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# Extent of Prophylactic Lymph Node Dissection in the Central Neck Area of the Patients with Papillary Thyroid Carcinoma: Comparison of Limited Versus Comprehensive Lymph Node Dissection in a 2-Year Safety Study

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**Background:** To compare the "comprehensive" (including bilateral paratracheal, pretracheal, prelaryngeal lymph nodes) (CCND) with "limited" (saving contralateral paratracheal lymph nodes) central node dissection (LCND) for postoperative complications and disease recurrence rate in sonographically node-negative papillary thyroid carcinomas.

**Materials and Methods:** From 2003 to 2005, 114 consecutive patients, diagnosed as sonographically node-negative thyroid papillary carcinomas, were included retrospectively. Among them, the LCND was performed in 56 patients and CCND in 58 patients, in combination with total thyroidectomy, based on the operator-dependent decision. We compared the complication rates and the recurrence rates between these two groups with a mean follow-up duration of 2 years.

**Results:** Transient hypocalcemia was more frequent in the CCND group than in the LCND group (48.3% vs 26.8%, $P = .02$, odds ratio [OR] = 2.55). However, the other complication rates were similar in the two groups. In addition, the immediate postoperative reduction of parathyroid hormone (PTH) was more evident in the CCND group. The postoperative PTH levels increased up to a similar level (12.4 vs 11.8 pg/mL) over 6 months. The incidence of permanent hypocalcemia did not differ significantly between the two groups. Four (7.1%) and five recurrences (8.6%) were found in two groups, respectively, implying similar oncological safety during the 2-year follow-up.

**Conclusion:** The LCND with total thyroidectomy could be an alternative treatment option for node-negative papillary thyroid carcinomas, because LCND had fewer short-term hypocalcemia and similar oncological outcomes during the 2-year follow-up. Further study enrolling a large number of patients with long-term follow-up is needed.

**Key Words:** Thyroid carcinomas—Papillary carcinomas—Lymph node dissection—Lymph node metastasis.

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The surgical extent and indications for prophylactic central compartment lymph node dissection in patients with papillary thyroid carcinomas remains a controversial issue.[1,2] In general, there is consensus

on performing lymph node dissection in patients with clinical lymph node metastases, that is, therapeutic lymph node dissection.[3] However, the indications and the extent of prophylactic lymph node dissection in patients without clinically evident lymph node metastasis are not clear. Thyroid cancer guidelines stated that near-total or total thyroidectomy without central node dissection may provide an alternative approach for papillary thyroid carcinoma when followed by radioactive iodine therapy, although routine central-compartment neck dissection should be considered for patients with papillary thyroid carcinoma.[3]

Even for clinically node-negative papillary thyroid carcinomas, lymph node metastases are found in 50–60% of the central lymph nodes.[4] Among them, lymph nodes in the contralateral central compartment are involved in 17.4% of cases with thyroid micropapillary carcinomas.[4] Interestingly, the nodal recurrence rate did not differ between the prophylactic dissection group and the no-dissection group and between the central node dissection group and the no dissection group.[4,5] Disease-free survival did not differ either, between the groups with pathologically proven central nodal metastasis and without them.[1] Therefore, the possible benefits of prophylactic lymph node dissection should be weighed against the potential risks.[2]

Conventional central lymph node dissection inevitably results in a higher rate of postoperative hypocalcemia compared to no dissection. However, it provides more accurate information on lymph node metastasis and prognosis grouping, and it may eradicate the potential source of nodal recurrence.[2,5,6] In nonthyroid head and neck cancers (squamous cell carcinomas), the clinical role of prophylactic neck dissection is mainly nodal staging; the extent of lymph node dissection is limited to the possible nodal groups that have more than a 20% chance of being involved with the primary tumors of the head and neck.[7–10] This surgical concept might be applicable to thyroid papillary carcinomas.

The conventional (i.e., comprehensive) central lymph node dissection (CCND) usually removes all lymph nodes from the carotid artery to the contralateral carotid artery. Here, we define the "limited central lymph node dissection (LCND)" as the removal of certain parts of the lymph nodes in the central lymph node group for nodal staging and possible guidance of postoperative radioactive iodine therapy,[11,12] which includes prelaryngeal, pretracheal lymph nodes, and only ipsilateral paratracheal lymph nodes to primary tumors.

