerve (RLN) or superior laryngeal nerve palsy, respiratory complications, trauma infection, bleeding and hematoma, permanent and temporary hypoparathyroidism. The procedure type, referring to lobectomy, total thyroidectomy with or without node dissection, affects complication rates and hospital length of stay. Hospitalization of underage patients usually requires accompany of a family member during hospitalization due to the emotional charge of the patient. One day hospitalization after pediatric thyroidectomy is the common practice (4,5).

In this review we aimed to evaluate the field of thyroid surgical practice in patients less than 18 years old. Our objective was to emphasize the value of preoperative examinations, the type of the procedure, the increasing preference of surgery instead of more conservative treatment, the recurrence rate and follow-up needed. We present this article in accordance with the PRISMA reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-16/rc).

Highlight box

Key findings

- This study underscores the efficacy and safety of thyroidectomy as a primary intervention for pediatric thyroid pathology. Female predominance was observed among patients. Hypoparathyroidism, whether transient or permanent, emerged as the principal complication. Despite potential recurrence in pediatric thyroid cancer, overall survival rates were consistently excellent. Surgical approaches are witnessing increased favor due to their demonstrated safety and efficacy in managing pediatric thyroid diseases.

What is known and what is new?

- In previous years, due to limited pediatric expertise, a relatively conservative approach was favored for managing thyroid disease in children and adolescents. This approach included antithyroid medication, radioiodine treatment, and restricted resections.
- Pediatric thyroid surgery, whether for malignancies or benign conditions, has been established as a safe procedure. Complications are notably rare, hospitalization periods are short, and the impact on healthcare resources remains minimal.

What is the implication, and what should change now?

- The results emphasize the effectiveness of thyroidectomy in children and adolescents, signaling a need for updated clinical guidelines, enhanced surgeon training, and specific patient education. Furthermore, essential research is required to identify factors contributing to favorable outcomes in pediatric thyroid surgery.

Methods

The literature search was conducted in the PubMed, Scopus and Embase databases until March 2023 using the following Mesh terms: (thyroidectomy) AND (pediatric), (thyroidectomy) AND (children), (thyroidectomy) AND (adolescence), (thyroidectomy) using the age frame child (from birth to 18 years old age). The search was limited to articles written in English without any restriction on period. Studies included patients older than 18 years old were excluded.

Data including time period, study design, patients' demographics, indication for thyroid surgery, surgical procedures, postoperative complications, and outcomes were collected.

Results

The literature search identified 11,225 articles, 11,108 of which were excluded from title and abstract screening and an additional 81 articles were excluded by the full text. Thirty-seven retrospective studies were included in our systematic review (*Figure 1*).

A literature review was performed and 37 articles of thyroid surgery in pediatric population were selected and summarized in (*Table 1*).

In this systematic review, we added cases from our Department and descriptive statistics was applied. The percentage of criteria fulfillment is shown in *Table 2*.

The main results were as follow:

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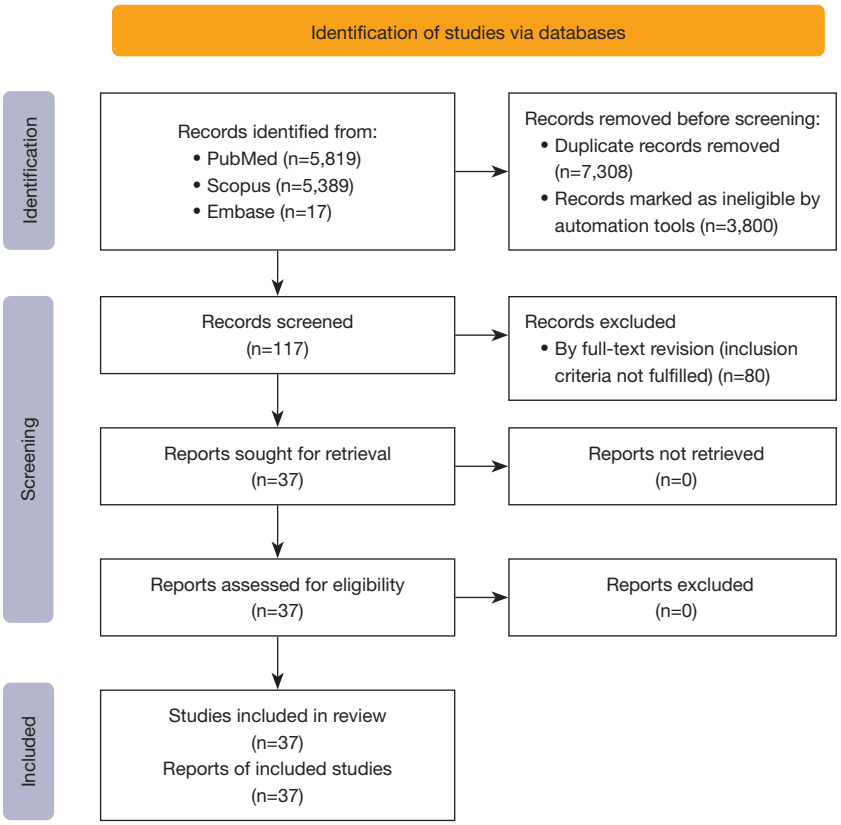

Figure 1 The PRISMA flowchart.

Demographics

In our study, 12,728 patients were enrolled, from whom 9,848 were females (77.4%). The mean age was 13.4±1.93 years old.

Indication for surgery

The indications for thyroid surgery were divided in two main categories; benign disease and malignancy. Benign disease included toxic adenoma, goiter, thyroid nodules, Graves' disease and congenital hyperthyroidism, which were found in 6,281/12,008 cases (52.3%). Malignant tumors (papillary, follicular and sporadic medullary TC) were found in 4,979/12,008 cases (41.5%), while prophylactic thyroidectomy for multiple endocrine neoplasia type 2 syndrome (MEN-2) was found in 295/12,008 cases (2.5%).

Type of procedures

The most common type of procedure was total thyroidectomy in 7,866/12,109 cases (64.9%), followed by hemithyroidectomy (HT) in 3,214/12,109 cases (26.5%). The percentage of lobectomy was 5.7% (693/12,109 cases), while near-total thyroidectomies were performed in 0.4% (48/12,109 cases). Completion thyroidectomy after HT or lobectomy was performed in 129/12,109 cases (1.1%), due to carcinoma in the final pathology report. The percentage of central and lateral lymph node dissection were 6% (732 cases) and 1.1% (128 cases), respectively.

