

## Effect of the application of prophylactic central compartment lymph node dissection on radioiodine ablation doses in patients with papillary thyroid carcinoma

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**Background/aim:** The aim of this study was to document the effect of the application of prophylactic central compartment dissection on radioiodine ablation activities for papillary thyroid carcinoma.

**Materials and methods:** This retrospective study included 452 (383 females, 69 males; mean age = 46.69 years, min-max: 13-71) patients who received ablative radioiodine activity between April 2010 and December 2014. The histopathological reports of thyroidectomy and the administered radioiodine activity were evaluated. Frequencies of prophylactic central compartment dissection according to T stage of the primary tumor, detection rate of lymph node metastases, and its effect on radioiodine ablation activities were calculated.

**Results:** Prophylactic central compartment dissection was applied for a total of 252 (56%) patients. The T stages of these patients were T1a, T1b, T2, and T3 in 85 (34%), 106 (42%), 41 (16%), and 20 (8%) cases, respectively. The administered radioiodine ablation activity was affected by central compartment lymph node metastases in 112 (44%) patients. While 32 (29%) of these patients had papillary microcarcinoma (T1a), 48 (43%), 20 (18%), and 12 (11%) of them had T1b, T2, and T3 tumors, respectively.

**Conclusion:** The application of prophylactic central compartment dissection affects the radioiodine ablation activity in approximately half of patients. This effect is more prominent in T1 stage tumors.

**Key words:** Papillary thyroid carcinoma, radioiodine ablation treatment, prophylactic central compartment dissection

### 1. Introduction

Papillary thyroid carcinoma (PTC) is the most common thyroid cancer and accounts for more than 80% of thyroid carcinomas (1-3). The extent of surgery in PTC patients who do not have clinically suspect lymph nodes (cN0) remains controversial. Despite the good long-term outcome of PTCs, approximately 50% of patients have cervical lymph node metastasis (1,4). The presence of lymph node metastasis is associated with a high locoregional recurrence rate (2,5). However, according to current concepts, there is no evidence of improvement in survival after prophylactic central compartment dissection (PCLND) despite the high rate of occult lymph node metastasis (6-8). In contrast, a large nested case-control study revealed that patients with lymph node metastasis have a higher mortality rate and that incomplete surgery is one of the most important factors in increasing mortality (9).

From the aspect of nuclear medicine, there is an element of safety in knowing the central compartment status when evaluating the need for radioiodine (RAI) ablation

treatment and calculating RAI activities. Preablative thyroglobulin (Tg) levels may be misleading due to the presence of different amounts of residual thyroid tissue. In addition, ultrasonographic evaluation of the central compartment becomes more difficult after thyroidectomy. Therefore, the present study was planned to document the effect of the application of PCLND on RAI ablation activities for papillary thyroid carcinoma.

### 2. Material and Method

#### 2.1. Patients

A retrospective review was conducted of the descriptive and clinical follow-up data of 568 patients who were referred to our department for RAI ablation treatment between April 2010 and December 2014. Ten patients with a diagnosis of follicular thyroid carcinoma and 106 patients with suspected lymph nodes during the preoperative evaluations were excluded from the analysis. All of the 452 patients included had undergone total or near-total thyroidectomy following neck ultrasound and fine-needle aspiration biopsy. None of the patients had

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any suspicious lymph nodes in the central or lateral neck compartments. As there were no indications for routine central compartment lymph node dissection in any patient, PCLND was applied to only 252 of the total 452 patients according to the surgeon's preference.

### 2.2. Radioiodine ablation treatment

Indications for RAI ablation treatments were evaluated and treatment was administered according to our routine fixed activity protocol if it was indicated. The given activities were in the range of 30–100 mCi for intrathyroidal tumors and 125–150 mCi for lymph node metastases. After RAI treatment, patients were hospitalized according to national regulations. Pinhole neck and parallel-hole whole-body scintigraphic images were obtained 6–8 days after treatment to evaluate residual tissue and possible metastases.

### 2.3. Data and statistical analysis

Descriptive features, surgical procedures, postoperative pathological examinations, and the given radioactive iodine activities were noted for statistical analysis. The application of PCLND and its effect on the administered RAI activities were calculated according to the T stage of tumors. Comparisons were made of sex, age, tumor dimension, capsule invasion, and preablative Tg and anti-Tg levels of patients with (Group 1) and without (Group 2) PCLND.

### 3. Results

PCLND was applied to 252 (56%) of the 452 patients, comprising 383 females and 69 males with a mean age of 46.69 years (min–max: 13–71 years). The T stages of these patients were T1a, T1b, T2, and T3 in 85 (34%), 106 (42%), 41 (16%), and 20 (8%), respectively. There was no statistically significant difference between the sex, mean age, tumor dimension, or preablative Tg and anti-Tg levels of patients who underwent central compartment dissection and those who did not. A statistically significant difference was determined between the groups for thyroid capsule invasion rates (25% vs. 14%,  $P = 0.001$ ) (Table 1).

Central compartment lymph node metastasis was detected in 112 (44%) of the 252 patients, thereby affecting the given RAI ablation doses. While 32 (29%) of these patients had papillary microcarcinoma (T1a), 48 (43%), 20 (18%), and 12 (11%) had T1b, T2, and T3 tumors, respectively. There was no significant difference in sex, mean age, or preablative Tg and anti-Tg levels between the patients with and without central compartment lymph node metastasis, while a significant difference was determined in mean tumor dimension (1.72 vs. 1.38 cm,  $P = 0.03$ ) and thyroid capsule invasion rate (10% vs. 42%,  $P = 0.001$ ) (Table 2).

**Table 1.** Difference between groups of patients with and without PCLND.

	CLN metastasis		P-value
Age (mean years)	Positive	46.7	0.18
	Negative	53.6	
Sex (F/M)	Positive	225/37	0.87
	Negative	160/32	
Tumor dimension (mean)	Positive	1.68	0.82
	Negative	1.55	
Thyroid capsule invasion	Positive	25%	<0.01
	Negative	14%	
Preablative Tg (mean)	Positive	8.84	0.50
	Negative	7.87	
Preablative anti-Tg (mean)	Positive	18.12	0.17
	Negative	10.57	

PCLND: Prophylactic central lymph node dissection, F: female, M: male, Tg: thyroglobulin, anti-Tg: antithyroglobulin.

**Table 2.** Difference between groups of patients with and without CLN metastasis.

	CLN metastasis		P-value
Age (mean years)	Positive	47.1	0.32
	Negative	59.6	
Sex (F/M)	Positive	124/5	0.05
	Negative	120/3	
Tumor dimension (mean)	Positive	1.72	0.03
	Negative	1.38	
Thyroid capsule invasion	Positive	42%	<0.01
	Negative	10%	
Preablative Tg (mean)	Positive	6.36	0.90
	Negative	11.35	
Preablative anti-Tg (mean)	Positive	24.32	0.18
	Negative	12.02	

CLN: Central lymph node, F: female, M: male, Tg: thyroglobulin, anti-Tg: antithyroglobulin.

#### 4. Discussion

Although central lymph node dissection is recommended for cN1 patients, the need for PCLND in cN0 PTC patients is still controversial (10–15). Generally, it is accepted that lymph node metastasis is associated with higher locoregional recurrence and distant metastasis rates. However, it does not affect survival (16). In contrast, a large-scale nested case-control study revealed that patients with lymph node metastasis experience higher mortality. Moreover, incomplete surgical excision is associated with higher mortality, particularly in Stage 1 patients (9).

Some surgeons do not prefer PCLND for cN0 patients due to morbidities related to recurrent nerve paralysis and hypoparathyroidism. However, others claim that because there could be lymph node metastasis, even in low-risk patients, and reoperation in this compartment is technically difficult, PCLND should be applied. Practice guidelines on this topic are also conflicting. While the American Thyroid Association guidelines suggest that PCLND can be considered for patients with advanced primary tumors (T3 and T4), the National Comprehensive Cancer Network guidelines recommend PCLND for cN0 patients at any stage of primary tumors (category 2B) (17,18).

Therefore, the outcome of applying PCLND or not has been a subject of interest for several authors. Calo et al. researched whether or not total thyroidectomy without PCLND in cN0 patients was adequate and concluded that total thyroidectomy appeared to be adequate for cN0 patients. However, PCLND could be recommended for high-risk patients as a more appropriate selection for RAI

treatment (19). In a large series, Jiang et al. investigated the clinical characteristics related to central lymph node metastasis in 916 cN0 PTC patients. Tumors located in the upper/middle pole/whole lobe, patient age of  $\leq 35$  years, tumor size of  $>1.5$  cm, and capsule invasion were found to be risk factors of central lymph node metastasis (20). From another aspect, Liu et al. investigated the long-term outcome of the observation of cN0 PTC patients. They concluded that observation without PCLND was safe for this patient group, particularly for those without extrathyroidal invasion (6).

In the current series, PCLND was applied to 252 of the 452 patients. Most of the patients (76%) who underwent PCLND had T1 stage tumors. As the expected macroscopic lymph node metastasis rate is higher in T2 and T3 tumors than T1 tumors, the therapeutic central compartment dissection indication rate in T2 and T3 tumors might be higher. Therefore, a large proportion of patients with a history of PCLND might have T1 tumors. The only significant difference between the group to which PCLND was applied and the group to which it was not was in the thyroid capsule invasion rates (25% and 14%). PCLND in cN0 patients might be an intraoperative choice of surgeons, depending on the location of the tumor and the appearance of the thyroid capsule and lymph nodes. At least some patients with thyroid capsule invasion could have had PCLND applied due to macroscopic suspicion of extrathyroidal invasion during the intraoperative observation.

Central lymph node metastasis was detected in 112 of the 252 patients and the need for RAI ablation or the given RAI ablation dose was affected by this in all cases. The most important result of this analysis is that the majority of those patients had T1 tumors. