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Dissection of Right Upper Paraesophageal Lymph Node for Management of Recurrent Nodal Lesion in Papillary Thyroid Cancer (PTC)

Sung-Dong Kim, Youngjin Cho, Yong-Il Cheon, Sung-Chan Shin, Byung-Joo Lee

Department of Otorhinolaryngology-Head and Neck Surgery, College of Medicine, Pusan National University and Biomedical Research Institute, Pusan National University Hospital, Busan, Korea

ABSTRACT

Background and Objectives: Although there is several published research about right upper paraesophageal lymph node (RUPELN) for the initial surgery in papillary thyroid cancer (PTC), reports of RUPELN in recurrent PTC are sparse. This study investigates the incidence of RUPELN metastasis and the complications of reoperation for management of recurrent nodal lesion in PTC. **Materials and Methods:** This is a retrospective study of 50 patients who underwent therapeutic or prophylactic central-compartment neck dissection (CCND) between Jan. 2005 and Dec. 2013. **Results:** Thirty-four among 36 patients (94.4%) who underwent therapeutic right CCND were found to have metastatic central compartment lymph node (CCLN). Eleven of 36 patients (30.6%) who underwent dissection for RUPELN exhibited nodal metastasis. Four among 14 patients (28.6%) who underwent prophylactic right CCND had metastatic CCLN in recurrent or persistent nodal PTC. Two of 14 patients (14.3%) who underwent prophylactic dissection for RUPELN had lymph node metastases. **Conclusion:** The dissection of RUPELN should be considered during right CCND for management of recurrent or persistent nodal lesion in patients with PTC.

KEY WORDS: Thyroid cancer; Reoperation; Lymph node excision; Paraesophageal lymph node.

Introduction

Papillary thyroid cancer (PTC) is the most common endocrine tumor and its prognosis is highly favorable, with the reported 5- year and 20- year survival rates being 94% and 87%, respectively.[1,2] Despite good prognosis, cervical lymph node metastases of PTC are common, occurring in 20% to 50% of patients. Although central-compartment neck dissection (CCND) is performed for clinically nodal-positive disease, its effect on survival with nodal metastasis is questionable.[1,2]

There are several clinical benefits of total thyroidectomy with prophylactic CCND, as it allows surgery without leaving additional scars except for the thyroidectomy incision, and has a low complication rate with hypocalcemia or recurrent laryngeal nerve palsy when conducted by an experienced surgeon. However, some reports found no significant increase in survival rate when compared to non-prophylactic CCND group.[3–5] Therefore, the need for prophylactic CCND during initial surgery is controversial.

Most PTC sequentially spreads to the lateral neck lymph node group via the central compartment lymph node (CCLN) group, whereas about 9.6% of PTC directly metastasizes to the lateral neck lymph node group, skipping metastasis

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Corresponding author: Byung-Joo Lee, Department of Otorhinolaryngology-Head and Neck Surgery, Pusan National University Hospital, Busan 49241, Korea
Tel: +82-51-240-7824, Fax: +82-51-246-8668, E-mail: voiceleebj@gmail.com

of the CCLN group.[3–8] ATA guidelines recommend prophylactic CCND in patients with lateral neck metastasis of PTC.[9] Rho et al. reported that the positive rate of ipsilateral prophylactic CCND in operation was 84.6% in patients with untreated CCND in initial surgery and recurrent lateral cervical lymph node metastasis.[10] Therefore they recommended prophylactic CCND in patients with recurrent lateral cervical lymph node metastasis and untreated CCND in initial surgery.[10]

Level VI lymph nodes include preoccipital, pretracheal paratracheal, and parathyroid lymph nodes.[11] The right and left recurrent laryngeal nerve ascends through the fibro-fatty tissue of level VI in a different course. There are some lymph nodes between the posterior of the right recurrent laryngeal nerve and anterior of esophagus and deep fascia. Lee et al.[12] reported it as a right upper para-esophageal lymph node (RUPELN). The RUPELN can be clearly distinguished from the right para-tracheal lymph nodes. It is important because these lymph node metastases are related to the lateral cervical lymph nodes and mediastinal lymph node metastases.[13–15] The surgical treatment of metastatic lymph nodes is important because lymph node recurrence or persistent disease is significantly related to the presence of metastatic lymph nodes at diagnosis. Although the management of RUPELN behind the right recurrent laryngeal nerve is controversial, the metastatic rate in RUPELN has been reported at 11.4% to 26.7% when simultaneously removed during the right CCND in initial surgery.[12,16–18]