Complications

The most common complication was hypoparathyroidism (HP) in 1,218/12,728 cases (9.6%), from which 148 cases had permanent HP (12.2%). The second most common complication was RLN palsy in 153/12,728 cases (1.2%), from which 25 cases had permanent nerve injury (16.3%). Other rare complications were wound infection in 18/12,728 (0.14%) cases, keloid formation in 32/12,728 cases (0.25%), hematoma in 8/12,756 cases (0.06%) and chylous leak in 1/12,728 cases (0.008%).

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Table 1 Characteristics of included studies on pediatric thyroid surgery

Source	Time period	Study design	Patients (n)	Mean age, years	Sex	Pathology	Type of surgery	Complications	Mean postoperative hospital stay (days)	Follow-up, mean (range)
Sosnowska-Sienkiewicz *et al.*, 2024 (6)	2013–2022	Retrospective study	148	15	Female 113 (76%), male 35 (24%)	Goiter 56; Graves' disease 3; Hashimoto's disease 13; PTC 48; follicular thyroid carcinoma 6; medullary thyroid carcinoma 2; lymphoepithelial cyst 1; sinus histiocytosis 2; hyalinizing trabecular adenoma 1; Burkitt's lymphoma 1; mature teratoma 1; thyroid tissue 5; thyroid adenoma 20	TT 64, HT 95, + LN dissection 45, reoperation 11	*Early complications 43 (39.05%)* -Transient retrograde laryngeal nerve palsy 6 -Transient hypoparathyroidism 37 *Late complications 3 (2.03%)* -Vocal cord paralysis (required a tracheostomy) 1 -Hypoparathyroidism 2	6	Until they were 18 years old
Quaglino *et al.*, 2023 (7)	2019–2022	Retrospective review study	25	12.64±3.86	Female 15 (60%), male 10 (40%)	Graves' disease 6 Uninodular thyroid goiter 3 Multinodular thyroid goiter 4 Papillary thyroid cancer 8 Medullary thyroid cancer 3 Completion thyroidectomy (in previous papillary thyroid cancer) 1	TT 20 (80%) TT + unilateral LN dissection of the central cervical compartment 3, HT 5 (20%)	Transient hypoparathyroidism 5 Persistent hypoparathyroidism 1	3.4 (range, 2.6–4.5)	3 months
Weber *et al.*, 2023 (8)	2017–2022	Prospective study	604	15.4	Female 453 (75%), male 151 (25%)	Nodular goitre (35.6%) Follicular adenoma (30.1%) Graves' disease (28.5%) *Malignancy 126* PTC 77.8% Follicular thyroid carcinoma 10.3% Medullary thyroid carcinoma 8.7%	Not reported	Early RLN injury 27 (4.9%) Persistent RLN injury 4 (0.7%)	Not reported	Not reported
Vieira *et al.*, 2023 (9)	2010–2021	Retrospective study	14	15.9	Female 12, male 2	Follicular adenoma 6 Colloid nodular goiter 6 Noninvasive follicular thyroid neoplasm with papillary-like nuclear features 1 Papillary carcinoma 1 MEN2A 1	TT 6 (including 1 completion thyroidectomy), HT 9	Persistent bilateral lesion of the RLN 1 Cervical hematoma 1 Transient hypoparathyroidism 1	Not reported	Not reported
Scholfield *et al.*, 2023 (10)	1986–2021	Retrospective review study	307	Not reported	Not reported	Well-differentiated thyroid carcinoma 307	TT 212 (69%), HT 95 (31%)	Temporary unilateral vocal cord palsy 1.06% Permanent vocal cord palsy 0.7% Transient hypocalcemia 32.6% Permanent hypocalcemia 5.2%		61 months
Reiter *et al.*, 2023 (11)	2015–2019	Retrospective cohort study	1,595	14.9	Female 1,234 (77.4%), male 361 (22.4%)	*Benign 1,091 (68.4%)* -Thyrotoxicosis 637 (58.4%) -Nontoxic goiter 153 (14.0%) -MEN 110 (10.1%) *Malignant 504 (31.6%)*	TT 1,595	Minor 8 Major 49 Readmissions 38 Reoperations 12	Benign 1.7 Malignant 1.9	30 days

Table 1 *(continued)*

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Table 1 *(continued)*

Source	Time period	Study design	Patients (n)	Mean age, years	Sex	Pathology	Type of surgery	Complications	Mean postoperative hospital stay (days)	Follow-up, mean (range)
Willobee *et al.*, 2023 (12)	1997–2012	Retrospective study	5,633	16	Female (79%), male (21%)	Malignancy (46%) Goiter (42%)	TT 3,253 HT 2,380	Hypocalcemia 174 (9%) Nerve injury 57 (3%)		
Elgendy *et al.*, 2022 (13)	2011–2021	Retrospective study	32	14 (range, 5–18)	Female 26 (81.25%), male 6 (18.75%)	Papillary carcinoma 24 (75%) Follicular carcinoma 6 (18.75%) Medullary carcinoma 2 (6.25%)	TT 25 (78%) TT only 9 TT and node dissection 16 TT and central node dissection 16 TT and central and lateral node dissection 7 HT 7 (22%)	Chylous leak 1 Transient hypoparathyroidism 3 Transient unilateral RLN palsy 3 Bilateral RLN injury 1 (required an urgent tracheostomy procedure)	Not reported	54 (range, 9–117) months
Bukarica *et al.*, 2022 (14)	2017–2022	Retrospective observational study and systematic literature review	17	14.8 (range, 5–17)	Female 14 (82.4%), male 3 (17.6%)	*Malignant (n=3)* -Papillary carcinoma *Benign (n=14)* -Hyperplastic diffuse colloid goiter -Cystic nodule -Follicular adenoma -Hashimoto thyroiditis -Toxic adenoma	*Total surgeries 19* -Total thyroidectomies 8 -Lobectomy 10 -Central neck dissections 3	Wound infection 1 Transient hypocalcemia 1 Transient RLN injury 2	4	Not reported
Alfonso *et al.*, 2022 (15)	2010–2020	Retrospective study	11	9.8±3.9	Female 7 (63%), male 4 (37%)	Thyroid nodule 1 Graves-Basedow disease 1 Follicular adenoma 1 Papillary thyroid cancer 5 Medullary thyroid cancer 3	TT 7 HT 4 Completion thyroidectomy 1	Transient hypocalcemia 1 (8.6%) Transient RLN neuropraxia 2 (16.6%)	2.35 (range, 1.25–5)	4 years
García-García *et al.*, 2022 (16)	2000–2020	Retrospective study	39	(range, 3.67–14)	Female 26 (66.7%), male 13 (33.3%)	MEN2A 25 (64.1%) Differentiated carcinoma 8 (20.5%) Medullary carcinoma 2 (5.1%) Simple MNG 4 (10.3%)	*Total surgeries 42* -TT 29 -HT 3 -Completion HT with central neck dissection 3 -TT with central neck dissection 7	Temporary hypoparathyroidism 9/39 (23.1%) Permanent hypoparathyroidism 3/39 (7.7%)	Not reported	Not reported
Al-Qurayshi *et al.*, 2022 (17)	2010–2014	Retrospective cross-sectional analysis	361	13.5±0.2	Female 288 (79.8%), male 73 (20.2%)	Thyroid cancer (19.0%) MEN2 (5.4%) Toxic nodular disease (33.6%) Non-toxic benign disease (42.0%)	Lobectomy 29.11% Lobectomy followed by completion thyroidectomy 3.22% TT 67.66%	Postoperative complications were reported in 14.2% of the sample and hypocalcemia was the most common complication (98.2%)	Pediatrics-only hospital 2.44, general hospital 2.11	Not reported

