The effectiveness of prophylactic ipsilateral central neck dissection in selected patients who underwent total thyroidectomy for clinically node-negative unilateral papillary thyroid carcinoma

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Background: Prophylactic central neck dissection (CND) in clinically node-negative (cN0) papillary thyroid carcinoma (PTC) remains controversial. The purpose of this study was to evaluate the benefits of prophylactic ipsilateral CND compared with bilateral CND in total thyroidectomy for cN0 unilateral PTC.

Methods: We retrospectively enrolled 174 patients who underwent total thyroidectomies with prophylactic CND for cN0 unilateral PTC between January 2009 and May 2010. The prophylactic CND patients were divided into group 1, the ipsilateral CND group (n=74), and group 2, the bilateral CND group (n=100). The incidence of central lymph node metastasis (CLNM) and postoperative complications, such as hypoparathyroidism, recurrent laryngeal nerve injury, and recurrence were assessed.

Results: CLNM was found in 22 (29.8%) in group 1 and 69 (69%) in group 2. The incidence of postoperative severe hypocalcemia less than 7.0 was also significantly different (six patients [8.1%] in group 1 and 23 [23%] in group 2; p=0.009). Permanent hypoparathyroidism was significantly more frequent in group 2 (4.1% vs. 19%; p=0.005). However, the incidence of transient hypoparathyroidism, recurrence, and recurrent laryngeal nerve injury was not significantly different.

Conclusion: Prophylactic ipsilateral CND has advantage not only to reduce incidence of some complications but also to have similar recurrence rate compared with bilateral CND. We suggest that prophylactic ipsilateral CND may be safe and effective for selected patients undergoing total thyroidectomy for cN0 unilateral PTC.

Keywords: Hypoparathyroidism; Lymph node; Neck dissection; Papillary thyroid carcinoma

Introduction

The treatment of differentiated thyroid carcinoma has shown excellent outcomes, with a 0.6% recurrence rate and over 95% 10-year disease-free survival [1]. Nevertheless, there are complications associated with total thyroidectomies, such as hypoparathy-roidism, recurrent laryngeal nerve and external branch of the superior laryngeal nerve injury, and locoregional recurrence. The risk of these complications may increase with the extent of surgery. Recently, there has been a growing interest in functional complications after total thyroidectomy. The typical long-term functional complication after total thyroidectomy is permanent

hypoparathyroidism, with a 10%–60% incidence [2]. Most endocrine surgeons follow a parathyroid preservation principle during thyroidectomy; however, hypoparathyroidism can occur because of devascularization, thermal or mechanical damage, and inadvertent removal of the parathyroid gland. Permanent hypoparathyroidism can lead to symptomatic hypocalemia, the need for lifetime calcium supplementation, and seriously impact the patient's quality of life. Furthermore, the incidence of permanent hypoparathyroidism after total thyroidectomy is greatly influenced by the experience of the operator and the decision of whether or not to perform central neck dissection (CND).

Central lymph node metastases (CLNM) have been reported in approximately 30%–80% of the patients with papillary thyroid carcinoma (PTC) [3]. It is difficult to detect metastatic central lymph node (LN) by ultrasound preoperatively because, while the specificity is 80%–93%, the sensitivity is only 53%–61% [4]. Tumor size and extrathyroidal extension are known risk factors for ipsilateral CLNM. And ipsilateral CLNM is a significant factor in contralateral LNM [3,5-8]. Prophylactic CND is defined as the removal of level VI LNs, which includes the pretracheal, prelaryngeal, and paratracheal LNs. Prophylactic CND is performed to remove occult nodal metastases with negative preoperative assessments. Several studies have reported that patients who underwent prophylactic CND had a higher rate of complications and no effect on survival, and prophylactic CND may not be routinely recommended [9-12]. Furthermore, according to the 2015 American Thyroid Association (ATA) guidelines, prophylactic CND should be considered for patients with advanced primary tumors (T3 or T4) and clinically involved lateral neck nodes (cN1b), while CND may not be appropriate for small (T1 or T2), clinically node-negative (cN0) PTC [13]. In contrast, some studies have reported that prophylactic CND should be performed because of the high incidence of central neck LNM and the poor sensitivity of ultrasound [14]. In another study, of the patients who underwent prophylactic CND with cN0 PTC, 45.8% had central neck LNM, 0.9% had recurrent laryngeal nerve injuries, 1.16% had a locoregional recurrence, 6.24% had transient hypoparathyroidism, and 0.13% had permanent hypoparathyroidism [15]. Nevertheless, prophylactic CND in cN0 PTC remains controversial.