Although a few papers have reported RUPELN metastases rates and risk factors in initial surgery, there are no studies reporting the frequency of the RUPELN metastasis in patient with untreated CCND in initial surgery and recurrent or persistent nodal lesions. Thus, this study evaluates the positive metastatic rate and complications during dissection of RUPELN to manage recurrent or persistent nodal lesions in patients with untreated CCND in initial surgery of PTC.

Materials ane Methods

This study is a retrospective study of 50 (38 females, 12 males) patients who performed total thyroidectomy without CCND in initial surgery and underwent reoperation to manage recurrent or persistent nodal lesion between Jan. 2005 and Dec. 2013. We categorized our 50 patients into two groups: group A (n=36) with therapeutic (node positive) repeat surgery, and group B (n=14) with prophylactic (node negative) repeat surgery (Table 1).

Preoperative evaluation for CCLN metastasis was done by fine-needle aspiration cytology, high-resolution ultrasound scan, and computerized tomography (CT) scan. Among 50 patients, thirty-three (66.0%) underwent only right CCND and seventeen (34.0%) underwent bilateral CCND. Among group A, twenty-six patients underwent right CCND and ten bilateral CCND. Among group B, eight patients underwent right CCND and six bilateral CCND.

In group A, CCND was performed in five patterns. First, six of 36 (16.7%) patients underwent only right CCND due to recurrence of right CCLN in preoperative CT finding and fine needle aspiration biopsy. Second, four of 36 (11.1%) patients underwent bilateral CCND due to recurrence of both CCLN. Third, nineteen of 36 (52.8%) patients underwent lateral neck dissection with right CCND due to recurrence of lateral neck lymph node and right CCLN. Fourth, six of 36 (16.7%) patients underwent lateral neck dissection with bilateral CCND due to recurrence of lateral neck lymph node and both CCLN. Lastly, one of 36 (2.7%) patients

Table 1. Demographics and clinical characteristics

	Therapeutic (n=36)	Prophylactic (n=14)	p-value
Age (years)	58.02±7.42	54.25±8.30	0.320
Gender (male)	9 (25.0%)	3 (21.4%)	1.000
Gender (female)	27 (75.0%)	11 (78.6%)	
Both central compartment	10 (27.8%)	6 (32.0%)	0.330
Right central compartment	26 (72.2%)	8 (68.0%)	

underwent completion thyroidectomy with right CCND due to recurrent cancer in right remnant thyroid tissue and right CCLN in fine needle aspiration biopsy. In group B, prophylactic CCND was performed in three patterns. First, although there was not abnormal finding in level VI, eight of 14 (57.1%) patients underwent lateral neck dissection with prophylactic CCND due to recurrence of lateral neck lymph node in preoperative CT finding and fine needle aspiration biopsy. Second, although there was not abnormal finding in contra-lateral level VI, five of 14 (35.8%) patients underwent bilateral CCND due to recurrent lymph node in ipsilateral thyroid bed in preoperative CT finding and fine needle aspiration biopsy. Lastly, although there was no abnormal finding in bilateral level VI, one of 14 (7.1%) patient underwent completion thyroidectomy and bilateral CCND due to recurrent cancer in ipsilateral remnant thyroid tissue in fine needle aspiration biopsy (Fig. 1).

The authors performed the repeat surgery for CCLN using the 'Back door approach' (Fig. 2). Briefly, the back door approach dissects lymph nodes of the thyroid bed through between the anterior border of sternocleidomastoid and the strap muscles, which through previous un-dissected surgical plain. Sterno-cleido-mastoid muscle traction can reveal the sterno-hyoid and underlying sterno-thyroid muscles. Para-tracheal soft tissue is exposed by traction of the carotid artery. It is important to dissect under the inferior thyroid artery to preserve the superior parathyroid gland. If necessary, cutting the strap muscle provides good exposure.