Table 1 *(continued)*

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Table 1 *(continued)*

Source	Time period	Study design	Patients (n)	Mean age, years	Sex	Pathology	Type of surgery	Complications	Mean postoperative hospital stay (days)	Follow-up, mean (range)
Pereira *et al.*, 2021 (18)	2000–2019	Retrospective study	47	8.9±3.9	Female 29 (61.7%), male 18 (38.3%)	MEN2A 29	TT 38 (73.7% of which were prophylactic)	Hematoma 0	1.3±0.6	29 (range, 6–171) months
						MEN2B 1	Double HT 3	Wound infection 0		
						Papillary carcinoma 5	HT 5	RLN injury 0		
						Follicular adenoma 5	+ Lymphadenectomy 5	Transient asymptomatic hypoparathyroidism 7		
						Multinodular goiter 4		Persistent symptomatic hypoparathyroidism 1		
						Follicular carcinoma 1				
						Thyroglossal duct papillary carcinoma 1				
						Graves' disease 1				
van Rooijen *et al.*, 2021 (19)	2013–2020	Retrospective study	48	14.6 (range, 3.9 –17.9)	Female 37 (77.1%), male 11 (22.9%)	Graves' disease 12 (25%)	*Total surgeries 52*	Rapid resolved hypocalcemia 3	Not reported	1.6 (range, 0.1–6.0) years
						Benign thyroid nodule(s) 16 (33.3%)	-HT 19 (39.6%)	Transient hypocalcemia 10		
						Hashimoto's disease 1 (2.1%)	-TT only 18 (37.5%)	Permanent hypocalcemia 6		
						Piriform sinus fistula 2 (4.2%)	-TT in two tempi only 2 (4.2%)	Transient RLN injury 4		
						Goiter due to Pendred syndrome 1 (2.1%)	-TT in two tempi with central neck dissection 1 (2.1%)	Permanent RLN injury 1		
						Goiter due to a congenital activating TSH receptor mutation 1 (2.1%)	-TT plus central neck dissection 3 (6.3%)	Keloid 8		
						MEN2A 3 (6.3%)	-TT plus central and lateral neck dissection 5 (10.4%)			
						Papillary carcinoma 12 (25%)				
de Jong *et al.*, 2021 (20)	2003–2018	Retrospective review study	72	12.7 (range, 1–18)	Female 52 (72%), male 20 (28%)	Papillary cancer 57 (79.2%)	HT 24	Bleeding 0	Not reported	39.7 months
						Follicular cancer 15 (20.8%)	TT alone 10	Wound infections		
						LN metastases 41 (56.9%)	TT + central neck dissection 4	Transient hypoparathyroidism 27		
							TT + central & lateral neck dissection 33	Permanent hypoparathyroidism 18		
							Debulking 1	Unilateral RLN injury		
							Completion thyroidectomy only 18	Excision of RLN owing to tumor infiltration		
							Completion thyroidectomy + central neck dissection 2			
							Additional central & lateral neck dissection 2			
Almosallam *et al.*, 2020 (21)	2000–2014	Retrospective study	103	13.2 (range, 2–18)	Female 80 (78%), male 23 (22%)	*Benign 37 (36%)*	*Total surgeries 112*	Operative complications were observed in 22 patients (19.6%)	Mean length of stay: benign 5.2; malignant 4	71.7 (median 60.0, range 9–148) months
						-Normal thyroid tissue 14 (13.5%)	-TT (50%)	Transient hypocalcemia 20		
						-Colloid nodule 14 (13.5%)	-HT (17%)	Permanent hypocalcemia 3		
						-Cyst 2 (1.9%)	-Completion thyroidectomy (31%)	Transient unilateral RLN palsy 3		
						-Adenoma 3 (2.9%)	-Subtotal thyroidectomy (1.7%)	Permanent unilateral RLN palsy 3		
						-Thyroiditis 3 (2.9%)	-Neck dissection was performed in 59 patients	Bleeding/hematoma 0		
						-Graves' disease 1 (1.0%)		Wound infection 0		
						Thyroid cancer 66 (64%)		Tracheal injury 0		
						-Papillary 61 (59%)				
						-Follicular 3 (2.9%)				
						-Medullary 2 (1.9%)				

