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Pediatric Thyroid Cancer at a Referral Center in Colombia: A 7-Year Observational Study (2016–2022)

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Abstract

Background/Objectives: Pediatric thyroid cancer is uncommon, and data from middle-income countries remain limited. This study aimed to describe the epidemiological, clinical, surgical, and histological characteristics of pediatric thyroid cancer at a Colombian referral center. Methods: This retrospective observational study included patients younger than 18 years with histopathologically confirmed thyroid cancer who underwent surgical management between January 2016 and December 2022. Demographic, clinical, imaging, surgical, pathological, and outcome data were collected. Univariate analyses explored factors associated with surgical reintervention and differences between patients with and without fine-needle aspiration cytology (FNAC). Results: Fifty-six patients were included; median age was 15 years and 78.6% were female. A palpable thyroid mass was the most common presentation (50.0%), and 51.8% had lymph node involvement at diagnosis. FNAC was performed in 80.4%, while 19.6% underwent surgery without FNAC. Patients without FNAC had larger nodules and a higher proportion of high-risk disease. Total thyroidectomy with central dissection was the most frequent procedure (57.1%). In exploratory, unadjusted comparisons, reintervention occurred in 16.1% and was associated with lymph node involvement (OR 9.90; $p = 0.0257$) and extrathyroidal extension (OR 11.73; $p = 0.0094$); no association remained significant after Holm adjustment. Estimates are imprecise (9 events) and hypothesis-generating. Papillary thyroid carcinoma was predominant (52/56, 92.9%). No deaths occurred during the index surgical hospitalization; one patient with medullary carcinoma and MEN2B died during follow-up, and vital status was unknown in 60.7% of patients. Conclusions: Pediatric thyroid cancer in this referral cohort was characterized by female predominance, predominance of papillary carcinoma, and substantial locoregional disease at diagnosis. In exploratory, unadjusted analyses, lymph node involvement and extrathyroidal extension were associated with surgical reintervention, but these associations did not remain statistically significant after adjustment for multiple comparisons. Incomplete follow-up limits conclusions regarding long-term outcomes, and postoperative complications were not recorded.

Keywords: pediatric thyroid cancer; thyroid neoplasm; papillary thyroid carcinoma; children; adolescents; fine-needle aspiration cytology; thyroidectomy; Colombia

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1. Introduction

Pediatric thyroid cancer is the most common endocrine malignancy in children and adolescents [1]. Its incidence has increased in recent decades, with annual growth rates exceeding 3% in some regions [2]. Despite this trend, data from middle-income countries, including Colombia, remain limited, hindering the understanding of population-specific characteristics [3].

Children often present with more advanced disease than adults, including a higher frequency of lymph node and distant metastases; however, long-term survival remains excellent, with 5- and 10-year survival rates close to 95% [4,5]. Pediatric tumors more frequently harbor oncogenic rearrangements such as RET/PTC and less often BRAF mutations [4,5].

Most pediatric thyroid cancers present as asymptomatic, euthyroid solitary nodules detected on physical examination or ultrasound. Forty percent of cases are detected by family members, another 40% by medical personnel, and the remaining 20% are identified incidentally during imaging studies performed for cervical lymphadenopathy [1].

The initial evaluation relies on ultrasound to characterize nodule morphology. Ultrasound findings, including microcalcifications, irregular margins, and abnormal vascularity, together with clinical characteristics and nodule size, guide the decision to perform fine-needle aspiration cytology (FNAC) [4]. Given the potential for interobserver variability, particularly in follicular-pattern lesions, evaluation by a pathologist experienced in pediatric thyroid pathology is recommended [4].

In Colombia and other Latin American middle-income countries, information on the epidemiology, clinical presentation, and outcomes of pediatric thyroid cancer is scarce, mostly derived from small series or isolated experiences [3]. This information gap complicates the adoption of local evidence-based guidelines and underscores the importance of gathering medium- and long-term follow-up data. To contribute to regional evidence, we conducted this retrospective observational study at a Colombian pediatric referral center covering 2016–2022. The primary objective was to describe the epidemiological, clinical, surgical, and histological characteristics of thyroid cancer in patients aged <18 years.

2. Materials and Methods

2.1. Study Design

We conducted a retrospective observational study at a pediatric referral hospital in Bogotá, Colombia, including patients diagnosed with histopathologically confirmed thyroid cancer between January 2016 and December 2022. The primary objective of this study was to describe clinical characteristics, evolution, and outcomes. Additionally, we compared factors associated with surgical reintervention. This study is reported in accordance with the STROBE guidelines [6].

2.2. Participants and Selection Criteria

All patients aged < 18 years with thyroid cancer who underwent surgical management during the study period were eligible. Patients were identified retrospectively from the institutional pathology database. All patients identified met the eligibility criteria, and none were excluded for incomplete clinical or pathological records. The selection and follow-up of the study population are shown in Figure 1.