Total thyroidectomy without CND helps to reduce the risk of hypoparathyroidism and recurrent laryngeal nerve injury, but it can leave metastatic LNs because of the high incidence of ipsilateral central compartment LNM. Finally, it can affect locoregional recurrence. In contrast, total thyroidectomy with bilateral CND has the advantage of identifying and controlling LNM, but it also has the disadvantage of increased risks of hypoparathyroidism and recurrent laryngeal nerve injury. The incidence of contralateral LNM is below 5%. If the risk factors for contralateral LNM are not present, ipsilateral CND may be reasonable. We focused on the extent of prophylactic CND during total thyroidectomies in cN0 PTC patients. The endpoints of this study were (1) the incidence of transient and permanent hypoparathyroidism, (2) transient and permanent recurrent laryngeal nerve injury, and (3) recurrence. The aim of this study was to evaluate the benefits of prophylactic ipsilateral CND compared with bilateral CND in total thyroidectomy for cN0 unilateral PTC.

Materials and methods

1. Ethics statements
This study was approved by the Institutional Review Board of Yeungnam University Hospital (IRB No: 2019-09-066).

2. Patients
We retrospectively enrolled 324 consecutive patients who underwent total thyroidectomies with prophylactic CND for cN0 unilateral PTC by a single experienced surgeon between January 2009 and May 2010. The inclusion criteria were patients (1) with a final postoperative diagnosis of PTC, (2) who underwent a total thyroidectomy with prophylactic CND, (3) had follow-up parathyroid hormone (PTH) and calcium testing, and (4) had no evidence of clinical node positivity. The exclusion criteria were patients (1) without follow-up examinations or laboratory tests, (2) concomitant modified radical neck dissection, (3) parathyroidectomy due to parathyroid adenoma, (4) bilateral PTC, (5) 11 male sex in only group 1, and (6) other types of pathological results. One hundred-fifty patients (bilateral carcinoma, male, modified radical neck dissection, lack of follow-up or laboratory tests and parathyroidectomy) who met the exclusion criteria were excluded among of 324 patients. Finally, 174 patients were divided into two groups according to the extent of CND. Seventy-four patients in group 1 underwent prophylactic ipsilateral CND with total thyroidectomy and 100 patients in group 2 received prophylactic bilateral CNDs with total thyroidectomy. Ipsilateral CND was defined as the removal of ipsilateral paratracheal, pretracheal, and prelaryngeal LNs. Bilateral CND was defined as the removal of paratracheal, pretracheal, and prelaryngeal LNs. All patients received prophylactic ipsilateral CNDs and whether or not a prophylactic bilateral CND was performed depended on the frozen biopsy result of the ipsilateral LN and enlarged contralateral LN intraoperatively.