Table 1 *(continued)*

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Table 1 *(continued)*

Source	Time period	Study design	Patients (n)	Mean age, years	Sex	Pathology	Type of surgery	Complications	Mean postoperative hospital stay (days)	Follow-up, mean (range)
Bilić *et al.*, 2020 (22)	2011–2020	Retrospective study	58	14.4 (range, 6–18)	Female 54 (93.1%), male 4 (6.9%)	Multinodular goiters 23 Follicular adenoma 9 Papillary cancer 25 + level VI cervical LN metastasis 4 + level II–IV cervical LN metastasis 10 Medullary cancer with unilateral RLN invasion 1	*Total surgeries 58* -Lobectomies 21 -Total thyroidectomies 37 -Paratracheal neck dissections 12 -Selective neck dissections 10 -Sternotomy with partial pleurectomy 1	Transient hypoparathyroidism 11 (19%) Permanent hypoparathyroidism 2 (3.4%) Permanent unilateral recurrent nerve palsy 1 Unilateral resection of spinal accessory nerve (nXI) 1 A few local wound infections	Not reported	Not reported
Dream *et al.*, 2020 (23)	2015–2019	Retrospective review study	51	15±0.3 (range, 9–18)	Female 40 (79%), male 11 (21%)	Graves' disease (55%) Thyroid cancer (17%) Thyroid nodule (11%) Multinodular goiter (7%) Hashimoto's disease (6%) Toxic adenoma (4%)	TT 36 HT 13 TT with neck dissection 2 Modified lateral neck dissection 2	Wound complication 3 Hematoma 1 Transient hypoparathyroidism 5 Transient hoarseness 1 Permanent hypoparathyroidism 2 Permanent RLN injury 0	6 h	13±7 days
Utria *et al.*, 2020 (24)	2015–2017	Retrospective study	1,300	14±3.5	Female 1,014 (78%), male 286 (22%)	Benign 834 (64%) Malignant 380 (29%)	Total thyroidectomies 805 Unilateral thyroidectomies 412 Modified radical neck dissection 83	*Total 39* • Readmissions (n=20) -Hypocalcemia/hypoparathyroidism 12 -Remainder included thyroid malignancy 4 -Nausea and vomiting 1 -Postprocedural endocrine disorder 1 -Localized swelling 1 -Unknown 1 • Infection 6, prolonged intubation 5, reoperation 5, DVT 2, transfusion 1, peripheral nerve injury 1, urinary tract infection 1, reintubation 1	1.7	30 days
Babala *et al.*, 2019 (5)	2006–2018	Retrospective study	22	12.6±4.0	Female 15 (68%), male 7 (32%)	Papillary carcinoma 12 (55%) MEN2 6 (27.3%) Medullary carcinoma 3 (13.7%) Follicular cancer 1 Neck LN metastases 8 (36.4%) Distant metastases 6 (27.3%) Both locations 4 (18.2%)	TT 18 (82%) Lobectomy 1 (4.5%) Primary surgery on the LNs 1 (13.6%)	*Transient hypoparathyroidism 6 (27.3%)* -Symptomatic 1 (4.5%) -Asymptomatic 5 (22.7%) Permanent unilateral vocal cord paralysis 1	Not reported	6 years
Patel *et al.*, 2020 (25)	2015–2016	Retrospective study	720	14.1	Female 555 (77%), male 165 (23%)	Not reported	HT 245 TT 376 TT with central neck dissection 99	Nerve injury 1, occurrences bleeding/transfusion 1, organ/space surgical site infection 1, related readmission 18, related reoperation 1, seizure 1, superficial incisional surgical site infection 3, superficial wound disruption/dehiscence 2, urinary tract infection 1	1 to 5 years of age: 7.8 Older: 2.1	30 days

Table 1 *(continued)*

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Table 1 *(continued)*

Source	Time period	Study design	Patients (n)	Mean age, years	Sex	Pathology	Type of surgery	Complications	Mean postoperative hospital stay (days)	Follow-up, mean (range)
de Jong *et al.*, 2020 (4)	1998–2018	Retrospective study	106	12 [range 0–18]	Female 68 (64.2%), male 38 (35.8)	Graves' disease 52 (49.1%) Hereditary medullary thyroid carcinoma 36 (33.9%) Multinodular goiter 3 (2.8%) Thyroid carcinoma (follicular or papillary) 15 (14.2%)	TT only 83 (78.3) TT plus central neck dissection 9 (5.7) TT plus central and lateral neck dissection 14 (13.2)	Post-operative transient hypocalcaemia 63 (59.4%) (within 24 h after surgery) Long-term hypoparathyroidism 23 (21.7%)	4 (range, 1–15)	6 months
Jiang *et al.*, 2019 (26)	2010–2016	Retrospective review study	38	14.3 (range, 4.3–18.4)	Female 32 (84.2%), male 6 (15.8%)	Medullary thyroid carcinoma (associated with MEN2) 4 (10.5%) Classic PTC 14 Follicular Variant of PTC 3 Diffuse Sclerosing Variant of PTC 1 Follicular carcinoma 3 Multinodular goiter 8 Graves' disease 5	TT 32 Completion thyroidectomy with prior lobectomy surgery 6 + neck dissection 14	24 (63.2%) hypocalcemia Permanent hypoparathyroidism 5.3% Transient or permanent RLN paralysis 0	2.5±1.3	7 years
Nordenström *et al.*, 2018 (27)	2004–2014	Retrospective study	274	14 (range, 0–17)	Female 215 (78.5%), male 59 (21.5%)	Graves' disease 214 (78.1%) Other benign disease 27 (9.9%) Thyroid cancer 33 (12%)	TT 174 + LN surgery 38	Permanent hypoparathyroidism 20 (7.3%)	No permanent 1 day Permanent hypoparathyroidism 2	4.8 years
Alkhars *et al.*, 2019 (28)	1997–2017	Retrospective review study	75	13.3±3.76 (range, 3–18)	Female 60 (80%), male 15 (20%)	Follicular adenoma, 54.7% (n=42) Graves' disease, 13.3% (n=10) Teratoma, 1.3% (n=1) Ectopic thymic nodule, 1.3% (n=1) Papillary carcinoma, 14.7% (n=11) Follicular carcinoma 8% (n=6) Medullary carcinoma 6.7% (n=5)	TT 54.7% (n=41/75) whereas 13.3% (n=10/75) had associated neck dissection Partial thyroidectomy 45.3% (n=34/75)	Wound infection 1 Transient XII paralysis which had rapidly recovered 1 Bilateral RLN paralysis 1 Dysphonia with paralysis of the right vocal cord 1 Transient hypoparathyroidism 4 Permanent hypoparathyroidism 1	Not reported	Not reported
Bussières *et al.*, 2019 (29)	2006–2015	Retrospective study	98	11.8±4.75	Female 73 (74.5%), male 25 (25.5%)	Thyroid nodule 63 (64%) [malignant 23, papillary carcinoma (22/23), follicular carcinoma (1/23)] MEN mutation carrier 21 (22%) [malignant 9, medullary carcinoma (9/21)] Hyperthyroidism 7 (7%) Goiter 7 (7%) (malignant 4, papillary carcinoma 4/7)	Total 118 surgeries -Prophylactic TT 21 (18%) -TT 24 (20%) -HT 58 (49%) -HT with branchial remnant excision 7 (6%) -LN dissection 3 (3%) -Other 5 (4%)	Wound infection 2 Postoperative hematoma 1 Parathyroid injury Transient hypocalcemia 16 (13.6%) Permanent hypocalcemia 2 (1.7%) RLN injury Transient VC paralysis 2 (1.7%) Permanent VC paralysis 3 (2.5%)	First surgery: 1.42±1.05; second surgery: 1.95±3.33	2.7±2.65 years
Zong *et al.*, 2018 (30)	2005–2016	Retrospective study	35	9.5 (range, 4–14)	Female 25 (71%), male 10 (29%)	Follicular adenocarcinoma 1, papillary carcinoma 34	TT 7, HT 6	Hypocalcemia without hypoparathyroidism 3 (lobectomies), hypoparathyroidism 6 (TT)	HT 4.1±1.8 TT 9.7±3.4	HT 3.75 (1.2–4.3) years TT 3.8 (1.3–7) years
Spinelli *et al.*, 2019 (31)	2000–2017	Retrospective study	30	13.73±3.83 (range, 5–18)	Female 22 (73%), male 8 (27%)	Follicular carcinoma 30	HT 21 (70%) [11 (52%) of them were operated a second time with completion of thyroidectomy], TT 9 (30%), + lymphadenectomy of the central and lateral cervical section was performed in 3 patients (10%)	Transitory hypoparathyroidism 4 (57%) Definitive hypoparathyroidism 2 (28%) Lesion of the RLN 1 (15%)	72.8±34.62 (range, 6–120) months	6±3.46 (0.5–10) years