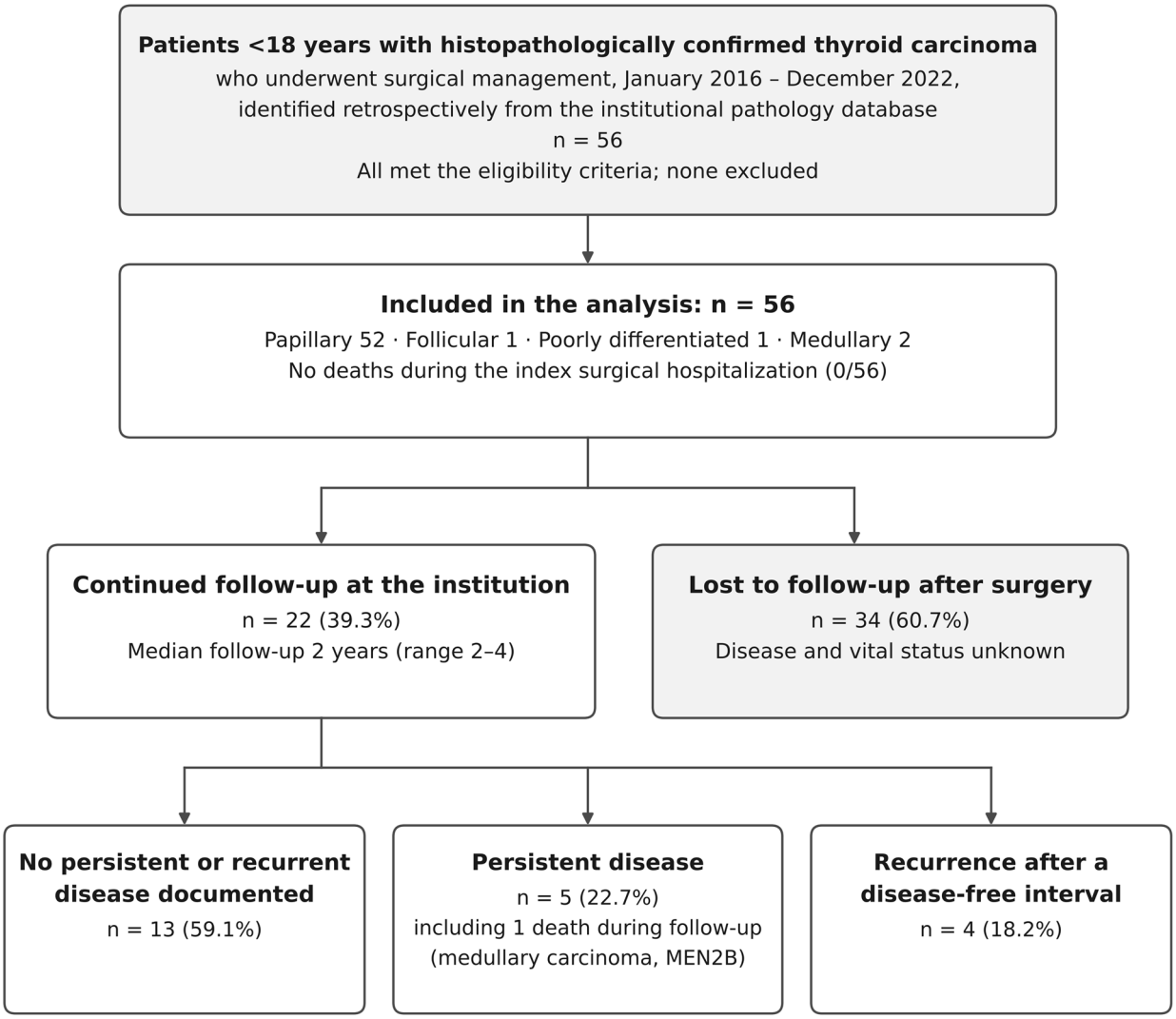

Figure 1. Flow diagram of patient identification and follow-up. Patients were identified from the institutional pathology database; all met the eligibility criteria and none were excluded. Disease status was assessed only in the 22 patients who continued follow-up at the institution. MEN2B, multiple endocrine neoplasia type 2B.

2.3. Variables

We collected information regarding:

Demographic and clinical data: age at diagnosis (in completed years), sex, family history of thyroid neoplasms, clinical presentation, pubertal stage (Tanner, as recorded in the clinical record at the consultation in which surgical treatment was planned), and thyroid function.

Imaging characteristics: ultrasound findings (nodule size, recorded in categories of <1, 1–1.9, 2–2.9, 3–3.9, and ≥4 cm; borders, calcifications, echogenicity, and lymph node involvement) and, when indicated, complementary chest studies (radiography or tomography).

Surgical and pathological data: intervention type (total thyroidectomy with central or modified radical neck dissection, or hemithyroidectomy [lobectomy with isthmectomy]), reinterventions, definitive histological subtype, TNM classification, and American Thyroid Association (ATA) recurrence risk stratification.

Fine-needle aspiration cytology (FNAC): performance (yes/no) and, if performed, cytological results classified according to the Bethesda system.

2.4. Diagnostic and Therapeutic Procedures

All patients with suspected thyroid carcinoma underwent cervical ultrasonography and, when performed, fine-needle aspiration cytology (FNAC). Ultrasonography was performed by pediatric radiologists with experience in childhood oncology. The indication for histopathological study was based on the ultrasound criteria for suspected malignancy established by the American Thyroid Association for pediatric populations [1]. Ultrasound reports followed the ATA 2015 pediatric sonographic criteria for suspicious nodules (presence of suspicious features rather than size thresholds); TI-RADS was not used, as it is not validated in children. Calcifications were recorded as present or absent, without distinction between micro- and macrocalcifications. Cervical lymph node involvement was recorded as present or absent; nodal mapping by compartment was performed only when ultrasound showed extensive nodal disease, so compartment-level data are not available for the whole cohort. Inter-observer agreement was not assessed. Diagnostic procedures included ultrasound-guided FNAC or diagnostic hemithyroidectomy for nodules greater than 4 cm in diameter.

The definitive surgical approach—total thyroidectomy with central dissection or total thyroidectomy with modified radical dissection—was determined according to ultrasound findings and preliminary pathological evaluation. Hemithyroidectomy was performed as a diagnostic procedure, and total thyroidectomy was completed once carcinoma was confirmed on histopathology. In a subset of patients, preoperative FNAC was not performed because of large nodule size and the simultaneous presence of multiple ultrasound features suggestive of malignancy.

2.5. Outcome Definitions

Outcomes included:

Surgical reintervention: any additional procedure related to the thyroid neoplasm performed during the same hospitalization or subsequent admissions; planned second-stage completion of an initial hemithyroidectomy was not counted as reintervention.

Reinterventions were classified by review of the clinical records as planned staged procedures, surgery for persistent disease (disease never cleared after initial treatment), or surgery for recurrent disease (disease reappearing after a disease-free interval).

Recurrence: documented structural disease appearing after a disease-free interval following initial treatment; persistent disease (never cleared after initial treatment) was not counted as recurrence. In patients with differentiated thyroid carcinoma, a disease-free interval required no evidence of disease on neck ultrasonography and no biochemical evidence of disease based on thyroglobulin measurements.

Follow-up surveillance consisted of cervical ultrasound and basal thyroglobulin (stimulated thyroglobulin when indicated); diagnostic radioiodine (123I) whole-body scanning is not available in Colombia and was not used. Mortality: death related to thyroid cancer.

Radioactive iodine eligibility: differentiated (papillary or follicular) thyroid carcinoma with intermediate or high pediatric ATA (2015) risk. TNM staging: patients were restaged according to the American Joint Committee on Cancer (AJCC) 8th edition; T and N categories are reported as recorded in the clinical records (AJCC 7th edition), and nodal status (N) was defined by histopathological examination of the surgical specimen. Patients without chest imaging were classified as having no known distant metastasis, not as having confirmed absence of distant metastasis; accordingly, in this study, M0 and stage I denote no known distant metastasis.

