

More Than Just Stuck in the Middle: Papillary Thyroid Cancer of the Isthmus Presents with More Aggressive Features

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Introduction:

Papillary thyroid cancer (PTC) originating from the isthmus is often more aggressive and may be associated with worse prognosis. Given the central location and unclear lymphatic drainage in these tumors, the extent of surgery remains controversial with no clear consensus guidelines for isthmusectomy (TI), lobectomy and isthmusectomy (TL), or total thyroidectomy (TT). The aim of this study was to examine the surgical management and outcomes of isthmus PTC.

Materials and Methods:

A retrospective review was performed of two tertiary referral centers of patients who underwent thyroidectomy between 2013-2021 with final pathology noting PTC within an isthmus nodule. This cohort included patients with benign or malignant indications for surgery, including metastatic lymphadenopathy, and nodules that were within or extended into the isthmus. Preoperative tumor characteristics, surgical pathology, and postoperative outcomes were compared.

Results:

A total of 140 patients underwent surgery for isthmus PTC in the study period. Median age was 46 years (IQR 35.5, 57.7) and 62.9% were female. Total thyroidectomy (TT) was most frequently performed, followed by lobectomy (TL), and isthmusectomy (TI).

Preoperative characteristics:

- Most patients who underwent TT (82%) had Bethesda V/VI nodules (TL:58%; TI:67%).
- Patients who underwent TI (28%) more frequently had Bethesda III/IV nodules (TT:1%; TL:17%; $p < 0.001$).

Table 1. Preoperative Characteristics by Surgical Approach

	Isthmusectomy (n=18)	Lobectomy + Isthmusectomy (n=24)	Total thyroidectomy (n=98)	P-Value
Median Tumor size on Imaging (cm)	1.0	1.2	1.6	0.40
Multiple Nodules on Imaging	3 (17%)	17 (71%)	77 (74%)	0.002
Enlarged Lymph Nodes on Imaging	0	1 (4%)	30 (31%)	<0.001
Central Neck Dissection	0	1 (4%)	67 (68%)	-
Lateral Neck Dissection	0	0	20 (20%)	0.02

Pathology findings:

- 37 (26.4%) patients had PTC variants (tall cell, follicular, solid, oncocytic, trabecular, warthin-like, infiltrative follicular, and diffuse sclerosing variants).
 - There was no difference in the incidence of these variants by surgical approach.
- 100 patients had lymph nodes removed on final pathology; 63 were node-positive
 - Of TT patients, 19 had both CND and lateral neck dissections.

Table 2. Pathology Findings by Surgical Approach

	Isthmusectomy (n=18)	Lobectomy + Isthmusectomy (n=24)	Total thyroidectomy (n=98)	P-Value
Tumor size (cm)	1.1	1.1	1.5	0.008
Multifocality	2 (11%)	12 (50%)	56 (57%)	0.001
Extrathyroidal Extension	2 (11%)	3 (13%)	28 (29%)	0.10
Lymphovascular Invasion	1 (6%)	2 (8%)	15 (15%)	0.41
Lymph Node Involvement	2	4	57	0.02
Persistent/Recurrent Disease	2	0	8	0.30

Postoperative outcomes:

Table 3. Characteristics of patients who underwent completion thyroidectomy

Case #	Initial Operation	Multifocal	Lymphovascular Invasion	Extrathyroidal Extension	PTC Variant
1	Isthmusectomy	Yes	Yes	Yes	Classic
2	Isthmusectomy	Yes	No	No	Tall cell
3	Lobectomy	No	Yes	Yes	Encapsulated follicular variant with capsular invasion
4	Lobectomy	Yes	No	No	Tall cell

Table 4. Postoperative Outcomes by Surgical Approach

	Isthmusectomy (n=18)	Lobectomy + Isthmusectomy (n=24)	Total thyroidectomy (n=98)	P-Value
Transient Hypoparathyroidism	0	0	21 (21%)	0.005
Permanent Hypoparathyroidism	0	0	5 (5%)	0.33
Hematoma	0	0	0	-
Nerve Injury	0	1 (4%)	1 (1%)	0.44
Reoperation	2 (11%)	2 (8%)	4 (4.1%)	0.41
Thyroid Hormone Replacement	1 (10%)	9 (56%)	-	0.018

Conclusion:

Isthmus PTC presents with high-risk pathologic variants in $\sim 1/3$ and positive nodes in $\sim 2/3$ of patients who had lymph nodes removed. TI may be appropriate in small tumors, with similar reoperation rates as TL and lower rates of thyroid hormone replacement.