Table 1 *(continued)*

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Table 1 *(continued)*

Source	Time period	Study design	Patients (n)	Mean age, years	Sex	Pathology	Type of surgery	Complications	Mean postoperative hospital stay (days)	Follow-up, mean (range)
Spinelli *et al.*, 2016 (32)	2000–2014	Retrospective review study	250	14.2 (range, 4–18)	Female 71 (28.4%), male 179 (71.6%)	Papillary carcinoma 250	TT 226/250 (90.4%) Thyroid lobectomy 24/250 (9.6%) Neck dissection followed TT in 109/115 (94.8%) patients. It followed lobectomy in the remaining 6/115 (5.2%) patients	Transient hypoparathyroidism 13.6% Permanent hypoparathyroidism 4.4% Unilateral vocal fold palsy 5 (2%) Bilateral vocal fold palsy 2 (0.8%) requiring an urgent tracheostomy	Not reported	5.8 (range, 1–15) years
Chen *et al.*, 2015 (33)	1992–2013	Retrospective study	171	15.4 (range, 2.5–18.9)	Female 141 (82.3%), male 30 (17.7%)	Benign 127 (68.3%), most common follicular adenoma (31.4%), Graves' disease (11.9%), malignant 59 (31.7%), papillary thyroid cancer 51 (27.4%) Medullary thyroid cancer 5 (2.7%) Follicular thyroid cancer 3 (1.6%)	186 operations TT 85 (45.7%), completion thyroidectomy 15 (8.1%), HT 79 (42.5%) Local excision or nodulectomy 7 (3.8%) + LN dissection 39 (21.0%) Central neck (level VI) 23 (12.4%) Central plus unilateral (levels II–IV) 12 (6.5%) Central plus bilateral 4 (2.2%)	Transient hypocalcemia 24 (12.9%) with 13 (7.0%) requiring intravenous calcium infusion. Permanent hypoparathyroidism 1 (0.9%). Temporary RLN injury 3 (1.6%). Permanent 0	1 (range, 0–8)	3 (range, 0–17) years
Sinha *et al.*, 2015 (34)	1987–2011	Retrospective study	61	Benign conditions 12 (range, 5–18) Malignant conditions 7.5 (range, 2–17)	Female 43 (70.5%), male 18 (29.5%)	*Benign:* -Graves disease 36 (84%) -Other 7 (16%) (toxic MNG 1, nontoxic MNG 2, and benign thyroid nodule 4) *Malignant:* -MEN-2 syndrome 9 (50%) -Papillary 6 (33%) -Follicular cancer 2 (11%) -B-cell lymphoma 1 (6%)	*Benign:* -Total 18 (42%) -Near-total 9 (21%) -Subtotal 12 (27%) -HT 4 (9%) *Malignant:* -Prophylactic TT for MEN-II 9 (50%) -TT 8 (44.5%) (± LNs dissection) -HT 1 (5.5%)	Transient hypocalcemia 7 Permanent hypocalcemia 4 Transient hoarseness 4 Permanent hoarseness 1 Bilateral RLN injury 1	Not reported	1.4 (range, 0.3–14.5) years
Akkari *et al.*, 2014 (35)	2004–2012	Retrospective study	64	12.5±0.7	Female 48 (75%), male 16 (25%)	Thyroid nodule 32 (49.2%) [2 of them had papillary adenocarcinoma (6.3%)] Toxic MNG 8 (12.3%) Graves' disease 14 (21.5%) Familial MTC 11 (16.9%) [36.3% of them presented one or more sites of C-cell carcinoma]	*Total surgeries 65* -Enucleation (9.2%) -Lobectomy with isthmusectomy (38.5%) -TT (44.6%) -TT and LN dissection (7.7%)	Permanent RLN paralysis 1 (1.1%) Transient hypoparathyroidism 3 (23.5% of the 34 total thyroidectomies) Permanent hypoparathyroidism 5 (14.7%)	Not reported	Range, 6–103 months
Fahrner *et al.*, 2014 (36)	2002–2012	Retrospective study	34	13 (range, 2–17)	Female 30 (83%), male 4 (17%)	Uni- or multinodular goitre 18 (50%) Graves' disease 9 (25%) Malignancy 6 (17%) Genetic tumour predisposition (MEN) 3 (8%)	*Total surgeries 36* -TT 24 (67%) -HT 12 (33%) (2 had a second operation on the contralateral side after initial HT) -+ LN dissection 5 (14%)	Persistent hypoparathyroidism 1 (3%) Persistent recurrent nerve palsy 1 (3%) Transient recurrent nerve palsy 2 (6%)	5 (range, 3–11)	57 (range, 14–130) months
Astl *et al.*, 2014 (37)	1991–2006	Retrospective review study	148	13.7 (range, 7–18)	Female 121 (81.7%), male 27 (18.3%)	*Benign 92 (62.2%)* -Graves' disease and toxic goiter 40 -Toxic adenoma 5 -Nodular goiter 16 -Solitary thyroid node 27	*Total surgeries 56* TT 52 (prophylactic 4) + neck dissections 19 Revision surgeries 4 Totalization of thyroidectomy 1 Totalization of thyroidectomy with neck dissection 2	Transitory hypocalcaemia 33 (58.9%) Permanent hypocalcaemia 4 (7.1%) Lasting hypocalcaemia 1 (1.8%) Scare hypertrophy 9 (16.1%) Unilateral permanent vocal fold paresis 1 (1.8%) (RLN encased by the tumor)	Not reported	37–168 (mean 78.4 months)

