

Research Article

Efficacy of thyroid isthmusectomy and its outcomes in patients with single isthmic papillary thyroid carcinoma: a single-center observational study

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Abstract

Background; Despite the total thyroidectomy is recommended for isthmic papillary thyroid carcinoma (PTC), the gold standard surgery is not well-known. We aimed to investigate the efficacy of isthmusectomy and its outcomes in the treatment of isthmic PTC. **Methods;** All patients with single isthmic PTC and underwent total thyroidectomy with or without central neck dissection (CND) were included in the study. Patients with cervical lymph node metastasis and neck extension or patients with their cancer in another place were omitted from the study. Included patients were subdivided into 3 groups; total thyroidectomy, lobectomy with isthmusectomy, and isthmusectomy. Clinical and pathologic data and surgical outcomes were collected. **Results;** Among the included 121 patients, 28 were males and 93 were females. Total thyroidectomy, isthmusectomy, and lobectomy with isthmusectomy were conducted in 70 (57.8%), 11 (9.1%), and 40 (33.1%), patients, respectively. Patients with total thyroidectomy showed increased postoperative hypoparathyroidism than patients with lobectomy and isthmusectomy. On the other hand, there were no significant differences in the recurrence rate or the survival between the 3 groups. **Conclusion;** Total thyroid isthmusectomy may be helpful in the surgical management of small single isthmic PTC. Further studies are needed to verify this result.

Keywords: Isthmusectomy, Papillary thyroid carcinoma

Introduction

Differentiated thyroid tumor is the most common cancer of the endocrinal glands, and accounting for nearly 33% of all head and neck tumors.¹ Its prevalence has been rapidly increasing through the last 20 years, and increased in females more than males.²

Papillary thyroid carcinoma (PTC) is considered the most common histologic subtype of differentiated thyroid tumor, as it accounts for 80-85% of patients with differentiated thyroid tumor, and has a relatively good prognosis with more than 90% exceeded 10-year survival.^{1,3} Despite most of PTC occurs in the thyroid lobes, around 1-9% is restricted to the thyroid isthmus.⁴⁻⁶ Tumors of the thyroid isthmus are proven to have an increased incidence of multifocality and invasion of the surroundings compared to tumors presenting in the thyroid lobes.⁷

The gold standard of treatment for PTC is surgery, and preoperative ultrasound (US) is important for deciding the extent of surgery. The surgical method is considered according to the size and number of thyroid nodules, extent of tumor, lymph node metastasis, and the age of the patients.⁸ Due to the low incidence, there is no optimum treatment for isthmic PTC.^{2,4,5,9,10} The total thyroidectomy was conducted mainly because of the increased rate of extra-thyroidal extension (ETE) and the neck invasion in isthmic PTC.

Moreover, to minimize surgical complications and preserve the thyroid function, thyroid isthmusectomy has been introduced for isthmic PTC. However, the outcomes of isthmusectomy has not been clearly discussed so far. We hereby aimed to assess the efficacy of thyroid isthmusectomy by evaluating the surgical outcomes and

survival based on the surgical procedures used in isthmic PTC.

Materials and methods

This study was a retrospective archive-based study that included 121 patients with a solitary PTC confined to the thyroid isthmus without lymph node involvement. These patients underwent thyroidectomy with or without prophylactic central neck dissection (CND). All patients were categorized as either Bethesda category V or VI on preoperative ultrasound-guided fine needle aspiration cytology (FNAC) for the nodule that located in the thyroid isthmus based on the preoperative US and the final histopathology-confirmed PTC.

Patients with suspected cervical lymph node involvement or gross extrathyroidal extension were omitted. Patients with suspicious nodules at the thyroid lobes or anywhere other than the thyroid isthmus on preoperative US or pathologic were also excluded. Patients with total thyroidectomy or lateral selective neck dissection were also omitted.