2.6. Statistical Analysis

Data were consolidated in a spreadsheet and analyzed using Stata 18 (StataCorp LLC, College Station, TX, USA). Categorical variables were described as frequencies and percentages and continuous variables as median (Q1–Q3). For univariate comparisons of qualitative variables, we used Fisher's exact test for 2 × 2 tables and the Fisher–Freeman–Halton exact test for tables with more than two categories. For 2 × 2 tables, odds ratios (ORs) are reported with exact (conditional) 95% confidence intervals (CIs). For quantitative variables, we used the Mann–Whitney U test and report the Hodges–Lehmann estimate of the location difference with its 95% CI. Statistical significance was set at $p < 0.05$. All between-group comparisons were exploratory and not preplanned; *p*-values are unadjusted for multiplicity (25 tests), and the result of Holm adjustment is reported for information. Percentages were rounded to one decimal place and are reported with their denominators. No imputation was performed for missing data.

2.7. Ethical Considerations

The study was approved by the institutional ethics committee (see Institutional Review Board Statement). Informed consent was not required for this retrospective study. All information was anonymized to ensure patient confidentiality.

3. Results

3.1. Demographic and Clinical Characteristics

Fifty-six patients were included, with a median age of 15 years (Q1–Q3, 14–16; range 6–17). Females accounted for 78.6% ($n = 44$) of the patients. The age distribution was 57.1% ($n = 32$) in the 11–15 years group. A family history of thyroid cancer in any relative was present in 6 patients (10.7%), 2 (3.6%) of whom had a first-degree relative. Normal nutritional status was present in 58.9% ($n = 33$). Normal thyroid function was observed in 67.9% ($n = 38$). These data are summarized in Table 1.

Table 1. Demographic, clinical, imaging, treatment and outcome characteristics of the cohort ($N = 56$).

Variable	*n* (%)
Demographic and clinical characteristics	
Sex	
Female	44 (78.6%)
Male	12 (21.4%)
Age at diagnosis (years), median (Q1–Q3); range	15 (14–16); 6–17
Age group (years)	
6–10	4 (7.1%)
11–15	32 (57.1%)
16–17	20 (35.7%)
Family history of thyroid cancer	
None	50 (89.3%)
First-degree relative	2 (3.6%)
Second-degree relative	2 (3.6%)
Third-degree relative	1 (1.8%)
More than one relative	1 (1.8%)

Table 1. *Cont.*

Variable	*n* (%)
Nutritional status	
Normal	33 (58.9%)
Risk of overweight	12 (21.4%)
Overweight	4 (7.1%)
Risk of malnutrition	4 (7.1%)
Malnutrition	3 (5.4%)
Pubertal stage (Tanner)	
1	4 (7.1%)
2	2 (3.6%)
3	0
4	48 (85.7%)
5	2 (3.6%)
Thyroid function	
Normal	38 (67.9%)
Subclinical hypothyroidism	13 (23.2%)
Hypothyroidism	3 (5.4%)
Hyperthyroidism	2 (3.6%)
Clinical presentation	
Mode of presentation/reason for referral	
Palpable neck mass	28 (50.0%)
Cervical lymphadenopathy or incidental finding during evaluation for other complaints	11 (19.6%)
Surveillance for hypothyroidism	6 (10.7%)
Goiter	4 (7.1%)
Surveillance for thyroiditis	4 (7.1%)
Surveillance after prior cervical radiotherapy	1 (1.8%)
No information	2 (3.6%)
Symptom duration (months)	
≤6	18 (32.1%)
7–12	12 (21.4%)
13–24	3 (5.4%)
25–36	3 (5.4%)
37–60	0
>60	1 (1.8%)
Not recorded	19 (33.9%)
Imaging findings	
Nodule size on ultrasound	
<1 cm	8 (14.3%)
1–1.9 cm	21 (37.5%)
2–2.9 cm	9 (16.1%)
3–3.9 cm	12 (21.4%)
≥4 cm	6 (10.7%)

Table 1. *Cont.*

Variable	*n* (%)
Lymph node involvement on ultrasound	
Yes	29 (51.8%)
No	27 (48.2%)
Margins	
Irregular	29 (51.8%)
Regular	20 (35.7%)
Not specified	7 (12.5%)
Calcifications	
Present	44 (78.6%)
Absent	12 (21.4%)
Echogenicity	
Hypoechoic	44 (78.6%)
Isoechoic	8 (14.3%)
Hyperechoic	4 (7.1%)
Extrathyroidal extension	
Yes	7 (12.5%)
No	49 (87.5%)
Chest radiography	
Normal	35 (62.5%)
Pulmonary metastasis	1 (1.8%)
Not performed	20 (35.7%)
Chest CT	
Normal	10 (17.9%)
Pulmonary metastasis	6 (10.7%)
Not performed	39 (69.6%)
No information	1 (1.8%)
Diagnosis, treatment and outcomes	
FNAC	
Performed	45 (80.4%)
Not performed	11 (19.6%)
Surgery	
Total thyroidectomy + central neck dissection	32 (57.1%)
Total thyroidectomy + modified radical neck dissection	19 (33.9%)
Hemithyroidectomy followed by total thyroidectomy	5 (8.9%)
Reintervention	9 (16.1%)
TNM stage (AJCC 8th edition) *	
I (no known distant metastasis)	48 (85.7%)
II	6 (10.7%)
III	0
IV	2 (3.6%)
Distant metastasis (M category)	
M0 (no known distant metastasis)	49 (87.5%)
M1	7 (12.5%)

Table 1. *Cont.*

Variable	*n* (%)
ATA risk	
Low	14 (25.0%)
Intermediate	24 (42.9%)
High	18 (32.1%)
Radioactive iodine	
Received, dose documented	16 (28.6%)
Received, dose not recorded	1 (1.8%)
Pending	3 (5.4%)
Not received	20 (35.7%)
Unknown	16 (28.6%)
Disease status during follow-up (patients with follow-up, $n = 22$)	
Persistent disease	5 (22.7%)
Recurrence after a disease-free interval	4 (18.2%)
No persistent or recurrent disease documented	13 (59.1%)
Not assessed (lost to follow-up)	34
Death	
During index hospitalization	0/56
During follow-up	1/22
Vital status unknown (lost to follow-up)	34 (60.7%)

Values are *n* (%) unless otherwise indicated. Percentages use $N = 56$ as denominator, except where another denominator is shown. Disease status was assessed only in the 22 patients who continued follow-up at the institution. * AJCC 8th edition. All patients were younger than 55 years; in differentiated thyroid carcinoma, stage I denotes no known distant metastasis (any T, any N, M0) and stage II denotes distant metastasis (M1); stage IV corresponds to medullary carcinoma (IVA 1, IVC 1). Nine patients without chest imaging were classified as having no known distant metastasis. ATA = American Thyroid Association; CT = computed tomography; FNAC = fine-needle aspiration cytology; Q1–Q3 = first to third quartile.