3. Study design
Patients with intraoperative findings, such as parathyroid color

change and autotransplantation, were excluded because of subjective evidence. Robotic or endoscopic thyroidectomies were also excluded because those techniques offer magnified views that can make it easier for the surgeon to preserve the parathyroid. We classified PTC according to the American Joint Committee on Cancer 7th edition and minimal extrathyroidal extension was categorized as T3. The indications for radioactive iodine ablation were extrathyroidal extensions and LN involvement. We reviewed basic characteristics of the patients (age, tumor location, size, multifocality, concomitant benign tumor, and length of the lobe), histopathological factors (lymphocytic thyroiditis, extrathyroidal extension, margin status, number of retrieved LN, metastasis, and parathyroid on tissue) and laboratory tests (postoperative PTH and calcium). We investigated the incidence of transient and permanent hypoparathyroidism, transient and permanent hoarseness, and recurrence by reviewing the patients' medical records. Recurrence was defined as tumor in the thyroidectomy bed or metastatic central or lateral cervical LN after surgery. Recurrent laryngeal nerve injury was assessed by patient's self-assessment and physician's objective assessment. Permanent recurrent laryngeal nerve injury was defined as persistent hoarseness and vocal cord palsy identified with laryngeal examination more than 6 months after surgery. Through this study, we sought to find evidence for two hypotheses. The first hypothesis is that prophylactic CND during total thyroidectomy in cN0 PTC should not be routinely discounted because of the rate of incidentally found CLNM. And second, prophylactic ipsilateral CND is more advantageous than bilateral CND according to the complication rate.

4. Hypoparathyroidism

Hypoparathyroidism was defined as PTH levels < 10 pg/mL (range, 10–65 pg/mL). Transient hypoparathyroidism was defined when a low PTH level returned to normal within the follow-up period. And permanent hypoparathyroidism was defined as PTH < 10 pg/mL with persistent low PTH levels during follow-up. PTH was tested on postoperative 1 day and then at annual follow-ups. Calcium levels less than 8.5 mg/dL were classified as hypocalcemia. We tested calcium level perioperatively, then regularly at follow-up. Calcium and vitamin D supplements were used to maintain the calcium and vitamin D levels as close to normal as possible, regardless of the patient's symptoms.

5. Statistical analyses

Chi-squared tests or Fisher exact test or linear and linear association was used to compare the categorical variables. Student t-tests were used for continuous valuables, which are expressed as mean ± standard deviation. All statistical analyses were performed

using IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA) and p-values < 0.05 indicated statistical significance.

Results

1. Patient characteristics

Table 1 shows a comparison of the characteristics of patients between the two groups. One hundred seventy-four patients were included in this study, of which 74 were assigned to group 1 and 100 to group 2 according to the extent of CND. All 174 patients were female. The mean age of the patients was 47.8 ± 11.2 years and 45.1 ± 10.2 years and the mean tumor size was 0.8 ± 0.5 cm and 0.9 ± 0.6 cm in groups 1 and 2, respectively. There was no significant difference in age, tumor size, location, multifocality, length of dominant lobe, minimal extrathyroidal extension, lymphocytic thyroiditis, positive margin or stage between the groups. However, radioactive iodine ablation was different in 31 patients (41.9%) and 62 patients (62%) in groups 1 and 2, respectively (p = 0.009). The mean follow-up period was 118.2 ± 4.6 and 115.5 ± 4.1 months in groups 1 and 2, respectively (p < 0.001).

Table 1. Patient characteristics

Characteristic	Group 1 (n = 74)[a]	Group 2 (n = 100)[b]	p-value
Female sex	74	100	NA
Age (yr)	47.8 ± 11.2	45.1 ± 10.2	0.097
Age < 45 yr	28 (37.8)	42 (42)	0.580
Tumor size (cm)	0.8 ± 0.5	0.9 ± 0.6	0.736
Tumor location			0.850
Upper	14 (18.9)	24 (24)	
Middle	52 (70.3)	65 (65)	
Lower	5 (6.8)	6 (6)	
Isthmus	3 (4)	5 (5)	
Multifocality	14 (18.9)	16 (16)	0.614
Length of dominant lobe	4.8 ± 0.8	4.6 ± 0.7	0.096
Minimal extrathyroidal extension	43 (58.1)	66 (66)	0.287
Lymphocytic thyroiditis	17 (23)	34 (34)	0.114
Margin positivity	10 (13.5)	13 (13)	0.675
Stage			0.614
I	45 (60.8)	57 (57)	
III	29 (39.2)	43 (43)	
Calcium replacement	59 (79.7)	88 (88)	0.136
RI ablation	31 (41.9)	62 (62)	0.009
Follow–up (mo)	118.2 ± 4.6	115.5 ± 4.1	< 0.001

Values are presented as mean±standard deviation or number (%).
NA, not applicable; RI, radioactive iodine; CND, central neck dissection.
[a]Group 1, ipsilateral CND group. [b]Group 2, bilateral CND group.