The included patients were divided into three groups; total thyroidectomy, lobectomy with isthmusectomy, and isthmusectomy. The type of surgery was decided according to the disease status and surgeon's experience. Of patients with total thyroidectomy, postoperative radioactive iodine (RAI) usage was performed in patients with minimal ETE, occult lymph node involvement, or higher risk histologic features. The RAI dose ranging from 30 mCi to 100 mCi.

The demographic characteristics of the patients, preoperative US results, surgical outcomes, histopathologic findings, and survival outcomes were extracted.

Fiberoptic laryngoscopy was conducted for all patients before and after the surgery. Hypoparathyroidism was defined as the level of serum parathyroid hormone below 15pg/ml regardless of hypocalcemic symptoms. Permanent hypoparathyroidism was defined as the persistence of low levels for > 6 months.

Statistical analysis was performed Using SPSS software version 22. The categorical variables were compared using chi-square test or Fisher's exact test. Furthermore, Student's t-test was utilized to compare continuous variables. The survival analysis was implemented using the Kaplan–Meier curve. All over the analysis, P value was set to be significant when $P < 0.05$

Results

During the study period, 121 patients with isthmic PTC were included with the mean age was $48.3(\pm 13.2)$ years. Among them, 28 were men (23.1%) and 93 were women (76.9%). The mean size of the tumor was 1.05 ± 0.5 cm. Total thyroidectomy was conducted for 70 patients, lobectomy with isthmusectomy was conducted for 40 patients, and only isthmusectomy was conducted for 11 patients underwent. Furthermore, prophylactic CND was conducted, according to the surgeon's decision, for 104 patients (Table 1).

Clinicopathologic characteristics

There were no differences between the three groups regarding the age ($p = 0.508$) or sex ($p = 0.498$). Prophylactic CND was conducted for 62 patients (88.6%) among the patients who underwent total thyroidectomy group, 32 patients (80.0%) among the patients who underwent lobectomy, and 10 patients (90.9%) among the patients who underwent isthmusectomy. Therefore, there was no difference between the three groups regarding it ($p = 0.492$).

Having the total thyroidectomy group, the preoperative US showed that all patients had a solitary isthmic PTC; however, the final histopathological examination revealed occult PTC in the unilateral lobe in six patients and at the bilateral lobes in one patient. According to the lobectomy group, all 40 patients revealed no occult PTC in the excised thyroid lob.

There were no differences between the three groups regarding the T classification ($p = 0.074$), N classification ($p = 0.776$), or overall classification ($p = 0.360$). However, the mean size of the tumor was significantly

larger in the patients with total thyroidectomy than the other two groups. The lymphovascular invasion was comparable among the three groups ($p = 0.036$), and the subgroup analysis revealed that the total thyroidectomy group revealed higher rate of lymphovascular invasion than the lobectomy group ($p=0.016$). There was no difference between the two groups as regard as the minimal extrathyroidal extension ($p = 0.251$).

The postoperative RAI ablation was conducted for 55 patients (78.6%) of the total thyroidectomy group. The mean follow-up periods were 68.3 ± 32.0 , 41.4 ± 24.8 , and 28.4 ± 26.8 months for the three groups, respectively. The duration of follow-up was significantly longer in patients with total thyroidectomy than patients in the lobectomy and isthmusectomy groups (Table 2).

The surgical outcomes and recurrence rate

Among the total thyroidectomy group, postoperative hematoma developed in three

patients (4.3%), while developed in one patient (2.5%) in the lobectomy group. Four patients in the total thyroidectomy and one patient in lobectomy group developed unilateral vocal cord paralysis which was temporary and returned to normal after three months. Hypoparathyroidism was developed in 33 patients (47.1%) with total thyroidectomy group.

Among them, two patients developed permanent dysfunction. Furthermore, it was higher in the total thyroidectomy group than the lobectomy and isthmusectomy groups. There was no difference between the three groups regarding the rate of recurrence ($p = 1.000$) as it occurred in two patients; one patient in the total thyroidectomy group and one patient in the lobectomy group (Table 2).