3.2. Clinical and Imaging Presentation

The most common reason for consultation was a palpable thyroid mass in 50.0% ($n = 28$) of cases, followed by incidental cervical lymphadenopathy in 19.6% ($n = 11$). The interval between symptom onset and thyroid cancer diagnosis was 6 months or less in 18 patients (32.1%), 7–12 months in 12 (21.4%), 13–24 months in 3 (5.4%), 25–36 months in 3 (5.4%), and more than 60 months in 1 (1.8%); duration was not recorded in 19 (33.9%). On ultrasound, nodule size was <1 cm in 8 patients (14.3%), 1–1.9 cm in 21 (37.5%), 2–2.9 cm in 9 (16.1%), 3–3.9 cm in 12 (21.4%), and ≥4 cm in 6 (10.7%) (Figure S1). Lymph node involvement was documented in 51.8% ($n = 29$), calcifications in 78.6% ($n = 44$), irregular margins in 51.8% ($n = 29$), and hypoechogenicity in 78.6% ($n = 44$). Ultrasound nodal status agreed with pathological N in 34 of 49 evaluable patients (69.4%); of 23 patients with negative nodal ultrasound, 13 had nodal metastases on pathology (N1a 5, N1b 7, N1 subcategory not recorded 1), and 2 of 26 with positive nodal ultrasound were pN0. Seven patients were not evaluable (NX 5, TNM not recorded 2). Extrathyroidal extension was identified in 12.5% ($n = 7$). Chest imaging was performed selectively (chest radiography in 36 patients and chest CT in 16; 9 patients had no chest imaging); pulmonary metastases were evidenced by chest radiography in 1.8% ($n = 1$) and chest tomography in 10.7% ($n = 6$); the patient with metastases on radiography was also among those detected by CT (Table 1).

3.3. Initial Cytological Evaluation of the Thyroid Nodule

FNAC was performed in 80.4% of patients, while 19.6% proceeded directly to surgery without FNAC due to high clinical and imaging suspicion. Patients without FNAC had larger nodules (median size category 3–3.9 vs. 1–1.9 cm; Fisher–Freeman–Halton $p = 0.020$), a higher proportion of high-risk disease (63.6% vs. 24.4%; Fisher's exact $p = 0.027$ for high vs. non-high risk; overall ATA risk distribution $p = 0.052$), and a distinct distribution of histological subtypes ($p = 0.035$). No differences were observed in terms of age, sex, or other clinical or imaging variables (Table 2). These comparisons are descriptive: the larger nodules and higher ATA risk in the no-FNAC group reflect the criteria used to proceed directly to surgery, and all comparisons were exploratory and unadjusted. In the FNAC group, 13 patients (28.9%) had benign or indeterminate cytology (Bethesda II–IV): 3 cases (6.7%) were Bethesda II, 4 (8.9%) Bethesda III, and 6 (13.3%) Bethesda IV (Table S5).

Table 2. Characteristics of patients with and without preoperative FNAC ($N = 56$).

Variable	Without FNAC ($n = 11$)	With FNAC ($n = 45$)	*p*
Sex			1.00
Female	9 (81.8)	35 (77.8)	
Male	2 (18.2)	10 (22.2)	
Age at diagnosis (years), median (range)	15 (9–17)	15 (6–17)	0.99
Age group (years)			0.77
6–10	1 (9.1)	3 (6.7)	
11–15	7 (63.6)	25 (55.6)	
16–17	3 (27.3)	17 (37.8)	
Pubertal stage (Tanner)			1.00
1	1 (9.1)	3 (6.7)	
2	0	2 (4.4)	
3	0	0	
4	10 (90.9)	38 (84.4)	
5	0	2 (4.4)	
Thyroid function			0.67
Normal	7 (63.6)	31 (68.9)	
Subclinical hypothyroidism	4 (36.4)	9 (20.0)	
Hypothyroidism	0	3 (6.7)	
Hyperthyroidism	0	2 (4.4)	
Nodule size category on ultrasound, median	3–3.9 cm	1–1.9 cm	0.020
Number of nodules, median (range)	1 (1–3)	1 (1–4)	0.51
Lymph node involvement on ultrasound			1.00
Yes	6 (54.5)	23 (51.1)	
No	5 (45.5)	22 (48.9)	
Margins			0.085
Irregular	4 (36.4)	25 (55.6)	
Regular	7 (63.6)	13 (28.9)	
Not specified	0	7 (15.6)	
Calcifications			0.69
Present	8 (72.7)	36 (80.0)	
Absent	3 (27.3)	9 (20.0)	
Extrathyroidal extension			0.61
Yes	2 (18.2)	5 (11.1)	
No	9 (81.8)	40 (88.9)	
Echogenicity			0.45
Hypoechoic	8 (72.7)	36 (80.0)	
Isoechoic	3 (27.3)	5 (11.1)	
Hyperechoic	0	4 (8.9)	
Surgery			1.00
Total thyroidectomy + central neck dissection	6 (54.5)	26 (57.8)	
Total thyroidectomy + modified radical neck dissection	4 (36.4)	15 (33.3)	
Hemithyroidectomy followed by total thyroidectomy	1 (9.1)	4 (8.9)	

Table 2. *Cont.*

Variable	Without FNAC ($n = 11$)	With FNAC ($n = 45$)	p
Reintervention			1.00
Yes	2 (18.2)	7 (15.6)	
No	9 (81.8)	38 (84.4)	
Disease status (patients with follow-up) †			0.23
Persistent disease	2/4 (50.0)	3/18 (16.7)	
Recurrence after a disease-free interval	1/4 (25.0)	3/18 (16.7)	
No persistent or recurrent disease documented	1/4 (25.0)	12/18 (66.7)	
Not assessed (lost to follow-up), n	7	27	
Histology			0.035
Classic papillary carcinoma	3 (27.3)	22 (48.9)	
Papillary carcinoma, mixed classic and follicular patterns	2 (18.2)	10 (22.2)	
Papillary carcinoma, follicular subtype	2 (18.2)	6 (13.3)	
Papillary carcinoma, diffuse sclerosing subtype	0	4 (8.9)	
Papillary carcinoma, tall cell subtype	3 (27.3)	0	
Follicular carcinoma (minimally invasive)	0	1 (2.2)	
Medullary carcinoma	1 (9.1)	1 (2.2)	
Poorly differentiated carcinoma	0	1 (2.2)	
ATA risk			0.052 ‡
High	7 (63.6)	11 (24.4)	
Intermediate	2 (18.2)	22 (48.9)	
Low	2 (18.2)	12 (26.7)	

Values are *n* (%) unless otherwise indicated; percentages are calculated within each column. Comparisons were performed using the Mann–Whitney U test for continuous variables (Hodges–Lehmann estimate of the location difference, without minus with FNAC: age 0 years, 95% CI −2 to 1; number of nodules 0, 95% CI 0 to 0), Fisher's exact test for 2 × 2 tables, and the Fisher–Freeman–Halton exact test for larger tables. All comparisons are exploratory and unadjusted for multiplicity. † Disease status was assessed only in the 22 patients who continued follow-up; percentages use these patients as the denominator. ‡ Overall distribution; high vs. non-high risk, Fisher's exact $p = 0.027$. ATA = American Thyroid Association; CI = confidence interval; FNAC = fine-needle aspiration cytology.

In this subgroup, surgical decisions were based on high-risk ultrasound characteristics (calcifications, lymph node involvement), with total thyroidectomy performed in nine patients and hemithyroidectomy in four, followed by completion thyroidectomy. As the cohort included only patients with histologically confirmed carcinoma, these cases do not inform the accuracy of cytology; final histopathology in this subgroup was predominantly classic papillary carcinoma, with one follicular carcinoma and one poorly differentiated carcinoma.

Molecular testing was not part of routine diagnostic work-up. BRAF V600E testing was performed in the first 17 consecutive patients of the series as part of a funded institutional research project; testing was not continued after the project ended. The assay was real-time PCR for BRAF V600E (COBAS 4800, Roche) on DNA extracted from formalin-fixed paraffin-embedded tumor tissue. We identified the BRAF V600E mutation in a 15-year-old female patient who presented with a mixed classic and follicular histological pattern, as well as cervical and pulmonary metastases.

Relevant medical histories were identified in two patients: one Hodgkin lymphoma survivor who had undergone cervical radiotherapy 10 years prior to receiving a thyroid cancer diagnosis, and another patient with a germline PTEN mutation. Cytology was malignant in 6 patients and suspicious for malignancy in 26; surgery proceeded without a diagnostic cytological result in the remaining 24. These 24 patients (42.9%; 11 without FNAC and 13 with benign or indeterminate cytology, Bethesda II–IV) underwent surgery based on clinical and ultrasound criteria.

3.4. Surgical Management, Adjuvant Treatment, and Outcomes

Total thyroidectomy with central dissection was the most frequent procedure (57.1%, $n = 32$); 33.9% ($n = 19$) required modified radical dissection, and 8.9% ($n = 5$) initially underwent hemithyroidectomy, subsequently completing total thyroidectomy with dissection. Reintervention occurred in 16.1% ($n = 9$): 5 for persistent disease, 3 for recurrent disease, and 1 planned staged procedure (a planned second-stage neck dissection); one patient operated for recurrence had also undergone completion thyroidectomy, which was not counted as reintervention. Patients had one to three additional procedures. In the reintervention group, eight binary factors were evaluated; lymph node involvement (OR 9.90; $p = 0.0257$) and extrathyroidal involvement (OR 11.73; $p = 0.0094$) were associated with reoperation in unadjusted analysis. Associations with the other factors (sex, pulmonary metastasis, size ≥ 2 cm, size ≥ 1 cm, irregular borders, and calcifications) were inconclusive ($p > 0.05$); pulmonary metastasis was assessed only among the 16 patients who underwent chest CT. The values are presented in Table 3. When the analysis was restricted to the 8 reinterventions for persistent or recurrent disease, 7 of the 8 patients had lymph node involvement (1/27 vs. 7/29; OR 8.27; Fisher $p = 0.052$), and extrathyroidal extension remained associated with reoperation (4/49 vs. 4/7; OR 15.0; $p = 0.0055$) (Table S3). Lymph node involvement and extrathyroidal extension overlapped: all 7 patients with extrathyroidal extension also had lymph node involvement. Reintervention for any cause occurred in 1 of 27 patients (3.7%) with neither factor, 4 of 22 (18.2%) with lymph node involvement alone, and 4 of 7 (57.1%) with both (Table S4). All comparisons in Tables 2 and 3 were exploratory and unadjusted for multiplicity (25 tests); after Holm adjustment, no association remained statistically significant.

Table 3. Factors associated with reintervention: univariate analysis.

Factor	Factor Absent: No Reintervention	Factor Absent: Reintervention	Factor Present: No Reintervention	Factor Present: Reintervention	OR (Exact 95% CI)	*p*-Value
Sex (absent = male; present = female)	11	1	36	8	2.444 (0.27–118.2)	0.6662
Pulmonary metastasis on chest CT ($n = 16$)	6	4	5	1	0.300 (0.01–4.88)	0.5879
Nodule size ≥ 2 cm	27	2	20	7	4.725 (0.77–50.00)	0.0733
Nodule size ≥ 1 cm	7	1	40	8	1.400 (0.14–70.88)	1.000
Lymph node involvement	26	1	21	8	9.905 (1.13–456.0)	0.0257
Irregular margin (absent = regular or not specified)	25	2	22	7	3.977 (0.65–42.17)	0.1456
Calcifications	10	2	37	7	0.946 (0.15–10.73)	1.000
Extrathyroidal involvement	44	5	3	4	11.733 (1.42–98.36)	0.0094

Values are numbers of patients ($N = 56$; 9 reinterventions). ORs are sample odds ratios with exact (conditional) 95% CIs; *p*-values from Fisher's exact test for 2 × 2 tables. Pulmonary metastasis was evaluated only among the 16 patients who underwent chest CT. A *p*-value < 0.05 was considered statistically significant.