Table 1 *(continued)*

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Table 1 *(continued)*

Source	Time period	Study design	Patients (n)	Mean age, years	Sex	Pathology	Type of surgery	Complications	Mean postoperative hospital stay (days)	Follow-up, mean (range)
						-Hashimoto's thyroiditis 3	Neck dissections 2	Bilateral RLN palsy 0		
						-Mechanic syndrome with diffuse goiter 1				
						Malignant 56 (37.8%)				
						Papillary cancer 42 (75%)				
						Follicular cancer 5 (8.9%)				
						Medullar cancer 9 (16.1%)				
						MEN2 3 (5.4%)				
Scholz *et al.*, 2011 (38)	1970–2004	Retrospective review study	175	12	Female 139 (79.4%), male 36 (20.6%)	*Nodules 146 (83%)*	Initial thyroid surgery in 146 patients referred for thyroid nodules	Hypocalcemia 12 (6.9%)	Not reported	Not reported
						-Papillary thyroid cancer 44	nTT 33	Transient hypocalcemia 10 (5.7%)		
						-Follicular thyroid cancer 5	Subtotal thyroidectomy 10	Permanent hypocalcemia 2 (1.1%)		
						-Clear cell cancer 1	Lobectomy 90	Vocal cord paralysis 3 (1.7%)		
						-Medullary thyroid cancer 2	Local excision 13	Transient 1 (0.6%)		
						-Benign nodule(s) 88 (cyst 14, adenoma 66, colloid 8)		Permanent 2 (1.1%)		
						-Thyroiditis 5				
						-Histiocytosis 1				
						Hyperthyroidism 13 (7%)				
						Goiter 13 (7%)				
						MEN II 3 (2%)				
Raval *et al.*, 2009 (39)	2000–2007	Retrospective review study	31	Benign 11.6 (range, 5–14)	Female 25 (80.6%), male 6 (19.4%)	Graves' disease 12	TT 31	Hematoma 0	Benign 2.2 (range, 1–6)	Benign 12.9 (range, 6–34) months
						Hyperthyroidism not classified as Graves' disease 2		Wound infection 0		
				Malignant 13 (range, 8–17)		Multinodular goiter 1		RLN palsy or paralysis 0	Malignant 2.1 (range, 1–6)	Malignant 17.7 (range, 6–52) months
						Papillary thyroid cancer 11		Keloid scar 1		
						Medullary thyroid cancer 3		Transient hypocalcemia 16		
						Follicular thyroid cancer 2		Permanent hypocalcemia 2		
Astl *et al.*, 2004 (40)	1991–2000	Retrospective study	114	Benign 15.5	Female 99 (86.1%), male 16 (13.9%)	Benign 82 (71.9%)	TT 49 (43%)	Transitory hypocalcaemia 27 (23.7%)	Not reported	0–12 months
				Malignant 14.7		Graves' disease 39 (34.2%)	nTT 6 (5.3%)	Lasting hypocalcaemia 1 (0.86%)		
						Toxic adenoma 5 (4.4%)	HT 36 (31.6%)	Keloid scar 12.3%		
						Polynodular goiter 13 (11.4%)	TT 18 (in 4 cases as a two-step procedure)	Unilateral RLN paresis 1		
						Hashimoto thyroiditis 3 (2.6%)	TT and selective modified neck dissection 11 (9.6%) (area II–V), nTT 2			
						Diffuse goiter 1 (0.9%)	Revision surgery 6 (2 completion of TT with selective neck dissection and 3 selective neck dissection, 1 simple completion of thyroidectomy)			
						Malign tumor 32 (28.1%)				
						Papillary cancer 25 (21.9%)				
						Follicular cancer 4 (3.5%)				
						Mononodular goiter 22 (19.3%)				
						Medullar cancer 3 (2.6%)				

PTC, papillary carcinoma; TT, total thyroidectomy; HT, hemithyroidectomy; LN, lymph node; RLN, recurrent laryngeal nerve; MNG, multinodular goiter; MEN, multiple endocrine neoplasia; TSH, thyrotropin; DVT, deep vein thrombosis; VC, vocal cord; MTC, medullary thyroid carcinoma; nTT, near TT.

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Table 2 Descriptive statistics

Criteria	Number of cases	%
Gender	12,421	97.6
Age	12,421	97.6
Indication for surgery	12,008	94.3
Type of surgery	12,109	95.1
Complications	12,728	100
Length of hospitalization	6,279	49.3

Length of hospitalization

The median length of hospitalization postoperatively was 2,35 days (range, 6 hours to 8.8 days) and the extension was due to postoperative hypocalcemia that emerged intravenous calcium supplementation.

Discussion

Key findings

Thyroidectomy is the treatment option for pediatric TC as well as for some benign thyroid conditions like Graves' disease and benign thyroid nodules. In cases where there's an increased risk of future TC, especially within familial syndromes, prophylactic thyroidectomy may be a consideration (19).

Indication for surgery

Bussières *et al.* in a series of 96 patients found that the most common indication for thyroidectomy in children is thyroid nodules (64%), as well Almosallam *et al.* and Chen *et al.* (21,29,33). Dream *et al.* in a study of 55 patients considered Graves' disease as the most common indication for operation (55%), followed by TC (17%), thyroid nodule (11%), multinodular goiter (7%), Hashimoto's disease (6%), and toxic adenoma (4%) (23). According to Fahrner *et al.*, thyroid nodules and Graves' disease were the leading indication for surgery (75%), while malignancy or familiar MEN-2 were indications in 25%; the incidence of TC was 17% (36). Among 271 patients treated by Nordenström *et al.*, indications for surgery were Graves' disease in 78.1%, other benign disease 9.9% and TC 12% (27). In a large series of 175 patients, Scholz *et al.* reported thyroid nodules as the leading indication for thyroidectomy (83%), followed by hyperthyroidism (7%) and goiter (7%); cancer was found in 36%, and thus papillary TC in 85% (38). In Bukarica *et al.* retrospective observational study, the prevalence of TC increased in adolescence (14). Al-Qurayshi *et al.* studied 361 patients operated over a period of 5 years in multiple centers; thyroid diseases included 19% TC, 5.4% MEN-2, 33.6% toxic nodular disease, and 42% non-toxic benign disease (17).

Thyroidectomy was conducted preventively in all cases where there was a familial background of medullary thyroid carcinoma by Akkari *et al.* and in three cases without clinical signs of thyroid tumor with diagnosed *RET* gene mutation by Astl *et al.* (35,37). In Raval *et al.*'s study, the majority of patients who underwent total thyroidectomy for benign conditions either had unsuccessful outcomes with long-term medical treatment (33%) or encountered thyroid storm despite medical management (27%). The efficacy of antithyroid medications like propylthiouracil and methimazole is constrained by issues related to patient compliance, frequent relapses, the onset of hypothyroidism, and the potential for toxicity, including rare instances of fatality. There remains a preference to minimize radioactivity exposure due to theoretical concerns of cancer in radioactive iodine treatment. Besides, total thyroidectomy and near-total thyroidectomy are safe and effective in Graves' disease in children (39).

Pediatric population with TC often present with advanced disease, namely cervical lymph node involvement (31.5%) and lung metastases (5.7%) (3,29,32,37,40).

Type of surgery

Thyroidectomy is more frequent in female patients (up to 80%) and approximately in individuals aged 14 years old (14,17,19,21,24,25).

Procedures of thyroid gland surgery by Almosallam *et al.* included total thyroidectomy (50%), HT (17%), completion thyroidectomy (31%), and subtotal thyroidectomy (2%) (21). Patel *et al.* demographic study of 720 cases stated 245 HT, 376 total thyroidectomies, and 99 total thyroidectomies with central neck dissection (25). Scholz and colleagues reserved near-total thyroidectomy for those patients with confirmed papillary TC. For individuals with unilateral nodules or intermediate cytologic abnormalities (Bethesda III and IV), they recommended lobectomy, followed by completion thyroidectomy if cancer diagnosis is confirmed through operative histology. Preventive total thyroidectomy was performed in 3 patients for MEN-2 syndrome. Another ten patients group underwent completion thyroidectomy for TC after lobectomy (38). According to Spinelli *et al.*, patients with unilateral

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lesions <2 cm, confined to one lobe, not demonstrating extrathyroidal invasion in neck ultrasound, and with no evidence of distant metastasis were selected for lobectomy. Nodal involvement did not rule out lobectomy (32). Astl *et al.* accept HT in differentiated TC conforming to T1 N0 M0 classification. Total thyroidectomy is suggested in medullary cancer or advanced papillary cancer. In case of lymph node metastases, therapeutic neck dissection is recommended (40). Bilić *et al.* advice total thyroidectomy along with occasionalparatracheal neck dissection, while lateral cervical lymph node dissection is only deemed essential when lymph nodes tested positive in fine-needle aspiration (FNA) (22).

Considering that thyroid carcinoma in children often occurs multifocal, and with early lymph node metastasis, Zong *et al.* found that total thyroidectomy did not have higher complication rate compared to lobectomy, except for the length of hospitalization that was shorter in lobectomy group. Contrariwise, the morbidity increased in staged operation following initial lobectomy because of the risk to identify the parathyroid glands and the RLN during the operation. Therefore, they recommended a primary total thyroidectomy in children with unilateral thyroid carcinoma (30). Multifocality in pediatric TC has been proved not to decrease disease free survival in highly selected cases after total thyroidectomy (41).

Type of TC

Papillary carcinoma (PTC) accounts for the majority of cases of TC (4). De Jong *et al.* reported 79.2% papillary and 20.8% follicular carcinoma (FTC), similarly Spinelli and Bilić found 90% PTC (4,20,22,31).

Thyroid nodule histology of 146 patients in Scholz *et al.* study was: TC in 52 cases (Papillary 44, Follicular 5, Clear cell 1, Medullary 2), Benign nodule(s) in 88 cases (Cyst 14, Adenoma 66, Colloid 8, Other 6 (Thyroiditis 5, Histiocytosis 1) (38).

Complications

RLN injury stands out undoubtedly as the most important complication -linked to thyroid surgery (34). Permanent RLN injury is extremely rare in all series reported. De Jong *et al.* reported a rate of 2.8% of RLN injury (20). Spinelli *et al.* reported bilateral RLN injury in two of 250 patients (0.8%) operated for papillary TC requiring an urgent tracheostomy (32). Sinha *et al.* reported two RLNs injury in their series of 61 patients with benign disease. Therefore, they suggested that referring patients for surgery earlier could prevent complications in benign thyroid disease (34). Bukarica *et al.* reported two transient RLN paralyses in their series of 19 operations, which were successfully treated with neurotropic medicines, glucocorticoids and vasodilators (14). In Scholz *et al.* series permanent unilateral vocal cord paralysis was documented in 2 children after resection for malignancy (38). Continuous intraoperative laryngeal nerve monitoring (if only it can be detected) has been used by many authors as standard care (22,39). Although intraoperative RLN monitoring may be applied, RLN palsy could still occur (35). According to American Head and Neck Society, intraoperative RLN monitoring should be discussed in every case of thyroid surgery in pediatric population (42).

