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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Causes, Timing, and Safety of Completion Thyroidectomy during the Follow-up Period after Lobectomy: a Single-Center Experience

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ABSTRACT

Purpose: Thyroid lobectomy is a standard procedure for patients with papillary thyroid carcinoma (PTC) with tumor size <4 cm and clinically negative lymph nodes (LNs) and is performed more frequently than total thyroidectomy. Completion thyroidectomy (CT) is an unexpected operation after lobectomy that has an unpredictable complication rate. In this study, we evaluated the causes, timing, and safety of CT based on our experience.

Methods: From January 2005 to December 2016, 7,731 patients underwent thyroid surgery in our institution. In this study, we included 63 patients who underwent CT for recurrent or contralateral thyroid disease during the follow-up period after lobectomy for PTC through retrospective chart review. We analyzed the causes and timing of CT, initial clinicopathologic factors of PTC, and the complication rate.

Results: All patients underwent initial thyroid lobectomy for PTC. On initial pathology, mean tumor size was 0.69 cm and 7.9% (5/63) patients had central LN metastasis. Patients underwent CT after a mean of 68.4 months (6–388 months). The cause of CT was local or regional recurrence in 52.4% (30/63) of patients, contralateral PTC in 49.2% (31/63), and contralateral benign nodule in 3.17% (2/63). After CT, persistent hypoparathyroidism occurred in 1.58% (1/63), hoarseness in 1.58% (1/63), and wound infection in 1.58% (1/63).

Conclusion: CT may be performed for recurrent or non-recurrent causes anytime during the patient's lifetime after lobectomy. The postoperative complication rate is relatively low. Special attention should be paid during CT.

Keywords: Papillary thyroid cancer; Recurrence; Reoperation; Postoperative complications

INTRODUCTION

Papillary thyroid carcinoma (PTC) is known to have an excellent prognosis with 10-year survival rates exceeding 90% (1). In the case of papillary thyroid microcarcinoma, the disease specific mortality rate has been reported to be less than 1%, with locoregional recurrence rates of 2%–6% (2,3). As a result, the extent of thyroid surgery and lymphadenectomy has become less aggressive. Moreover, since the 2015 American Thyroid Association (ATA) guidelines, the incidence of thyroid lobectomy has been increasing in patients with PTC up to 4 cm, despite continuing controversy about the appropriate extent of surgery (4).

Completion thyroidectomy (CT) is a procedure to remove remnant thyroid after thyroid surgery, and it is known to have a higher complication rate compared to primary surgery due to adhesion and fibrosis (5,6). Immediate postoperative CT can be performed in patients who were diagnosed with cancer postoperatively, who have remaining thyroid cancer, or who have to undergo radioactive iodine treatment due to aggressive pathological features. During the follow-up period after thyroid lobectomy, CT can be performed in cases of recurrences, contralateral thyroid cancer, or symptomatic benign thyroid disease. In these cases, it is challenging for surgeons to predict the timing and complications of CT.

In this study, we analyzed the patients who underwent CT during the follow-up period after thyroid lobectomy for PTC and evaluated the causes, timing, and safety of CT.

MATERIALS AND METHODS

1. Patients and data collection

This study was a retrospective analysis of a single-center experience with CT. Institutional Review Board's committee approval (2019-08-059) was granted. From January 2005 to December 2016, 7,731 patients underwent thyroid operations in Yeungnam University Medical Center according to the prospectively maintained thyroid surgical database. Among those patients, 109 underwent CT after thyroid lobectomy. Through a chart review, we included patients aged >18 years diagnosed with PTC at the time of primary surgery. The exclusion criteria were immediate CT after lobectomy due to aggressive pathologic features or multiple lymph node (LN) metastases requiring postoperative radioactive iodine therapy. A flow chart of the study cohort selection process is presented in **Fig. 1**. Clinicopathologic characteristics of patients and their primary surgery were investigated. The time interval between the primary surgery and CT, causes of CT, and complications after CT were analyzed.

2. CT and complications

In our institution, postoperative ultrasound and thyroid function testing were conducted every 6 or 12 months after thyroid lobectomy. When locoregional recurrence or contralateral malignancy was suspected, fine-needle aspiration cytology was conducted. When operative bed recurrence or LN metastasis was confirmed, ultrasound-guided skin marking or charcoal suspension tattoo localization was performed. When lateral neck LN metastasis was confirmed, modified radical neck dissection (MRND) was conducted. A new primary tumor in the contralateral lobe without ipsilateral LN metastasis was considered as new primary cancer and not a recurrence. All CT was performed through the previous incision as an open procedure.