Kaplan–Meier survival analysis showed no significant difference between the three groups as regard the disease free survival ($p = 0.505$) (Figure 1).

Table 1: Demographic characteristics of the included patients

Variables	(N = 121)
Sex	
Male/Female	28 (23.1%)/93 (76.9%)
Age (years)	48.3 ± 13.2
Extent of thyroidectomy	
Total thyroidectomy	70 (57.8%)
Lobectomy with isthmusectomy	40 (33.1%)
Isthmusectomy	11 (9.1%)
Central neck dissection (CND)	
No CND	17 (14.0%)
Prophylactic CND	104 (86.0%)
Staging	
I	116 (95.9%)
II	5 (4.1%)
T classification	
T1	111 (91.7%)
T2	8 (6.6%)
T3	2 (1.7%)
N classification	
Nx	17 (14.0%)
N0	65 (53.7%)
N1a	39 (32.2%)
Tumor size (cm)	1.05 ± 0.5

Table 2: Comparison between the study group regarding clinical characteristics and surgical outcomes.

Variables	Total thyroidectomy (N =70)	Lobectomy with isthmusectomy (N= 40)	Isthmusectomy (N = 11)	p-value
Sex				
Male	19 (27.1%)	7 (17.5%)	2 (18.2%)	0.498
Female	51 (72.9%)	33 (82.5%)	9 (81.8%)	
Age (years)	49.1 ± 13.8	48.0 ± 13.0	44.2 ± 9.8	0.508
Pathologic multiplicity				
Isthmus only	63 (90.0%)	40 (100%)	11 (100%)	0.267
Isthmus with unilateral lobe	6 (8.6%)	0	–	
Isthmus with bilateral lobe	1 (1.4%)	–	–	
No CND	8 (11.4%)	8 (20.0%)	1 (9.1%)	0.492
Prophylactic CND	62 (88.6%)	32 (80.0%)	10 (90.9%)	0.360
Staging				
I	68 (97.1%)	38 (95.0%)	10 (90.9%)	
II	2 (2.9%)	2 (5.0%)	1 (9.1%)	
T classification				0.074
T1	60 (85.7%)	40 (100%)	11 (100%)	
T2	8 (11.4%)	0	0	
T3	2 (2.9%)	0	0	
N classification				0.776
Nx	8 (11.4%)	8 (20.0%)	1 (9.1%)	
N0	38 (54.3%)	21 (52.5%)	6 (54.5%)	
N1a	24 (34.3%)	11 (27.5%)	4 (36.4%)	<.001
Tumor size (cm)	1.2 ± 0.6	0.8 ± 0.3 [†]	0.7 ± 0.3 [†]	
Lymphovascular invasion	26 (37.1%)	6 (15.0%) [†]	2 (18.2%)	0.036
Minimal ETE	38 (54.3%)	18 (45.0%)	8 (72.7%)	0.251
Complications				
Hematoma	3 (4.3%)	1 (2.5%)	0	1.000
RLN palsy	4 (5.7%)	1 (2.5%)	0	0.553
Transient/Permanent	4/0	1/0	–	
Hypoparathyroidism	33 (47.1%)	2 (5.0%) [†]	1 (9.1%)	<.001
Transient/Permanent	31/2	2/0	1/0	
Radioactive iodine ablation	55 (78.6%)	0 [†]	0 [†]	<.001
L-thyroxine replacement	70 (100%)	17 (42.5%) [†]	1 (9.1%)	<.001
Recurrence	1 (1.4%)	1 (2.5%)	0	1.000
Follow-up period (months)	68.3 ± 32.0	41.4 ± 24.8 [†]	28.4 ± 26.8	<.001