2. Central neck dissection: ipsilateral versus bilateral

The number of ipsilateral paratracheal LNs was 3.8 ± 2.8 and 4.8 ± 3.1 in groups 1 and 2, respectively ($p = 0.034$). The number of pretracheal and prelaryngeal LNs were 0.6 ± 1.2 and 1.8 ± 2.3, respectively ($p < 0.001$). Ipsilateral paratracheal LNM was found in 21 patients (28.4%) and 44 patients (44%) in groups 1 and 2, respectively ($p = 0.035$). Pretracheal LNM was found in one patient (1.4%) and 15 patients (15%) in each group ($p = 0.002$). Contralateral paratracheal LNM was 10 (10%) in group 2. The final pathologic results showed that the parathyroid gland was inadvertently removed in 15 patients (20.3%) and 22 patients (22%) in groups 1 and 2, respectively. Among these, the ipsilateral parathyroid was removed in 12 patients (16.2%) and 12 patients (12%) ($p = 0.425$) in groups 1 and 2, respectively, the contralateral parathyroid in 2 (2.7%) and 8 (8%) ($p = 0.193$) and both in 1 (1.4%) and 2 (2%). There was no significant difference in the removal of parathyroid glands inadvertently between the groups (Table 2).

3. Postoperative parathyroid hormone and calcium levels

The postoperative PTH and calcium level are shown in Table 3. Postoperative PTH levels were measured at 1 day, 1 year, and 2 years then annually at follow-up. By linear and linear association, there was a decreasing trend of the hypoparathyroidism (PTH < 10 pg/mL) over time ($p < 0.001$). The 1-day PTH levels (average) were significantly different (19.3 ± 12.1 in group 1 and 13.2 ± 9.4 in group 2; $p < 0.001$). One-year PTH levels (average) were 22.9 ± 10.2 and 19.6 ± 10.6 ($p = 0.003$) and 2-year PTH lev-

els (average) were 26.1 ± 10.9 and 19.6 ± 10.6 in groups 1 and 2, respectively ($p < 0.001$). The calcium levels in groups 1 and 2, respectively, were 9.1 ± 0.5 and 8.9 ± 0.4 preoperatively and 8.1 ± 0.6 and 7.8 ± 0.6 postoperatively. The perioperative calcium levels were not different (1.0 ± 0.7 in group 1 and 1.1 ± 0.6 in group 2; $p = 0.302$). But there was a significant difference in the incidence of postoperative severe hypocalcemia defined as calcium levels ≤ 7.0 mg/dL (6 patients [8.1%] in group 1 and 23 [23%] in group 2; $p = 0.009$).

4. Hypoparathyroidism, recurrent laryngeal nerve injury, and recurrence

Postoperative transient hypoparathyroidism was observed in 25 patients (33.8%) and 38 patients (38%) ($p = 0.527$), whereas permanent hypoparathyroidism occurred in three patients (4.1%) and 19 patients (19%) in groups 1 and 2, respectively. There was significant difference in the incidence of postoperative permanent hypoparathyroidism ($p = 0.005$). Transiently recurrent laryngeal nerve injury after total thyroidectomy with CND was estimated through medical record review, at 14 patients (18.9%) and 17 patients (17%) in groups 1 and 2, respectively ($p = 0.744$). Permanently recurrent laryngeal nerve injury totally occurred in three patients (1.7%). One patient in group 1 underwent nerve shaving because of recurrent laryngeal nerve invasion. In two patients in group 2, one patient received nerve repair and returned to a normal voice after 6 months. Laboratory tests and ultrasound examination were performed every 6 months until 2 years after surgery

Table 2. Comparison of ipsilateral versus bilateral prophylactic central neck dissection