Postoperative laryngeal evaluation was conducted when vocal cord palsy was clinically suspected. Temporary hypoparathyroidism was defined as hypocalcemia under a lower normal range of calcium or hypocalcemic symptoms such as a tingling sensation within 6 months. Permanent hypoparathyroidism was defined as persistently decreased parathyroid hormone below the normal range after 6 months. Other complications were described according to the chart.

3. Data analysis

Microsoft Excel and IBM SPSS for Windows v25.0 (IBM Co., Armonk, NY, USA) were used to store and analyze data. Chi-square test and independent samples t-test was used to analyze correlations between clinicopathologic factors and the cause of CT or the time interval

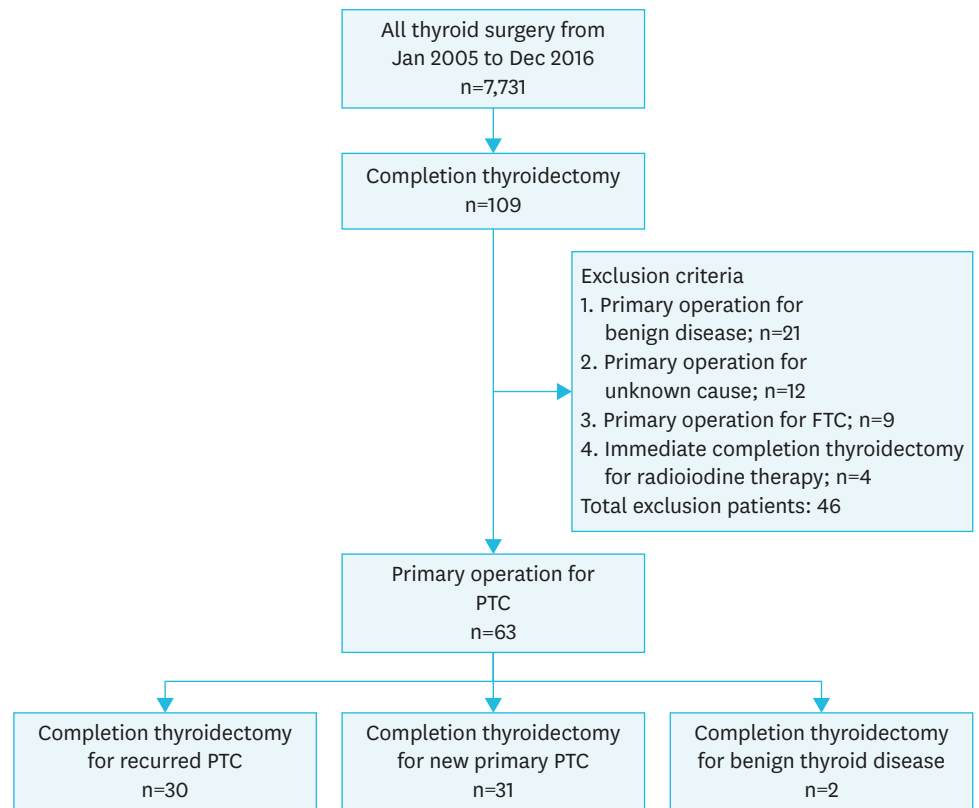


Fig. 1. Study cohort.

FTC = follicular thyroid carcinoma; PTC = papillary thyroid carcinoma.

between the primary operation and CT. Univariate and multivariate analyses using logistic regression were performed. A statistical significance was accepted for P values of <0.05.

RESULTS

1. Patients' demographics and tumor characteristics at the time of primary surgery

A total of 63 patients were included in this retrospective study. They all had received initial thyroid lobectomy for PTC and had a mean age of 42.0 ± 9.5 years at the time of the primary operation. Clinical thyroiditis was observed in 17.5% (11/63) patients, and contralateral nodules were observed on ultrasound in 25.4% (16/63). Central compartment neck dissection (CCND) was conducted in 65.1% (41/63). On initial pathology, mean tumor size was 0.69 ± 0.66 cm and 7.9% (5/63) patients had 1 or 2 central LN metastases. Multiple PTCs were observed in 28.6% (18/63) of patients, vascular invasion in 4.8% (3/63), and extrathyroidal extension in 60.3% (38/63). Thyroid hormone replacement was administered in 47.6% (30/63).