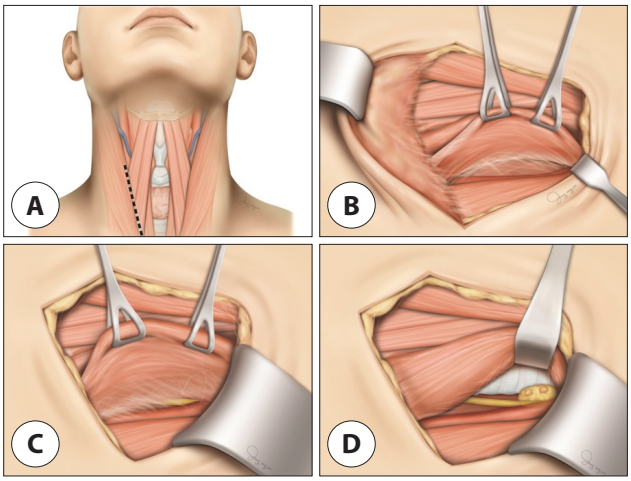

Fig. 2. Surgical procedure of the 'Back door approach'. The procedure dissects lymph nodes of the thyroid bed through between the anterior border of sternocleidomastoid and the strap muscles (A, B). Sternocleidomastoid muscle and strap muscle traction can reveal the recurrent laryngeal nerve, carotid artery and right upper paraesophageal lymph nodes (C, D).

Lymph node compartments

The CCLN were divided into two nodal sites: right para-tracheal lymph nodes, and RUPELN. The nodes were classified by the operating surgeon. The pre-tracheal and pre-laryngeal lymph nodes were included in the right para-tracheal lymph nodes according to the site of operation. The patients were considered to have a positive site when one or more nodes in the particular site contained a tumor.

Statistical analysis

Statistical analysis was performed using SPSS (IBM.

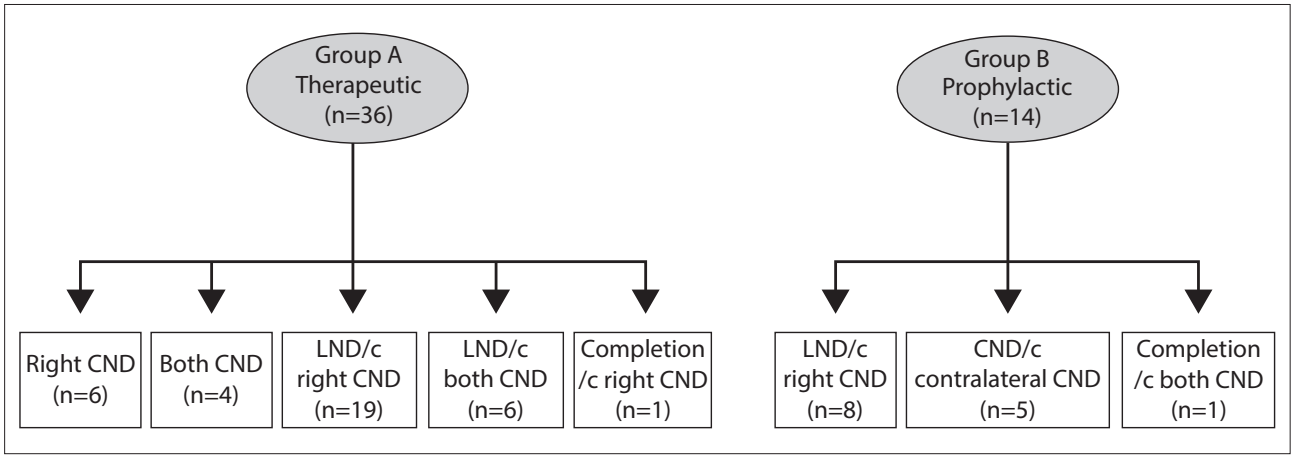

Fig. 1. The model diagram of the surgical procedures. CND: central neck dissection, LND: lateral neck dissection.

Released 2014. IBM SPSS Statistics for Windows, Version 23.0, IBM, Armonk, NY, USA). Univariate analysis was performed using the chi-square test and Fisher's exact test, and multivariate analysis was performed using logistic regression analysis.