Variable	Group 1 (n = 74)[a]	Group 2 (n = 100)[b]	p-value
Numbers of retrieved LN			
Ipsilateral paratracheal LN	3.8 ± 2.8	4.8 ± 3.1	0.034
Pretracheal and prelaryngeal LN	0.6 ± 1.2	1.8 ± 2.3	< 0.001
Contralateral paratracheal LN	0	4.0 ± 3.0	NA
Metastasis in level VI LN			
Ipsilateral paratracheal LN	21 (28.4)	44 (44)	0.035
Pretracheal and prelaryngeal LN	1 (1.4)	15 (15)	0.002
Contralateral paratracheal LN	0	10 (10)	NA
Parathyroid in tissue			
Ipsilateral	12 (16.2)	12 (12)	0.425
Contralateral	2 (2.7)	8 (8)	0.193
Both	1 (1.4)	2 (2)	NA

Values are presented as mean±standard deviation or number (%).
LN, lymph node; NA, not applicable; CND, central neck dissection.
[a]Group 1, ipsilateral CND group. [b]Group 2, bilateral CND group.

Table 3. Postoperative PTH and calcium level

Factor	Group 1 (n = 74)[a]	Group 2 (n = 100)[b]	p-value
Postoperative PTH (< 10 pg/mL)			< 0.001
1 Day	28 (37.8)	57 (57)	
1 Year	6 (8.1)	23 (23)	
2 Years	3 (4.1)	19 (19)	
Postoperative PTH (pg/mL)			
1 Day	19.3 ± 12.1	13.2 ± 9.4	< 0.001
1 Year	22.9 ± 10.2	18.3 ± 9.6	0.003
2 Years	26.1 ± 10.9	19.6 ± 10.6	< 0.001
Preoperative Ca	9.1 ± 0.5	8.9 ± 0.4	0.029
Postoperative Ca	8.1 ± 0.6	7.8 ± 0.6	0.007
Difference of Ca (perioperative level)[c]	1.0 ± 0.7	1.1 ± 0.6	0.302
Postoperative Ca ≤ 7.0 (severe hypocalcemia)	6 (8.1)	23 (23)	0.009

Values are presented as mean±standard deviation or number (%).
PTH, parathyroid hormone; Ca, calcium; CND, central neck dissection.
[a]Group 1, ipsilateral CND group. [b]Group 2, bilateral CND group.
[c]Perioperative level=postoperative–preoperative calcium level.

Table 4. Hypoparathyroidism, recurrent laryngeal nerve injury, and recurrence after total thyroidectomy with ipsilateral or bilateral CND

Variable	Group 1 (n = 74)[a)]	Group 2 (n = 100)[b)]	p-value
Hypoparathyroidism			
Transient	25 (33.8)	38 (38)	0.527
Permanent	3 (4.1)	19 (19)	0.005
Recurrent laryngeal nerve injury			
Transient	14 (18.9)	17 (17)	0.744
Permanent	1 (1.4)	2 (2)	NA
Recurrence	1 (1.4)	1 (1)	NA

Values are presented as number (%).
CND, central neck dissection; NA, not applicable.
[a)]Group 1, ipsilateral CND group. [b)]Group 2, bilateral CND group.

and then annually during follow-up. Among the 174 patients, only two patients (1.1%) had a recurrence. Contralateral paratracheal LNM was found in one patient in group 1, 8 years after surgery and another in group 2 was identified with lateral neck LNM 3.5 years after surgery (Table 4).