Final histopathological analysis revealed papillary thyroid carcinoma in 52 patients (92.9%), medullary carcinoma in 2 (3.6%), follicular carcinoma in 1 (1.8%), and poorly differentiated carcinoma in 1 (1.8%). Among the 52 papillary carcinomas (WHO 2022 subtypes), classic papillary carcinoma was the most frequent (25/52, 48.1%), followed by papillary carcinoma with mixed classic and follicular patterns (12/52, 23.1%), the follicular subtype (8/52, 15.4%, including 2 with infiltrative pattern), the diffuse sclerosing subtype (4/52, 7.7%), and the tall cell subtype (3/52, 5.8%). The follicular carcinoma was minimally invasive. Of the patients with medullary carcinoma, one had multiple endocrine neoplasia type 2B (MEN2B) and the other was a sporadic non-syndromic case. The patient with poorly differentiated carcinoma was an adolescent with a family history of thyroid carcinoma in a second-degree relative (maternal grandmother) of unspecified subtype who died from the disease; this patient was lost to follow-up.

According to ATA risk stratification, 14 patients (25.0%) were low risk, 24 (42.9%) intermediate risk, and 18 (32.1%) high risk. The T, N, and M components are shown in Table S2. Distant metastases (M1) were present in 7 patients (12.5%): pulmonary metastases in 6 patients with differentiated carcinoma, all classified as stage II, detected on chest CT in 5 and on the post-ablation radioiodine scan in 1 patient whose chest radiograph was normal and who had not undergone chest CT; and pulmonary, pleural, mediastinal and hepatic metastases in the patient with MEN2B (stage IVC). The remaining 49 patients had no known distant metastasis, including 9 without chest imaging, in whom the absence of distant metastasis was not confirmed by imaging. Restaging according to the AJCC 8th edition did not change any stage assignment. Mortality was 1.8% ($n = 1$) and was associated with advanced medullary carcinoma (Table 1).

In terms of follow-up, only 39.3% ($n = 22$) of patients continued to attend follow-up visits at the institution. The median follow-up period was 2 years (range 2–4 years). Disease status was evaluated exclusively in this subgroup. Structural disease was documented during follow-up in 9 of the 22 patients (40.9%), and no persistent or recurrent disease was documented in 13 (59.1%). Following individual review of the clinical records, 5 patients had persistent disease (5/22, 22.7%) and 4 had recurrence after a disease-free interval documented by neck ultrasonography and thyroglobulin (4/22, 18.2%). The patients with persistent disease included the patient with MEN2B, who had stage IVC medullary carcinoma at diagnosis and died during follow-up, and a patient with pulmonary uptake on the post-ablation scan whose thyroglobulin became undetectable during the first year and later rose with new cervical lesions; this patient was classified as having persistent disease because a complete structural response of the pulmonary metastases had not been demonstrated, despite an initial favorable biochemical response. Six of the 9 patients underwent surgical reintervention: 3 with persistent disease and 3 with recurrence. One patient with recurrence had previously undergone surgery for persistent disease, followed by a documented disease-free interval before the recurrence. In 3 of the 4 patients with recurrence, radioactive iodine had been delayed or not administered; these observations are descriptive. Disease status could not be established for the remaining 34 patients (60.7% of the cohort); these proportions therefore describe only patients with available follow-up and should not be interpreted as cohort-wide estimates. Baseline characteristics of patients with and without follow-up are compared in Table S1. No statistically significant differences were found, although the comparison is underpowered and patients with follow-up had numerically more advanced disease. Reintervention was required in 16.1% ($n = 9$) of patients, with one to three additional procedures per patient. No deaths occurred during the index surgical hospitalization (0/56). Among the 22 patients with follow-up, one died of advanced medullary carcinoma associated with MEN2B after three years of follow-up;

vital status was unknown in the remaining 34 patients (60.7%), so the overall mortality of 1.8% ($n = 1$) is a lower bound.

Radioactive iodine (RAI) eligibility was defined as differentiated (papillary or follicular) thyroid carcinoma with intermediate or high ATA risk ($n = 39$; patients with medullary or poorly differentiated carcinoma were not included). Among eligible patients, 16 (41.0%) received RAI: 15 with a documented dose and 1 without a recorded dose. For the remaining 23 (59.0%), RAI was clinically indicated, but treatment was recorded as not administered, pending, or undocumented in the available clinical records. One patient with low-risk papillary carcinoma also received RAI. Administered doses ranged from 30 to 123 mCi.

4. Discussion

Thyroid carcinoma is the most common endocrine neoplasm in childhood, with an estimated incidence of 1.1 cases per 100,000 inhabitants under 18 years of age; papillary thyroid carcinoma (PTC) accounts for approximately 86% of pediatric cases, followed by follicular (9%) and medullary carcinoma (4%) [4].

This study, conducted at a Colombian pediatric referral center, describes a series of 56 patients aged < 18 years with thyroid cancer treated over a 7-year period. In our study, classic papillary thyroid carcinoma was the most frequent histological subtype (25/52 papillary carcinomas, 48.1%). According to ATA risk stratification, 24 of 56 cases (42.9%) were classified as having intermediate risk, with a high proportion of locally advanced disease at diagnosis (51.8% with lymph node involvement). Follow-up was available in 22 patients; persistent or recurrent disease was documented in 9 of them (40.9%), including recurrence after a documented disease-free interval in 4 (18.2%); disease status was unknown in the 34 patients without follow-up, so no cohort-level proportion is reported.

No deaths occurred during the index hospitalization, and one death was recorded during follow-up (1.8%, a lower bound), corresponding to advanced medullary carcinoma. Lymph node involvement was consistent with the international literature, whereas persistent disease was frequent among patients with follow-up; survival could not be compared because vital status was unknown in 34 patients. Major pediatric thyroid cancer cohorts with complete follow-up have reported long-term survival between 95% and 98% [1].

The demographic distribution in our series, with 78.6% female patients and a median age of 15 years, aligns with international studies documenting marked female predominance and incidence peaks in adolescence for pediatric thyroid cancer [5].