RLN, Recurrent laryngeal nerve; ETE, Extrathyroidal extension

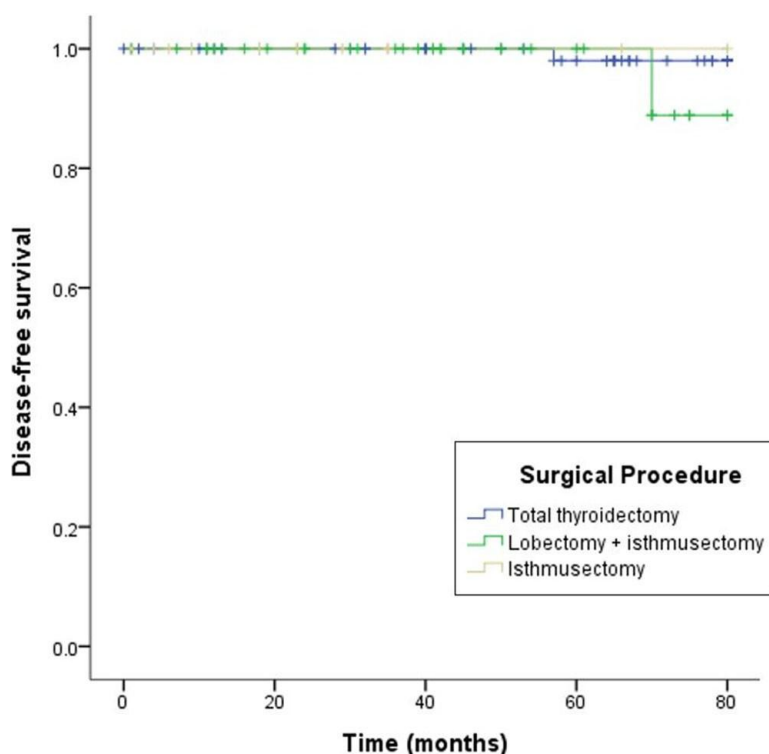


Figure 1. Kaplan–Meier curve for the disease-free survival of patients with single isthmic papillary thyroid carcinoma.

Discussion

Surgery was proven to be the gold standard for management of differentiated thyroid cancer. The aims of surgery are complete removal of the primary tumor, accurate staging of the tumor, and improving the survival by minimizing the risk of complications. Due to the good prognosis, there has been renewing interest in reducing surgical complications

There is a debate regarding the amount of tissue needed to be excised. Total thyroidectomy is indicated for patients with thyroid cancer more than 4 cm, with gross extension (cT4) or with local node metastasis (cN1) or distant metastasis (cM1). For patients with thyroid cancer more than 1 cm and less than 4 cm without any extension and without any evidence lymph node metastasis (cN0), total thyroidectomy and thyroid lobectomy need to be conducted. Moreover, thyroid lobectomy alone may be an effective treatment for small, intrathyroidal, and unifocal carcinomas in the absence of head and neck radiation or familial thyroid carcinoma.⁸ In the case of thyroid cancer restricted to the isthmus, there have been many controversies regarding whether total thyroidectomy,

lobectomy, or isthmusectomy are efficient for managing patients with single isthmic PTC.

Total thyroidectomy can be beneficial as it can treat multiple tumors that have not been discovered before surgery, and RAI ablation is beneficial for diagnosis and treatment after the operation. Furthermore, thyroglobulin is beneficial for recurrence assessment. However, the rate of complications was reported to be more present in total thyroidectomy.^{11,12} However, the incidence of hypothyroidism in isthmusectomy is decreased as there is a preservation of normal thyroid tissue and less possibility of nerve injury and parathyroid injury. However, the possibility of recurrence is high due to the remaining occult carcinoma at the thyroid lobes.