By comparing the CCND with LCND for disease recurrence and postoperative complications in sonographically node-negative papillary thyroid carcinomas, we aimed to determine the optimal extent of prophylactic central compartment lymph node dissection.

## METHODS

From 2003 to 2005, 114 patients, diagnosed as having thyroid papillary carcinomas without lymph node metastasis based on the findings from preoperative ultrasonography and needle aspiration, were included in this study. The approval of the Institutional Review Board of the Samsung Medical Center was obtained for this study. Patient informed consent was not required for this retrospective analysis, but written informed consent was obtained from all patients for surgical options. All subjects underwent total thyroidectomy in conjunction with one of two types of central compartment lymph node dissection (lymph node level VI). The diagnosis of papillary thyroid carcinomas was reconfirmed by the surgical pathology in all patients. This was a retrospective analysis of the surgical outcomes from two types of prophylactic central node dissection, performed by different surgeons and not intended to compare with each other initially.

Two types of central compartment lymph node dissection were "limited" and "comprehensive" central compartment lymph node dissection (Fig. 1). A "comprehensive" central lymph node dissection (CCND) was defined as lymph node dissection of the lymph nodes from one carotid artery to the other side, that is, bilateral paratracheal lymph node dissection, pretracheal lymph nodes and prelaryngeal lymph nodes. "Limited" central lymph node dissection (LCND) was defined as lymph node dissection confined to the ipsilateral paratracheal lymph nodes, pretracheal and prelaryngeal lymph nodes. In those cases, contralateral paratracheal lymph nodes were not removed after palpation and inspection for any suspicious findings. If enlarged lymph nodes were detected at the contralateral paratracheal lymph node groups, a frozen biopsy analysis during surgery of only suspicious lymph nodes was performed to rule out metastasis. We performed the frozen section analysis of contralateral suspicious lymph nodes in three patients during a limited central node dissection, and the results were all negative for malignant cells in the contralateral nodes. Thus, there was no case of conversion from a limited node dissection to

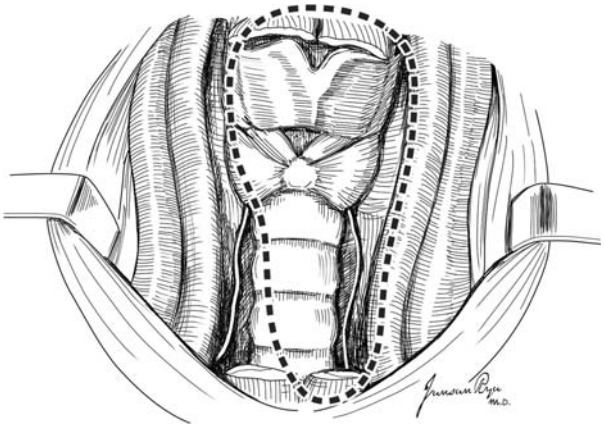

**FIG. 1.** Extent of prophylactic "limited" lymph node dissection in the central neck area. "Limited" lymph node dissection included the lymph nodes of ipsilateral paratracheal lymph nodes, pretracheal and prelaryngeal lymph nodes and the contralateral paratracheal nodes are not dissected.

**TABLE 1.** *Subject characteristics*

| | Extent of central neck dissection | | |
|---|---|---|---|
| | LCND | CCND | *P* value |
| No. subjects | 56 | 58 | |
| Gender (M/F) | 15/41 | 13/45 | .66 |
| Age | | | |
| Mean ± SD | 48.1 ± 10.7 | 48.7 ± 10.4 | .77 |
| Age group<45/≥45 | 20/36 | 21/37 | .95 |
| MACIS score | | | |
| Mean ± SD | 4.7 ± 0.9 | 4.9 ± 1.0 | .36 |
| <6/≥6 | 49/7 | 50/8 | .83 |
| Preoperative sonography findings | | | |
| Multiple tumors | 5 (8.9%) | 10 (17.2%) | .18 |
| Bilateral tumors | 4 (7.1%) | 4 (6.9%) | .98 |
| Additional procedures during surgery | | | |
| RLN sacrifice | 0 (0.0%) | 1 (%) | .32 |
| No. parathyroid gland preserved | 3.4 ± 0.8 | 3.3 ± 0.6 | .72 |
| Parathyroid autotransplantation | 1.4 ± 0.5 | 1.1 ± 0.3 | .78 |