Results

We divided our 50 patients into two groups: group A (n=36) with therapeutic CCND, and group B (n=14) with prophylactic CCND. In group A, thirty-four among 36 (94.4%) patients were found to have metastatic lymph nodes of PTC in the right CCLN. Eleven of 36 (30.6%) patients who underwent the dissection for RUPELN exhibited metastatic lesions in RUPELN (Table 2). In group B, four among 14 (28.6%) patients had metastatic lesions of PTC in the right CCLN. Two of 14 (14.3%) patients who underwent prophylactic dissection for RUPELN had metastatic lymph nodes (Table 3).

Thyroglobulin (TG) value was statistically significant between before and after surgery (Table 4). There was one case of permanent vocal cord paralysis in group A. Transient hypoparathyroidism was a complication in 16 of 36 patients (44.4%) in group A and five of 14 (35.7%) in group B. In group A, two (5.6%, 2/36) had permanent hypoparathyroidism requiring calcium supplements. The complication rate of group A was not significantly higher than group B (Table 5).

Discussion

Cervical lymph node metastasis is commonly detected, and present in 20%–90% of papillary thyroid carcinoma.[19] As the CCLN are generally the first and most commonly involved with metastasis, there may be a significant risk of recurrence in level VI.[19] In patients with a primary tumor that has extended beyond the thyroid capsule and spread to the cervical lymph nodes, complete surgical resection is important in prognosis because residual metastatic lymph nodes are the most common sites of persistent or recurrent disease.[20,21] If resection of metastatic lymph node is incomplete, there is more risk of local recurrence. The authors focused on the metastatic rate of RUPELN in patients who did not performed CCND in initial surgery and were planned to do right therapeutic or prophylactic CCND.

In the group B with prophylactic CCND, the metastatic rate of the RUPELN was 14.3%, compared to 30.6% in the group A with therapeutic CCND. Lee et al.[12] reported that

Table 2. Numbers and metastatic rates of therapeutic (node positive) repeat surgery compartment neck dissection (CCND)

	Right CCND		p-value*
	Paratracheal LNs	Upper paraesophageal LNs	
No. of removed LNs	2.83±2.70	2.12±1.04	
No. of metastatic LNs	2.07±1.66	0.60±0.44	
Metastatic LNs rate	94.4% (34/36)	30.6% (11/36)	<0.001†

* Student t-test.
† p<0.05 when comparing the preoperative and postoperative values.
CCND: central compartment neck dissection, LNs: lymph nodes; No.: numbers.

Table 3. Numbers and metastatic rates of prophylactic (node negative) repeat surgery central-compartment neck dissection (CCND)

	Right CCND		p-value*
	Paratracheal LNs	Upper paraesophageal LNs	
No. of removed LNs	0.72±1.46	1.96±0.87	
No. of metastatic LNs	0.62±1.19	0.58±0.44	
Metastatic LNs rate	28.6% (4/14)	14.3% (2/14)	0.056†

* Mann-Whitney test.
† p<0.05 when comparing the preoperative and postoperative values.
LNs: lymph nodes, No.: numbers.

Table 4. Thyroglobulin value between the preoperative and postoperative periods.

	Preoperative (n=50)	Postoperative (n=50)	p-value*
	Median (25^{th}–75^{th})	Median (25^{th}–75^{th})	
Thyroglobulin value	1.33 (0.32–5.75)	0.52 (0.14–1.50)	<0.001†
Prophylactic	1.33 (0.32–9.04)	0.54 (0.22–1.50)	<0.001†
Therapeutic	1.28 (0.14–6.20)	0.51 (0.09–1.55)	<0.001†

* Wilcoxon signed rank test.
† p<0.05 when comparing the preoperative and postoperative values.

Table 5. Postoperative complications between prophylactic and therapeutic repeat surgery

	Group A (n=36)	Group B (n=14)	p-value*
None	17 (50.2%)	9 (64.3%)	0.628
Transient hypoparathyroidism	16 (44.4%)	5 (35.7%)	
Permanent hypoparathyroidism	2 (5.6%)	0 (0%)	
Transient vocal cord palsy	0 (0%)	0 (0%)	
Permanent vocal cord palsy	1 (2.8%)	0 (0%)	

* Fisher's exact test.

the positive metastatic rate of RUPELN at initial surgery was 11.4% and another recent study reported that the rate of RUPELN metastasis was 15.4% among the 1,107 PTC patients. In one study, a meta-analysis of six papers reported that the metastatic rate of RUPELN in PTC patients ranged from 5.8% to 26.7%.[22] These results are comparable with the metastatic rate (14.3%) of prophylactic CCND at repeat surgery. However, when therapeutic CCND at reoperation was conducted, the metastatic rate of RUPELN (30.6%) was much higher than prophylactic CCND performed at reoperation and initial surgery.