Discussion

Prophylactic CND (ipsilateral or bilateral) can be considered in cN0 PTC with advanced tumors (T3 or T4) or cN1b [13]. Other study reported routine prophylactic CND is a treatment option for cN0 PTC [15]. It remains controversial. Our study uniquely compared ipsilateral with bilateral CND according to the extent of prophylactic CND. Furthermore, no previous studies have reported the details of postoperative hypoparathyroidism among CND groups. The starting point of our study was whether the need for prophylactic CND could be discounted. Our study was subject to two well-known facts. First, there is a relatively higher possibility of complications in CND patients than in non-CND patients. Second, there is a high incidence of CLNM incidentally in cN0 PTC patients. Surgeons might feel comfortable when only thyroidectomy is performed through capsular dissection, which can lead to decreased operative times and easy preservation of the parathyroid. Until now, the main idea was not to perform a prophylactic CND, which is prudent, except in the case of large tumors and clinically suspicious factors. Nevertheless, many endocrine surgeons might feel uneasy because of the high incidence of CLNM. If prophylactic CND is not preformed, the status and number of metastatic LNs cannot be determined. Ipsilateral CLNM might lead to contralateral central LN and lateral neck LNMs. Whether microscopic metastasis of the central LNs

should be ignored is still debatable. However, it is clear that prophylactic CND has an important role in controlling metastatic LNs found incidentally. The incidence of recurrent laryngeal nerve injury can decrease according to the surgeon's experience but the preservation of the parathyroid is more complex. To preserve the parathyroid more experience and strong preservation intent are needed. CND is known to be associated with a higher incidence of hypoparathyroidism. We considered how to decrease the incidence of hypoparathyroidism and to get similar oncologic safety. Finally, we focused on prophylactic ipsilateral CND after considering the pros and cons of prophylactic CNDs. The aim of our study was to evaluate the benefits of prophylactic ipsilateral CND with total thyroidectomy in cN0 PTC patients.

Several studies have reported the risk factors of central and lateral neck LNM [7,14,16,17]. Male sex, age (> 45 years), tumor size (> 5 mm), lower lobe, total tumor diameter (> 10 mm), and extracapsular spread were statistically significant factors for CLNM in multivariate analysis [7]. One study showed that young age (< 45 years), male sex, extrathyroidal extension, multifocal tumors, bilaterality, and tumor size (≥ 1 cm) were significant factors for CLNM, except in Hashimoto's thyroiditis [15]. Based on the above studies, the common risk factors for CLNM were young age, male sex, tumor size, and extrathyroidal extension. Furthermore, several studies found that CLNM was a significant risk factor for lateral neck LNM [18-20]. If some risk factors for CLNM are present preoperatively, prophylactic CND must be considered to control CLNM and reduce the possibility of lateral neck LNM. However, the role of prophylactic CND remains controversial, despite the high incidence of CLNM. A previous study found no significant difference in locoregional recurrence with or without CND and routine CND did not reduce lateral neck recurrence in cN0 PTC patients [21]. Higher complication rates and similar recurrence rates were found in patients who underwent total thyroidectomies with CND than total thyroidectomies alone. Specifically, transient hypocalcemia was significantly higher in total thyroidectomies with CND [12]. CND is associated with higher rates of transient hypoparathyroidism (12.6% in total thyroidectomy, 23.3% in total thyroidectomy with ipsilateral CND, and 36.7% in total thyroidectomy with bilateral CND) and a total thyroidectomy alone may be adequate treatment for patients with cN0 PTC [21]. However, recently, one study reported that CND reduced locoregional recurrence (6.9% difference at 10 years) [22]. Total thyroidectomy with CND resulted in a greater reduction in local recurrence than total thyroidectomy alone. Additionally, total thyroidectomy with bilateral CND showed significantly lower recurrence than total thyroidectomy alone [23]. This raises a question regarding how recurrence was assessed. Most studies used ultraso-

nography to assess preoperative and recurrent CLNM. However, in our experience, most paratracheal LNs were classified as indeterminate by preoperative ultrasonography. Furthermore, we performed regular ultrasonographic examinations during follow-up. At that time, it was difficult to identify LNM by ultrasonography. Hypoechoic lesions or indeterminate LNs at paratracheal lesions were often found postoperatively which were difficult to completely assess, unless fine needle aspiration was performed. Actual CLNM recurrence might not be detected because of ambiguous ultrasonographic results. This hypothesis can explain why the no-CND group had a recurrence rate similar to the CND group but a high incidence of CLNM. Preoperative ultrasonography has a 77% detection rate for LNM. Detection of CLNM using ultrasound, which has 92% specificity, 81% positive predictive value, 51% sensitivity, and 76% negative predictive value, is difficult [24,25]. Another study also reported the poor diagnostic accuracy of ultrasound for CLNM. Prophylactic CND is recommended due to the low diagnostic efficacy of ultrasound and high incidence of CLNM [14]. As discussed above, prophylactic CND can remove up to 50% of the metastatic LN unidentifiable in ambiguous ultrasound results.