LCND, limited central neck dissection; CCND, comprehensive central neck dissection.

comprehensive one. If multiple thyroid tumors were noted in the preoperative ultrasonography, the side of paratracheal lymph node dissection was the side where the main, large tumor in thyroid gland was located.

Patients were assigned to either type of neck dissection in addition to a total thyroidectomy solely by the operator. One surgeon performed the CCND in case of proven thyroid papillary carcinoma; however, two other surgeons did LCND for clinically node-negative papillary carcinomas.

The characteristics of the patients in each group are presented in Table 1. Fifty-six patients received a LCND, and 58 patients a CCND. Gender ratio, age distribution, and MACIS (Metastasis, Age at diagnosis, Completeness of primary tumor resection, Invasion of extrathyroidal tissues, and Size of primary tumor) scores[13,14] were similar in the two groups. The presence of multiple tumors on the preoperative ultrasonography was slightly more frequent in the CCND group. However, this difference did not reach statistical significance. During the operation, one side of the recurrent laryngeal nerve was sacrificed due to overt invasion by primary thyroid tumor to the nerve in one patient of CCND group. Subsequently, this patient was managed with thyroplasty to improve the vocal quality.

After the thyroidectomy with LCND or CCND, all subjects received low-dose (30–50 mCi) 131-I radioactive iodine treatments within 2–3 months after surgery. Then, based on the serum thyroglobulin level, antithyroglobulin antibody level, and the findings of post 131-I radioactive iodine scans, it was determined whether subsequent 131-I radioactive iodine treatments were needed. Ultimately, 103 patients (90.4%) had two or more 131-I radioactive iodine treatments with a dose of 30–200 mCi.

The numbers of parathyroid glands preserved and the numbers of parathyroid autotransplanted into the sternocleidomastoid muscles were similar in the two groups.

The data of the final surgical pathology are presented in Table 2. The thyroid tumor was slightly larger in the CCND group. Approximately 60% of tumors, in both groups, exhibited extrathyroid invasion. Similar to the findings of the preoperative ultrasonography, multifocality and bilaterality of the thyroid tumors had a tendency to be more frequent in the CCND group than in the LCND group. The number of dissected lymph nodes in the central compartments was 4.9 ± 2.7 in the LCND group and 9.3 ± 6.7 in the CCND group; the difference between these findings was statistically significant. The rate of metastasis to the lymph nodes in the central compartment was around 40% in both groups, and the metastases to the contralateral paratracheal lymph node groups were noted in five cases (8.6%) of subjects in the CCND group. Among them, multifocal tumors were found only in one patient; while the other four had single primary tumor, confined in one lobe of the thyroid gland.

We compared the complication rates and the recurrence rates between the two groups during 2 years of follow-up. Hypocalcemia was defined as at least one episode of symptoms or signs of hypocalcemia (perioral numbness, paresthesia of hands and feet,

**TABLE 2.** *Pathology data*

| | Extent of central neck dissection | | |
|---|---|---|---|
| | LCND ($N$ = 56) | CCND ($N$ = 58) | $P$ value |
| Primary tumor | | | |
| Diameter, mean ± SD | 1.1 ± 0.8 | 1.4 ± 0.9 | .063 |
| Multifocality, No. (%) | 12 (21.4%) | 22 (37.9%) | .067 |
| Bilateral tumors, No. (%) | 10 (17.9%) | 14 (24.1%) | .41 |
| Extrathyroid invasion, No. (%) | 33 (58.9%) | 34 (58.6%) | .97 |
| Lymph nodes in the central compartment | | | |
| No. LN examined, mean ± SD | 4.9 ± 2.7 | 9.3 ± 6.7 | <.0001 |
| Positive LNs, mean (range) | 1.2 (0–11) | 1.3 (0–10) | .79 |
| Malignancy positive rates of LNs, per subject, No. (%) | 24 (42.9%) | 23 (39.7%) | .72 |
| Metastasis to contralateral LNs rates, No. (%) | – | 5 (8.6%) | – |

LN, lymph node; LCND, limited central neck dissection; CCND, comprehensive central neck dissection.