The most frequent complication observed in pediatric thyroidectomy is either transient or permanent HP (17,20,33,34). HP leads to hypocalcemia of which its expression will be proportional to its severity and speed of onset. Studies reported transient HP after thyroidectomy in individuals under 18 years old from 13.6% to 34.1%, while permanent HP from 1.5% to 23.8% (17).

De Jong *et al.* claimed that the only factor associated with HP after total thyroidectomy in children was the number of parathyroid glands preserved in situ. HP can occur, and even be permanent, even parathyroid glands remain *in situ* but not intact (e.g., devascularization) (4,20). The frequency of HP in a 39 patients' study by García-García *et al.* was 4 out of 4 when two parathyroids were dissected, 2 out of 10 when only one was dissected, and 6 out of 25 when none were dissected (16). Scholz *et al.* reported permanent HP up to 4.7%, found only in individuals with bilateral resection; no incidence of permanent HP was found in the remaining operations (38). Nordenström *et al.* reported an overall incidence of permanent HP after total thyroidectomy in 273 patients up to 7.3% which is higher compared to previous studies (1.5%). This study did not identify any statistically significant risk factors for permanent hypoparathyroidism, and the autotransplantation of parathyroid glands did not prevented it (27). Chen *et al.* in a cohort of 171 patients reported 12.9% transient HP with 7.0% requiring intravenous calcium correction; only one patient (0.9%) presented with permanent hypoparathyroidism; the risk factors correlated to this included total thyroidectomy, central and bilateral lateral neck dissection, Graves' disease, and malignancy (33). In Sinha *et al.* cohort (61 patients), transient hypocalcemia was infrequent following HT. However, its occurrence

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notably rose with total thyroidectomy, particularly when coupled with lymph node dissection (34). In a series of 29 total thyroidectomies for thyroid malignancy, permanent HP was only seen in patients who underwent lymph node dissection (19).

No correlation between the incidence of HP and indication for surgery was found. Total thyroidectomy and neck dissection carry an increased risk of postoperative hypocalcemia (26).

The increased incidence of postoperative hypocalcemia among patients with Graves' disease in comparison to the remaining nonmalignant group could be ascribed to the localized thyroiditis-induced inflammation, which leads to greater adherence of the parathyroid glands and renders surgical dissection more challenging (33,35).

Van Rooijen *et al.* administered active vitamin D (calcitriol) preoperatively to patients undergoing total thyroidectomy in order to mitigate the risk of postoperative hypocalcemia. They also suggested intraoperative localization of the parathyroid glands by fluorescence (19).

Age, cancer type, type of surgery, reoperation, central neck dissection or lateral neck dissection are not significant reasons for these complications. On the contrary, Scholfield *et al.* showed that N stage and central neck dissection were independent factors for HP and RLN injury (5,10). Aggressive dissection of the central compartment is a risk factor of RLN injury and permanent hypoparathyroidism, or sporadic hemorrhage and readmission to the operation room (23,43).

Explanations of findings

In our study, we found that the most common type of surgery in pediatric population indicated for thyroid surgery was total thyroidectomy, which is in concordance with American and European Thyroid Associations Guidelines (44,45). Papillary thyroid carcinoma seems to be the most common type of TC in pediatric population, which in comparison to adults, pediatric individuals frequently exhibit advanced disease at the time of diagnosis, characterized by increased lymph node involvement, distant metastasis, and multifocal disease (45). There is no consensus about HT and lobectomy oncological outcomes in cases of microcarcinoma and further studies should be applied (45).

In our study, the most common indication for surgery was benign disease, in compliance with most studies in the international literature (17,21,29,38). What should be discussed is that in some studies the main indication for surgery was Graves' disease, for which medical treatment has been already proposed except for the cases of a thyroid nodule in a background of Graves' thyroiditis which indicates FNA and surgery (23,27,36,46). Only Raval *et al.* indicates surgery for Graves' disease after medical treatment failure (39).

Regarding complications, the most common complication found in our systematic review was transient HP in 9.5% of cases, while in the literature this ranges from 13.6% to 34.1% (17). The percentage of permanent HP in our study was 12.2%, which is claimed as high but in concordance with the literature (1.5% to 23.8%) (17). Nordenström *et al.* found the rate of permanent HP 7.3% (27). The RLN injury was found in 1.2% of cases, which justifies its rarity. Among these cases, the percentage of permanent nerve palsy was 16.3%, a high one, meaning that in case of nerve injury in children, the palsy is permanent in the majority of cases, may be due to anatomical differences of the young nerve compared to adult cases. Intraoperative neuromonitoring is advised in pediatric thyroid surgery (42).

Pediatric thyroid surgery should be performed by high-volume endocrine surgeons with experience in both pediatric and adult endocrine surgery and of course in endocrine surgical oncology (47). Pediatric thyroid patients have better outcomes when operated on by higher volume surgeons, while Moreno Alfonso *et al.* suggest that surgeons even if below high-volume threshold but specialized in pediatric surgery can perform thyroidectomies without increase in morbidity and mortality (15,48). Although the UK consensus on pediatric endocrine surgery supports high-volume surgeon to perform thyroidectomies in pediatric population, there is still a debate in the international literature (47,49). In our experience, we suggest pediatric thyroid surgery to be performed by high-volume endocrine surgeons with great experience in both pediatric and adult endocrine surgery.

Conclusions

Thyroidectomy in children and adolescence is a secure and efficient procedure regardless of its being total, HT, or lobectomy. It remains safe even if it is accompanied by central and/or lateral neck dissection. Nowadays, total thyroidectomy has also become the treatment of choice for benign pathology of the thyroid gland. Thyroid gland surgery in patients younger than 18 years is rare, most centers do not have adequate experience, nevertheless

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surgeons have made the procedure simple, not requiring extra armament, complications are rare or extremely rare, length of stay is short, and the burden on the health system is low. It is of great importance to direct pediatric thyroid surgery in reference with adult centers in order to reduce oncological malpractice, risk of complications and recurrence. The family of these younger patients is emotionally charged but this lasts for only 1 to 2 days.

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Footnote

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