Hypoparathyroidism is a common complication after total thyroidectomy, which was transient in 6.9%–46% of the patients and permanent in 0%–10% of the patients. During surgery, the parathyroid gland can be damaged by thermal or mechanical injury, vascular injury, or removed inadvertently [26]. Permanent hypoparathyroidism is usually defined as PTH levels below normal for more than 1 year. However, in our study, it was defined as persistent PTH levels below normal at follow-up because there have been many cases where PTH levels were shown to improve or decrease after 1 year. Large tumors (≥ 4 cm) or gross extrathyroidal extension were significant factors for permanent hypoparathyroidism postoperatively. Of 65 patients who underwent total thyroidectomies with bilateral CND, postoperative transient and permanent hypoparathyroidism were found in 44 (68%) and 12 (18%), respectively [27]. Other study showed the risk factors of hypoparathyroidism following total thyroidectomy with CND. Of 903 patients who underwent total thyroidectomy plus CND, 399 patients (44.2%) had transient hypoparathyroidism and 10 patients (1.1%) had permanent hypoparathyroidism. On multivariate analysis, female, nonuse of carbon nanoparticles, parathyroid autotransplantation, accidental parathyroid resection and bilateral CND were the independent factors of transient hypoparathyroidism. Nonuse of carbon nanoparticles and a tumor in the upper pole of thyroid gland were significant risk factors for permanent hypoparathyroidism [28]. Our study found severe postoperative hypocalcemia (calcium level ≤ 7.0) in six patients (8.1%)

and 23 patients (23%) in groups 1 and 2, respectively ($p = 0.009$). Parathyroid was found on the tissue in 15 (20.3%) of the ipsilateral CND patients and 22 (22%) bilateral CND patients. Permanent hypoparathyroidism was found in three patients (4.1%) and 19 patients (19%) in groups 1 and 2, respectively ($p = 0.005$). CND was associated with a higher incidence rate of hypoparathyroidism and complications. As shown in our study, 21 and 44% of the ipsilateral CLNM was found in cN0 PTC patients incidentally. In contrast, the incidence of permanent hypoparathyroidism and severe hypocalcemia (calcium level ≤ 7.0) in the ipsilateral CND group was significantly lower than in the bilateral CND group. The above results show that ipsilateral CND has the advantages of decreasing complication. A limitation of our study was that it was based on treatments performed 10 years ago. At that time, we focused on complete resection of the tumor burden, rather than preservation of the parathyroid. In conclusion, there were many cases of parathyroid present on removed tissue. Furthermore, we were notified of the loss of parathyroid inadvertently after surgery. If the inadvertent removal of parathyroid could be corrected, we could confidently state the advantages of ipsilateral CND. In group 2, there were higher incidence of RI ablation (41.9% vs. 62%; $p = 0.009$) and ipsilateral LNM (28.4% vs. 44%; $p = 0.035$). These could be caused by advanced disease than extent of CND. There were many cases of total thyroidectomy despite tumor size less than 1 cm, because of contralateral nodule or patient's preference. It might be a variable in determining the role of prophylactic ipsilateral CND.

In conclusion, our study showed lower permanent hypoparathyroidism and severe hypocalcemia rates in prophylactic ipsilateral CND compared with bilateral CND patients. Furthermore, there was no significant difference in recurrence rate between groups. We suggest that prophylactic ipsilateral CND may be safe and effective for selected patients undergoing a total thyroidectomy for cN0 unilateral PTC.

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