Six patients (10.7%) had a family history of thyroid cancer in any relative, and 2 (3.6%) of them in a first-degree relative. First-degree relatives of patients with differentiated thyroid cancer have a fourfold increased risk of the disease, and close surveillance appears most beneficial in kindreds with three or more affected members [4]; recording a detailed family history therefore remains relevant in this population.

As pediatric thyroid cancer is frequently asymptomatic, diagnosis is often established in advanced phases. In our cohort, the most common clinical manifestation was palpable thyroid mass (50.0%), followed by incidental cervical lymphadenopathy (19.6%). These findings align with those of a previous series where up to half of pediatric cases were diagnosed after nodule detection during physical exploration or lymph node findings on clinical examination [4].

Symptom duration was recorded in 37 patients and was 6 months or less in 18 (32.1% of the cohort); the remaining documented durations ranged from 7 months to 6 years. Although socioeconomic and access-related variables were not collected in this study, delays in diagnosis may reflect inequalities in timely diagnostic access in middle-income

contexts, where systematic use of ultrasound and fine-needle aspiration cytology (FNAC) may be limited by logistical, economic, or professional training barriers.

Regarding nutritional status, 58.9% of patients presented normal values; however, 21.4% were classified as at risk of overweight. This finding is relevant given the growing evidence suggesting a possible association between excess adiposity and thyroid nodule appearance in pediatric populations, particularly in pubertal girls, although the literature remains heterogeneous and occasionally contradictory [7].

Ultrasound was the primary diagnostic tool for thyroid nodule characterization in our cohort. Nodules measured ≥2 cm in 48.2% of patients, 51.8% presented lymph node involvement, and 78.6% showed calcifications. These findings align with the literature, indicating that pediatric patients with differentiated thyroid cancer typically present with more advanced disease at diagnosis, with a greater frequency of lymph node involvement and, in some cases, pulmonary metastases [8]. Ultrasound underestimated nodal disease in this series, as 13 of 23 patients with negative nodal ultrasound had pathological nodal metastases; because the extent of nodal dissection depended on ultrasound findings, this comparison is subject to verification bias and does not estimate the diagnostic accuracy of ultrasound. In our series, extrathyroidal involvement was documented in 12.5% of cases, a condition associated with an increased risk of lymph node metastases [9].

This series originated from a fourth-level institution and a national pediatric oncology referral center in Colombia. At this institution, ultrasound studies were performed and interpreted by a pediatric radiology team highly specialized in oncological pathology. Because this series included only patients with histologically confirmed carcinoma, nodules with suspicious ultrasound features that proved benign were not captured, and the diagnostic accuracy of ultrasound or cytology cannot be inferred from these data. Chest imaging was performed selectively, in accordance with the ATA 2015 pediatric guidelines, which do not require chest imaging in all patients: chest radiography and/or CT may be considered in children with substantial cervical lymph node disease, whereas routine chest CT is not recommended in those with minimal neck disease, because pulmonary metastases are likely to be identified at postoperative staging [1]. Nine patients had no chest imaging: 7 of them had no lymph node involvement on preoperative ultrasound, and in the remaining 2, the decision was individualized, considering the extent of cervical disease, the indication for radioactive iodine therapy, and the need to limit diagnostic radiation exposure in children. The absence of chest imaging precludes retrospective determination of pulmonary metastasis at diagnosis in these patients. These 9 patients were initially classified as MX, following the TNM classification reproduced in the 2015 ATA pediatric guidelines, which includes this category for distant metastasis not assessed [1]. In line with current AJCC staging rules, in which the MX designation is no longer used and the clinical M category does not require imaging, they were reclassified as M0 for this report. In these patients, M0 therefore indicates no clinical evidence of distant metastasis rather than its exclusion by imaging.

FNAC is the standard initial diagnostic tool for pediatric thyroid nodules, with reported sensitivity of 94% and specificity of 81–100% [10,11].

Pediatric guidelines accept proceeding to surgery without repeat cytology in selected situations, such as indeterminate cytology, large nodules (>4 cm), nodular growth, or compressive symptoms [1]. In our series, 42.9% of patients underwent surgery without a diagnostic cytological result (11 without FNAC; 13 with benign or indeterminate cytology, Bethesda II–IV), a decision taken case by case on the basis of clinical and ultrasound suspicion, guideline criteria, and the risk of loss to follow-up; this includes an adolescent with MEN2B and metastatic medullary carcinoma, for whom total thyroidectomy with lymph node dissection is standard management. Because the cohort includes only patients with confirmed carcinoma, these data cannot validate the omission of FNAC, and the

differences between patients with and without FNAC reflect selection rather than a property of the disease.

Series from other settings have reported comparable malignancy rates in children operated with or without preoperative FNAC [12,13]; those data and ours are retrospective and subject to selection bias, and molecular testing of indeterminate nodules, which could refine patient selection, is not routinely available in our setting [4].

Current pediatric thyroid cancer management is risk-adapted; despite the greater frequency of metastases at diagnosis, mortality is low, thus seeking selective aggressive treatment while avoiding overtreatment. In our cohort, total thyroidectomy with central dissection was the most frequent approach (57.1%) and modified radical dissection was indicated in 33.9%, in line with guidelines prioritizing total resection in high-risk or confirmed PTC given the elevated locoregional burden in patients aged < 18 years. Reintervention was required in 16.1% (one to three additional procedures per patient), within the 10–30% described in pediatric series. Among patients with follow-up, recurrence after a documented disease-free interval (18.2%) was within the range reported in pediatric series (10–30%), whereas persistent or recurrent disease was documented in 40.9%; given the small denominator and incomplete, possibly selective follow-up, these proportions are descriptive. The frequency of persistent disease, possibly reflecting referral selection, supports prolonged surveillance and individualized surgical decisions.

In our cohort, the reintervention rate was 16.1%, with lymph node involvement (OR ≈ 10) and extrathyroidal extension (OR ≈ 12) associated with higher reoperation probability in unadjusted exploratory analyses; no association remained statistically significant after Holm adjustment for the 25 comparisons. Because most reinterventions were neck dissections for persistent or recurrent nodal disease, the association with lymph node involvement is partly circular; when the analysis was restricted to reinterventions for persistent or recurrent disease, the association with extrathyroidal extension persisted, whereas that with lymph node involvement was no longer statistically significant (Table S3). Although lymph node involvement and extrathyroidal extension carry different weights in ATA risk stratification (limited nodal disease may remain low risk, whereas extrathyroidal extension increases risk), in this cohort the two overlapped: all 7 patients with extrathyroidal extension also had lymph node involvement (Table S4). Given the number of events, no multivariable model was fitted. This pattern is consistent with the literature linking greater initial extension with the need for additional surgery: a classic pediatric series ($n = 74$) identified age < 15 years and cervical lymphadenopathy as predictors of reoperation [14].