Chvostek sign, Trousseau sign, muscle cramp, and tetany) or biochemical hypocalcemia, that is, ionized Ca level under 1.0 mmol/L at any time during the hospital stay. There was no difference in hospital stay between the two groups (mean 3.15 days in LCND group and 3.50 days in CCND group after surgery).

Permanent hypocalcemia was defined as persistent symptomatic or biochemical (Ca level below 8.0 mg/dL) hypocalcemia at more than 6 months after thyroidectomy. Intact parathyroid hormone (PTH) levels were also measured at 1 hour after surgery and early the morning after the surgery using immunoradiometric assay (ELSA-PTH, October 2004-model 13, Cis bio international, France), and then serially up to 6 months after surgery.

The cases with elevation of thyroglobulin or antithyroglobulin antibody compared with the basal levels suggested a disease recurrence. The site of recurrence was proven by 131-I radioactive iodine whole body scan, ultrasonography, CT, and PET/CT (in one case). We also compared the serum thyroglobulin levels and antithyroglobulin antibody status between the two groups.

The chi-square test and Fisher exact test were used to analyze the significance of differences in the proportion of variables between the two groups. The difference of continuous variables was analyzed by employing the $t$ test. The Standard SPSS (version 11.0, Statistical Package for Social Science, Chicago, IL) was used for the statistical analyses. A two-tailed $P$ less than .05 was considered significant.

## RESULTS

### Complications

Acute complications such as immediate postoperative bleeding and wound infection were not different between the two groups; one case of bleeding occurred in the LCND group. The occurrence of temporary vocal fold palsy was similar in the two groups. Permanent vocal fold palsy (more than 6 months after surgery) was present in one case, in which purposeful sacrifice of ipsilateral recurrent laryngeal nerve was required due to gross tumor invasion of the nerve (Table 3). However, transient hypocalcemia, defined as either serum hypocalcemia or hypocalcemia symptoms, was more frequent in the CCND group than in the LCND group from the immediate postoperative period until 6 months after surgery (48.3% vs 26.8%, $P$ = .021, odds ratio [OR] = 2.55). The patients with hypocalcemia inevitably took large doses of calcium supplements and an active vitamin D formula to relieve their symptoms until recovery. In addition, the immediate postoperative reduction in parathyroid hormone (PTH) levels was more evident in the CCND group (Table 4). Compared with 5.4% in the LCND group, 19.0% of the CCND group had postoperative PTH levels below 3 pg/mL ($P$ = .043). However, the difference was eliminated over the following 6 months at which time the levels in two groups were 12.4 and

**TABLE 3.** *Postoperative complication rates*

| | Extent of central neck dissection | | |
|---|---|---|---|
| | LCND ($N$ = 56) | CCND ($N$ = 58) | $P$ value |
| Postoperative bleeding | 1 (1.8%) | 0 (0.0%) | .49 |
| Wound infection | 0 (0.0%) | 0 (0.0%) | 1.0 |
| Vocal fold palsy | | | |
| Temporary | 2 (3.6%) | 3 (5.2%) | 1.0 |
| Permanent | 0 (0.0%) | 1 (1.7%) | 1.0 |
| Hypocalcemia | | | |
| Transient | 15 (26.8%) | 28 (48.3%) | .021 |
| Permanent | 1 (1.8%) | 3 (5.2%) | .62 |

LCND: limited central neck dissection; CCND: comprehensive central neck dissection.