2. Causes of CT

The cause of CT was local or regional recurrence in 52.4% (30/63), contralateral PTC in 49.2% (31/63), and contralateral benign nodule in 3.17% (2/63). When contralateral PTC and benign nodules were regarded as non-recurrent causes of CT (non-recur CT group), there were no differences in the clinicopathologic characteristics of the primary surgery between the group who underwent CT due to recurrence (recur CT group) and the non-recur CT group (**Table 1**). In terms of the extent of lymphadenectomy, all patients underwent CCND and 60% (18/30) in the recur CT

Table 1. Clinicopathologic characteristics of primary surgery according to the cause of CT

Characteristic	Non-recur CT group (n=33)	Recur CT group (n=30)	P value
Sex			0.962
Female	33 (100.0)	29 (96.7)	
Male	0 (0.0)	1 (3.3)	
Age (yr)	42.1±8.5	41.9±10.7	0.948
Presence of clinical thyroiditis	9 (27.3)	2 (6.7)	0.069
Presence of contralateral nodule	10 (30.3)	6 (20.0)	0.517
Tumor size (cm)	0.59±0.25	0.81±0.92	0.216
LN dissection			0.284
CCND	24 (72.7)	17 (56.7)	
No	9 (27.3)	13 (43.3)	
Multiplicity			0.813
Yes	9 (27.3)	9 (30.0)	
No	20 (60.6)	16 (53.3)	
Unknown	4 (12.1)	5 (16.7)	
Vascular invasion			0.672
Yes	1 (3.0)	2 (6.7)	
No	28 (84.8)	23 (76.7)	
Unknown	4 (12.1)	5 (16.7)	
Extrathyroidal extension			0.312
Yes	18 (54.5)	20 (66.7)	
No	11 (33.3)	5 (16.7)	
Unknown	4 (12.1)	5 (16.7)	
LN metastasis	2 (6.1)	3 (10.0)	0.912
Time interval between primary surgery and CT (yr)	69.9±83.0	66.8±75.5	0.879
≤4	16 (48.5)	15 (50.0)	1.000
>4	17 (51.5)	15 (50.0)	

Values are presented as mean±standard deviation or a number (%).

CT = completion thyroidectomy; LN = lymph node; CCND = central compartment dissection.

group received MRND at the same time as the CT. The primary tumor size appeared to be larger in the recur CT group than in the non-recur CT group, but there was no statistical difference ($P=0.216$).

3. Time interval between primary surgery and CT

CT was performed after a mean of 68.4 months (6–388 months) and within 4 years of the primary surgery in 49% (31/63) of patients. The time intervals were similar between the recur CT and non-recur CT groups (**Fig. 2**). There was no difference between patients who received

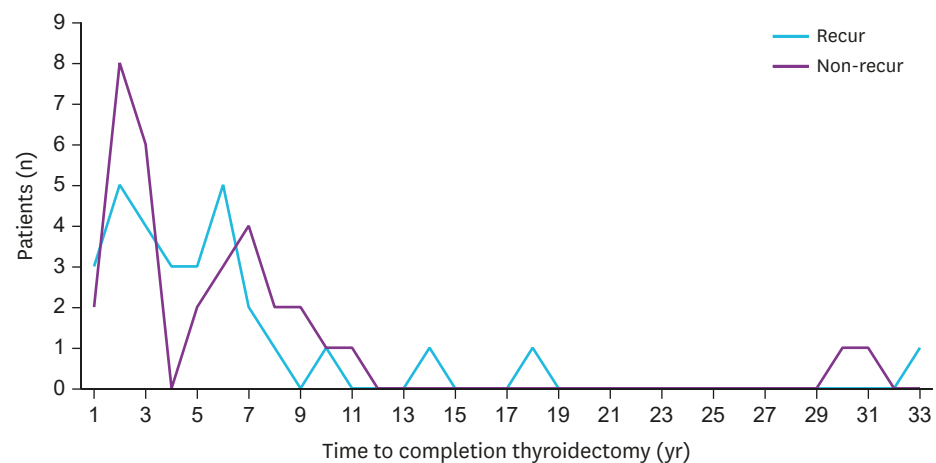


Fig. 2. The number of patients who received CT for recurrence (recur CT group) and non-recurrent causes (non-recur CT group) during the follow-up period after thyroid lobectomy. Within 4 years after lobectomy, 48.4% of patients in the recur CT group and 51.6% in the non-recur CT group underwent CT. CT = completion thyroidectomy.