Lee et al., reported that total thyroidectomy is an efficient surgical procedure for isthmic PTC due to the increased rates of capsular invasions and presence of multiple foci⁴. Furthermore, Vasileiadis et al., also reported that total thyroidectomy may be an effective treatment for patients with isthmic PTC due to the increased rate of central lymph node involvement in isthmic PTC.²

Moreover, Wang et al., preferred the avoidance of thyroid isthmusectomy in patients with a size of tumor more than 0.6 cm and in patients under 38 years due to the high probability of lymph node involvement¹⁰.

On the other hand, Nixon et al., revealed that isthmusectomy for patients who have a small, well-differentiated tumor confined to the thyroid isthmus may be efficient treatment as it decreases the risk of postoperative hazards by avoiding injury of the recurrent laryngeal nerve and parathyroid glands.⁵ Skilbeck et al., also reported results in the favor of thyroid isthmusectomy as it preserve other lobes and the surrounding structures.⁹

The literature studying isthmic PTC reported no difference between the total thyroidectomy, lobectomy, and isthmusectomy regarding the rate of recurrence as shown in our study.^{5,10,13-18} It is worthy mentioning that recurrence may occur with occult carcinoma that is confined to the thyroid lobes. All our patients had no evidence of loco affection as shown by the preoperative US.

Having the low probability of recurrence, recurrence from occult carcinoma in the thyroid lobes is not an important issue in clinical practice. Moreover, our data revealed that 90% of patients with isthmic PTC and without occult cancer may not require resection of the bilateral thyroid lobes. Thus, thyroid isthmusectomy might be an effective procedure for isthmic PTC as a progression for thyroidectomy.

Furthermore, it has upper hand from the view of quality of life. In total thyroidectomy, all patients required hormone replacement due to a permanent thyroid dysfunction, whereas few patients with isthmusectomy group needed hormonal replacement.

Previous literature revealed that the complications of total thyroidectomy were about 4.7%-5.6% regarding the transient vocal cord palsy, 0.5- 1.6% regarding the permanent vocal cord palsy, 33.7%-43.7% regarding the transient hypoparathyroidism, 1.2%-3.6% regarding the permanent hypo-

parathyroidism, and 0.6%- 2.3% regarding the postoperative hematoma.^{13-16,19} A previous meta-analysis revealed that the total thyroidectomy showed an increased risk of complications than the lobectomy ($p= 0.04$). On the other hands, most study showed that lobectomy or isthmusectomy were associated with less complications (less than 5%) as transient hypoparathyroidism.^{5,10,14,16,17}

In general, routine prophylactic CND is not preferred to be prescribed for PTC patients with a clinically negative lymph node, albeit therapeutic CND is prescribed in conjunction with complete thyroidectomy when preoperative imaging results indicate presence of suspicious lymph node metastasis. Prophylactic CND can however be found in patients with advanced primary tumors (T3 or T4) with clinically uninvolved central neck lymph nodes (cN0).^{8,20,21}

In our study, 104 (86 %) patients received prophylactic CND. Among prophylactic CND patients, 24 patients (34.3%), 11 patients (27.5%) and 4 patients (36.4%) displayed occult central cervical lymph node metastasis (N1a) in complete thyroidectomy, lobectomy, and isthmusectomy classes, respectively. In one recurring case of this study, PTC recurred to the central lymph node in the contralateral. Song et al., proposed that full bilateral central neck dissection due to the higher risk of bilateral central lymph node metastasis than that of non-isthmic PTC should be considered for isthmic PTC ($p < 0.001$).⁷ Wang et al., also found that in isthmic PTC patients 46.6 percent and 38.4 percent respectively, occult central lymph node metastasis and paratracheal lymph node metastasis were identified. Hence, in patients with isthmic PTC, the need for prophylactic CND may be considered given the high risk of occult metastasis and recurrence in the central lymph node compartment.¹⁰

In conclusion, thyroid isthmusectomy, given its low complication levels and appropriate oncological outcomes, may be useful in the surgical treatment of small single isthmic PTC. Further studies are needed to verify the results of this study.

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