**TABLE 4.** *Postoperative parathyroid hormone levels*

| | Extent of central neck dissection | | |
|---|---|---|---|
| | LCND ($N = 56$) | CCND ($N = 58$) | $P$ value |
| Immediate postoperative PTH level, No. (%) | | | |
| <7 pg/mL | 21 (37.5%) | 30 (51.7%) | .14 |
| <5 pg/mL | 15 (26.8%) | 24 (41.4%) | .117 |
| <3 pg/mL | 3 (5.4%) | 11 (19.0%) | .043 |
| PTH level at 6 months after surgery, pg/mL, mean ± SD | 12.4 ± 8.7 | 11.8 ± 10.0 | .73 |

PTH, parathyroid hormone; LCND, limited central neck dissection; CCND, comprehensive central neck dissection.

**TABLE 5.** *Clinical outcome data*

| | Extent of central neck dissection | | |
|---|---|---|---|
| | LCND ($N = 56$) | CCND ($N = 58$) | $P$ value |
| Recurrence | | | |
| Local | 0 (0.0%) | 0 (0.0%) | 1.0 |
| Regional | 3 (5.4%) | 1 (1.7%) | .36 |
| Distant | 1 (1.8%) | 4 (6.9%) | .364 |
| Serum TG level at last follow-ups, ng/mL, mean ± SD | 0.29 ± 0.27 | 0.25 ± 0.17 | .34 |
| Patient No.(%) with TG antibodies | | | |
| 0–50 lg/mL | 46 (82.1%) | 46 (79.3%) | .814 |
| 50–100 lg/mL | 8 (14.3%) | 9 (15.5%) | 1.0 |
| >100 lg/mL | 2 (3.6%) | 3 (5.2%) | 1.0 |
| Follow-up (months, mean ± SD) | 24.2 ± 4.9 | 24.1 ± 6.6 | .92 |

LCND, limited central neck dissection; CCND, comprehensive central neck dissection.

11.8 pg/mL. As a result, permanent hypocalcemia (>6 months) remained in only one patient in the LCND group and in three in the CCND group; this difference was not statistically significant.

### Oncological Safety During the 2-Year Follow-Up

There was no local recurrence, that is, in the surgical bed of the thyroidectomy, in either group. Regional recurrence occurred in three cases in the LCND group and one in the CCND group (Table 5). Interestingly, all of the regional recurrences were detected in the lateral lymph node groups: two in the lower jugular and supraclavicular lymph node groups and two in the mid jugular lymph node groups. As for the regional recurrences, high-dose 131-I radioactive iodine treatment (≥150 mCi) was used in one patient. In another three patients, subsequent salvage lymph node dissection was performed after the additional 131-I radioactive iodine treatment. Distant metastases to the lung were found in five patients during the 2-year follow-up after surgery: one in the LCND group and four in the CCND group. The patients have been treated with high-dose 131-I radioactive iodine treatment.

At the last follow-up, the serum thyroglobulin levels remained low in most patients (0.29 vs 0.25 ng/mL). Among all subjects, around 15% of patients showed an antithyroglobulin antibody level of more than 50 μg/mL in both groups. There were 3–5% of patients who had a markedly elevated level of antithyroglobulin antibody over 100 μg/mL. These levels of antithyroglobulin antibody were similar in the two groups.

## DISCUSSION

Patients who underwent prophylactic lymph node dissection with thyroid papillary microcarcinomas were found to have a high risk of lymph node metastasis in the central compartment (40–60%).[4,6,12] According to one of these reports, the cancers from nonpalpable lymph nodes usually remain indolent and rarely become clinically significant; thus, prophylactic node dissection for thyroid papillary microcarcinomas is not recommended.[4] However, many other studies have reported that the presence of lymph node metastasis in thyroid papillary carcinoma is related to recurrence, but not survival.[4,15–19] One recent report suggested significantly higher mortality rates for differentiated thyroid cancer involving lymph nodes.[20] Therefore, the exact staging of the lymph node status at initial treatment is one of the most important factors for assessing the risk of recurrence, which is essential to determine the adjuvant 131-I treatment and to decide on the follow-up strategy as well as to remove the potential source of recurrence.[12]