Table 2. Clinicopathologic characteristics of primary surgery according to the operation timing of CT

Characteristic	CT within 4 yr (n=31)	CT over 4 yr (n=32)	P value
Age at the time of primary operation	45.6±10.0	38.5±7.7	0.002
Presence of clinical thyroiditis	7 (22.6)	4 (12.5)	0.470
Presence of contralateral nodule	8 (25.8)	8 (25.0)	1.000
Extent of LN dissection			0.484
CCND	22 (71.0)	19 (59.4)	
No	9 (29.0)	13 (40.6)	
Tumor size (cm)			1.000
≤1	29 (93.5)	24 (96.0)	
>1	2 (6.5)	1 (4.0)	
Multiplicity			0.020
Yes	14 (46.7)	4 (16.7)	
No	16 (53.3)	20 (83.3)	
Vascular invasion			0.082
Yes	0 (0.0)	3 (12.5)	
No	30 (100.0)	21 (87.5)	
Extrathyroidal extension			0.594
Yes	22 (73.3)	16 (66.7)	
No	8 (26.7)	8 (33.3)	
LN metastasis			0.970
Yes	3 (9.7)	2 (6.2)	
No	28 (90.3)	30 (93.8)	
Cause of CT			1.000
Non-recur	16 (51.6)	17 (53.1)	
Recur	15 (48.4)	15 (46.9)	

Values are presented as mean±standard deviation or a number (%).

CT = completion thyroidectomy; LN = lymph node; CCND = central compartment dissection.

CT within and after 4 years, except for age at primary operation and presence of multiple PTCs (**Table 2**). According to the univariate and multivariate analyses, older age and multiple PTCs were correlated with undergoing CT within 4 years (**Table 3**).

3. Complication rate of CT

The incidence of temporary and persistent hypoparathyroidism after CT was 25.3% (16/63) and 1.58% (1/63). Temporary recurrent laryngeal nerve palsy and wound infection were each observed in one patient (1.58%). Suspicious thoracic duct injury and Horner's syndrome related with MRND occurred in 3.2% (2/63) and 1.6% (1/63) of patients, respectively. Most complications occurred irrespective of the timing and cause of CT (**Table 4**).

DISCUSSION

The 2015 ATA guidelines recommended thyroid lobectomy in low-risk patients with tumors up to 4 cm and clinically negative LN (4). Several studies have demonstrated that thyroid lobectomy and total thyroidectomy had similar overall survival rates in patients with 1–4 cm-sized PTCs (7-9). Recurrence rates during the follow-up period after lobectomy are reported

Table 3. Clinicopathologic factors affecting completion thyroidectomy performed within 4 years

Factor	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age at the time of primary operation	0.907	0.846–0.972	0.006	0.921	0.849–0.998	0.045
Multiplicity	4.375	1.203–15.911	0.025	4.812	1.240–18.668	0.023
Extrathyroidal extension	1.375	0.426–4.442	0.595			

OR = odds ratio; CI = confidence interval.

Table 4. Complication rates of CT

Characteristic	Cause of CT			Timing of CT		
	Non-recur (n=33)	Recur (n=30)	P value	Within 4 yr (n=31)	Over 4 yr (n=32)	P value
Wound infection	1 (3.0)	0 (0.0)	1.000	1 (3.2)	0 (0.0)	0.987
Chyle leakage	0 (0.0)	2 (6.7)	0.431	1 (3.2)	1 (3.2)	1.000
Hoarseness	0 (0.0)	1 (3.3)	0.962	1 (3.2)	0 (0.0)	0.987
Horner syndrome	0 (0.0)	1 (3.3)	0.962	0 (0.0)	1 (3.2)	1.000
Hypoparathyroidism	9 (27.3)	7 (23.3)	0.945	7 (22.6)	9 (28.1)	0.829
Temporary	9 (27.3)	7 (23.3)	0.945	7 (22.6)	9 (28.1)	0.829
Permanent	1 (3.0)	0 (0.0)	1.000	0 (0.0)	1 (3.2)	1.000

Values are presented as a number (%).
CT = completion thyroidectomy.

to be very low and to have no effect on the survival rate if properly treated (7,9,10). For these reasons, the preferences of surgeons regarding the necessary extent of thyroidectomy has shifted from total thyroidectomy to lobectomy, despite continuing controversy.

CT is usually recommended for patients who would have been treated by total thyroidectomy if they had been diagnosed with malignancy before surgery or those who must undergo radioactive ablation treatment. According to the National Comprehensive Cancer Network (NCCN; <http://www.nccn.org>), postoperative CT is recommended in cases of tumor size >4 cm, positive resection margin, macroscopic nodal metastasis (>5 mm) or multiple LN metastasis (the number of LNs >5), macroscopic multifocal disease (>1 cm), or vascular invasion on the pathologic report. In these cases, most completion thyroidectomies are conducted within 6 months by the same surgeon and the complications are predictable. In this study cohort, the number of cases of immediate postoperative CT was 4 for PTC and 4 for follicular thyroid cancer during the study period. In our institution, intraoperative frozen section analysis was conducted for suspicious LNs, and when metastasis was confirmed, the extent of thyroidectomy was changed to total thyroidectomy during surgery. Thus, the incidence of immediate postoperative CT was relatively low.

Despite an excellent prognosis, many patients with PTC are anxious and fearful of recurrence (11). Although thyroid lobectomy has advantages in terms of avoiding lifelong thyroid hormone replacement therapy, many patients worry about remnant thyroid tissue. Recent studies reported locoregional recurrence rates of less than 1%–4% and a CT rate of less than 10% after thyroid lobectomy (9,12). Typically, recurrence of PTC occurs within first 3–4 years, and most of the cases are considered disease persistence with possible enlargement rather than true recurrence (13,14). In our study, half of the completion thyroidectomies were conducted within 4 years in both the recur CT and non-recur CT groups, with the other half occurring anytime after 4 years. We analyzed the clinicopathologic characteristics of primary surgery based on median timing, 4 year. Multiple PTCs and older age were correlated with CT within 4 years. It is well known that PTC can have multiplicity, and the rate of occult carcinoma in contralateral lobe is reported at 13%–56% (15,16). A new primary lesion in the contralateral lobe is likely to be a persistent tumor in patients who underwent CT within 4 years. The odds ratio of 0.921 for the age is not impressive. The factor of age seems to be correlated with timing due to the differences in remaining lifespan between the patients underwent CT within and after 4 years.

Reoperation is considered to have a higher risk of postoperative complications. Tissue inflammation, adhesions, and scar tissue formation after primary surgery make it difficult to distinguish normal tissue (6,17,18). This leads to an increased risk of recurrent laryngeal

nerve or parathyroid gland injury during tissue dissection. However, in the case of CT after lobectomy, recurrent laryngeal nerve and parathyroid glands are less affected by the previous surgery. Rafferty et al. (19) reported similar complication rates between CT and total thyroidectomy with incidences of temporary recurrent laryngeal nerve paresis of 2.0% and 3.3% and permanent hypoparathyroidism of 2.5% and 3.3% in completion and total thyroidectomy, respectively. Rudolph et al. (20) reported a significantly lower rate of permanent recurrent laryngeal nerve palsy and hypoparathyroidism during reoperation after thyroid lobectomy than after bilateral subtotal thyroidectomy (0.77% vs. 3.4% and 1.5% vs. 5.1%, respectively). In our institution, one patient complained of hoarseness after CT with MRND due to ipsilateral LN recurrence at 33 months after primary surgery, though the symptom returned to normal within several months. There was no recurrent laryngeal injury, though severe adhesion was reported. Temporary hypoparathyroidism was reported in 25.3% (16/63) of the patients in this study. In most cases, their symptoms improved within 6 months, and persistent hypoparathyroidism was observed in only 1.58% (1/63). One patient received CT with CCND due to contralateral PTC at 76 months after the primary surgery, and there was no evidence of parathyroid gland injury. One patient was re-admitted with wound swelling and pus-like discharge on the seventh postoperative day.

To reduce the complication rate of CT during the follow-up period after lobectomy, a clear understanding of the operative findings of the primary surgery and a thorough preoperative evaluation are very important. Surgeons must ascertain whether there was any recurrent laryngeal nerve or parathyroid gland injury or if any other events occurred at the time of primary surgery. In the absence of information about the primary surgery, it is necessary to evaluate vocal cord function and a neuro-monitoring device may also be helpful. Exact localization is also critical, especially in cases of operative site bed recurrence or ipsilateral LN recurrence. Ultrasound-guided skin marking or charcoal suspension tattoo localization may reduce the extent of dissection.

This study has limitations of retrospective study. Information about complications was obtained solely from the chart records, and the rates may have been somewhat underestimated owing to the possibility of complications that the patients did not report. However, the low number of complications in this report may help reduce patients' anxiety about reoperation.

In conclusion, along with the increased rate of thyroid lobectomy, the frequency of CT is expected to increase. CT is an unexpected event that may occur anytime during the patients' lifetime after lobectomy. However, it is no longer a challenging surgery and the postoperative complication rate is relatively low. Special attention should be paid during surgery.

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