The series by Puga et al. reported a persistence/recurrence of 31.6%, at the upper limit described by other cohorts (≈17–30%) [15]. This performance suggests that estimating the real metastatic risk and postsurgical events requires more than lymph node or distant involvement at diagnosis; additional predictors are needed. Postoperative complications were not among the variables collected in this study, so surgical morbidity could not be assessed. Such morbidity is not negligible in children: a Brazilian series of 59 pediatric thyroidectomies for benign and malignant disease reported transient hypoparathyroidism in 22 patients, permanent hypoparathyroidism in 8, and vocal fold paralysis in 3 [16].

Molecular data in our series are too sparse for interpretation: BRAF V600E was tested in only 17 patients and found in one, who was lost to follow-up.

In our series, 16 of 39 eligible patients (41.0%) received radioactive iodine (RAI), 15 of them with a documented dose, in line with the current approach reserving it for intermediate/high risk (pediatric ATA) and extensive or persistent locoregional disease. Its use in children remains prudent due to their greater susceptibility to late effects, including secondary neoplasms, although it may be useful for tumor burden reduction when clearly indicated. For the remaining 23 eligible patients, treatment was recorded as not administered,

pending, or undocumented; incomplete follow-up, a frequent reality in middle-income countries, is a plausible contributor, although this could not be established individually. Regarding systemic treatment, a tyrosine kinase inhibitor with palliative intent was considered for the adolescent with MEN2B and metastatic medullary carcinoma; the family declined treatment.

Regarding mortality, no deaths from papillary thyroid carcinoma were recorded during the index hospitalization or among patients with follow-up; because vital status was unknown in 34 patients, this cannot be compared with the long-term survival of 95–98% reported in series with complete follow-up [1]. The only death corresponded to medullary carcinoma in an adolescent with multiple endocrine neoplasia type 2B, diagnosed at age 16 (stage IVC) with functional metastases and chronic diarrhea, involving cervical nodes, lung, liver, and brain; she carried a germline RET p.M918T mutation, with an aggressive clinical course and unfavorable prognosis, consistent with the literature reporting 21% 10-year survival for stage IV medullary carcinoma [17].

This study has limitations inherent to its retrospective design, including the inability to perform multivariable analysis and the lack of prolonged follow-up, which prevents accurate estimation of long-term outcomes (e.g., biochemical recurrence and disease-free survival). Thyroglobulin and anti-thyroglobulin antibodies were part of follow-up monitoring in patients followed at the institution, but these values and post-therapy whole-body scan results were not systematically collected in the study database and are not reported. Ultrasound findings were not graded with a standardized reporting system, microcalcifications were not distinguished from macrocalcifications, and nodal compartment data were not available for all patients. Pubertal stage was recorded retrospectively and may not reflect individual examination in all patients. Pulmonary metastasis prevalence is unknown in patients not imaged (9 patients had neither chest CT nor chest radiography). Health system fragmentation and frequent interinstitutional transfers complicated structured follow-up and the capture of late events. Postoperative complications were not systematically recorded, as noted above, and calcitonin and carcinoembryonic antigen were used in the management of the two patients with medullary carcinoma but were not collected in the study database.

5. Conclusions

This seven-year retrospective study conducted at a pediatric oncology referral center in Colombia highlights the substantial burden of locoregional disease at the time of thyroid cancer diagnosis, with lymph node involvement in 51.8% of patients and extrathyroidal extension in 12.5%. Surgical reintervention was required in 16.1% of cases. Lymph node involvement and extrathyroidal extension were associated with reintervention in exploratory, unadjusted analyses; however, neither association remained statistically significant after correction for multiple comparisons.

Overall, 42.9% of patients underwent surgery without a diagnostic cytological result, based on clinical and ultrasonographic findings. However, the study design does not allow conclusions regarding the appropriateness or diagnostic accuracy of this approach. Persistent or recurrent structural disease was documented in 9 of the 22 patients with available follow-up (40.9%), including recurrence after a documented disease-free interval in 4 (18.2%), whereas outcomes could not be ascertained for the remaining 34 patients.

In addition to its retrospective design, a major limitation of this study was the substantial loss to follow-up (60.7%), which may have been influenced by socioeconomic factors and barriers to healthcare access and continuity of care affecting the population served. Although these factors were not directly assessed, they warrant consideration when interpreting the findings, as incomplete follow-up precludes reliable estimation of recurrence and survival outcomes for the overall cohort.

These findings underscore the importance of individualized, risk-adapted management and the need to strengthen long-term surveillance, continuity of care, and coordination across healthcare institutions while accounting for the socioeconomic circumstances of patients and the challenges faced by healthcare systems in middle-income countries.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/pediatric18060155/s1, Figure S1. Distribution of thyroid nodule size on ultrasound (N = 56). Size was recorded in categories in the institutional database. Table S1. Baseline characteristics of patients with and without follow-up. Table S2. TNM components and stage. Table S3. Factors associated with reintervention for persistent or recurrent disease ($n = 8$): univariate analysis. Table S4. Cross-tabulation of lymph node involvement and extrathyroidal extension with reintervention. Table S5. Cytological results of fine-needle aspiration according to the Bethesda System for Reporting Thyroid Cytopathology ($n = 45$).

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Informed Consent Statement: Informed consent was not required for this retrospective study. All information was anonymized to ensure patient confidentiality.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to confidentiality and privacy restrictions related to patient clinical information. Access to the data may be granted upon reasonable request and subject to appropriate institutional and ethical considerations.

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Abbreviations

ATA	American Thyroid Association
CI	confidence interval
FNAC	fine-needle aspiration cytology
MEN2B	multiple endocrine neoplasia type 2B
OR	odds ratio
PTC	papillary thyroid carcinoma
RAI	radioactive iodine
TBSRTC	The Bethesda System for Reporting Thyroid Cytopathology
TNM	tumor, node, metastasis

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