Even with the benefits from the prophylactic central compartment dissection, central lymph node dissection inevitably results in a higher rate of postoperative hypocalcemia than does no dissection.[2,5,6] Therefore, to balance the benefits and risks from prophylactic central nodal dissection, an alternative management option for the central nodal compartment is needed. We considered the previous results that the lymph node metastasis to the contralateral central compartment was not high (less than 20%) in clinically node-negative thyroid papillary microcarcinomas.[4,11] This implied that the contralateral central compartment (contralateral paratracheal nodes) may not need to be dissected in the prophylactic central node dissection. In one trial, it was reported that in clinically node-negative papillary thyroid

carcinomas the addition of routine ipsilateral central compartment dissection resulted in lower postablation levels of thyroglobulin and higher rates of athyroglobulinemia when compared with total thyroidectomy alone, and the long-term complication rates were the same in the two study groups.[21,22] However, little information is available comparing conventional CND (bilateral nodal dissection in the central compartment) and ipsilateral CND for complication rates and oncological safety. This is the first study to compare the ipsilateral CND with conventional bilateral CND.

In this study, we defined the prophylactic nodal dissection of the ipsilateral paratracheal nodes, prelaryngeal nodes as well as pretracheal nodes as the "limited" CND. Because the chance of occult metastasis was relatively high (40.0%) in the pretracheal nodes,[4] we routinely included the pretracheal nodes in the LCND. Moreover, the dissection of the prelaryngeal and pretracheal nodes can be performed relatively easily without significant surgical morbidities. Therefore, we used the LCND even with the paraisthmic tumors of the thyroid gland.[11]

The results of our study showed that during a relatively short-term follow-up (approximately 2 years), similar thyroglobulin levels after 131-I radioactive iodine treatments could be achieved with both types of CND. In addition, the recurrence rates were similar in the two groups. These results imply that the information on the nodal status from the LCND might be sufficient for decisions about the adjuvant 131-I radioactive iodine treatments and the follow-up management.

Transient vocal fold palsy has been reported to occur in 3–6% of cases.[2,5,23] The occurrence of temporary vocal fold palsy in our series was similar (3.6% in the LCND group, 5.2% in the CCND group). Permanent vocal fold palsy (more than 6 months) did not develop except in the one case where section of the recurrent laryngeal nerve was performed for complete tumor removal.

Although the rates of permanent hypocalcemia were similar in the two groups, transient hypocalcemia was significantly higher in the CCND group than in the LCND group (48.3% vs 26.8%). Compared with the previous data (14–23.2%),[2,5,23] our results on the rate of transient hypocalcemia rate in the CCND were slightly higher. This might be explained by differences in the definition of "hypocalcemia" by using the different tools; we included symptomatic evaluation and biochemical assay of serum calcium or ionized calcium. To confirm the higher incidence of transient hypocalcemia in the CCND group, we also reviewed the postoperative levels of PTH in the two groups. The data showed that reduced PTH levels were more prominent in the CCND group. In our series, the number of parathyroid glands preserved and autotransplanted was not different in the two groups. Thus, transient hypoparathyroidism in the CCND group was probably related to a compromise of the blood supply due to the bilateral paratracheal nodal dissection.[2] The difference in the immediate postoperative PTH levels recovered to similar level in the two groups after 6 months, and the occurrence of permanent hypocalcemia did not differ in the two groups.

Our findings suggest that the LCND with total thyroidectomy for clinically node-negative papillary thyroid carcinomas offers acceptable oncological results in a 2-year follow-up and a reduction in the postoperative transient hypocalcemia. The prophylactic bilateral CND could diminish the quality of life during the early postoperative period. This may prolong the hospital stay after thyroid surgery.

This study contains some limitations. First, this is a retrospective analysis with a relatively short-term follow-up. Therefore, selection bias for allocating patients into each group may exist. Prospective randomized studies with a larger number of cases are needed to assess the exact clinical role of the LCND vs CCND. In addition, to determine the impact on the disease recurrence and survival with the two methods of CND, data from longer follow-up is needed. Nevertheless, this study provides the short-term evidence of the safety of the prophylactic LCND for the management of papillary thyroid carcinomas.

In conclusion, the LCND with total thyroidectomy could be an alternative surgical option for clinically node-negative papillary thyroid carcinomas, because it results in a reduced transient hypocalcemia and similar oncological outcomes during a 2-year follow-up. Further study with a larger number of patients and long-term follow-up is needed.

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