The benefit and extent of prophylactic CCND in PTC patients is controversial, especially in RUPELN. Because the anatomical location of RUPELN is near the esophagus, it is very hard to diagnose lymph node metastasis through preoperative ultra-sonographic examination. In addition, there is more possibility of injury of the right recurrent laryngeal nerve due to traction when the RUPELN was dissected. However, Grodski et al.[23] recommend that some lymph nodes (RUPELN) posterior to the right recurrent laryngeal nerve should be sectioned in routine CCND.

Reoperation of CCND commonly poses more difficulty for the head and neck surgeon than the initial surgery because of trouble detecting the nerve due to post-operative wound scar and tissue adhesion. Furthermore, removal of RUPELN could increase bleeding and nerve injury, from traction and elevation during removal of those lymph nodes. So, the risk of complications, such as hypoparathyroidism, vocal cord palsy and chyle leakage, is higher. Several researchers reported that the incidence of permanent recurrent laryngeal nerve paralysis is higher in repeat surgery than primary thyroid surgery.[24–26] Although there were two cases of permanent hypoparathyroidism in group A, and one permanent vocal cord paralysis in group B in our study, there were no significant difference in the incidence of permanent vocal cord paralysis (1%–1.5%) and permanent hypocalcemia (0.4%–13.8%) when CCND was performed in initial surgery.[27,28]

Lee et al.[12] recommended that the RUPELN may be preserved in routine CCND for left thyroid cancer in patients without metastatic lesions in the right paratracheal lymph nodes. Metastases of the RUPELN were more frequent at the right side than left (31.1%: 4.6%). Park et al. reported that the rate of RUPELN metastasis significantly increased with tumor size, location, a higher number of metastatic central lymph nodes, and lateral lymph node metastasis.[18]

Although there is a risk of complications due to dissection of RUPELN, there is no significant difference in the incidence of complications as compared with initial surgery, as reported in our study. In addition, the rate of lymph node

metastasis is higher during therapeutic surgery than initial surgery or prophylactic surgery. Therefore, the authors recommend that RUPELN should be removed in therapeutic reoperation for management of right side recurrent nodal lesion in PTC.

Unlike the well-known risk factors that affecting metastasis to RUPELN during initial surgery,[13–15] the risk factors for recurrence of RUPELN were difficult to find in this study. Although pathologic status in initial surgery is important for determining lymph node metastasis in reoperation, there are insufficient information about initial surgery in our study and the method of operation is inconsistent due to the initial surgery was performed by several hospitals and surgeons. Furthermore, several bias such as tumor characteristics, initial surgical methods and patient selection are some limitations of our study and further research is needed for larger numbers of patient with more clinical information.

Conclusion

In reoperation for CCLN, the rate of RUPELN metastasis was higher when there was recurrent or persistent lymph node metastasis in the right central cervical lymph node, and resection of RUPELN resulted in a more significant decrease in postoperative TG.

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

ORCID
Sung-Dong Kim, https://orcid.org/0000-0002-8436-5722
Youngjin Cho, https://orcid.org/0000-0002-1765-2000
Yong-Il Cheon, https://orcid.org/0000-0003-0288-0542
Sung-Chan Shin, https://orcid.org/0000-0003-2329-0648
Byung-Joo Lee, https://orcid.org/0000-0001-7091-6688

Author Contribution
Conceptualization: Lee BJ.
Data curation: Cho Y.
Formal analysis: Shin SC.
Methodology: Cheon YI.
Software: Cheon YI.
Validation: Shin SC.
Investigation: Kim SD.
Writing - original draft: Kim SD.
Writing - review & editing: Kim SD, Cho Y, Cheon YI, Shin SC, Lee BJ.

Ethics Approval
The institutional review board (IRB) of the Pusan National University approved this study before patient enrollment at each location (IRB number: H-1503-001-027).

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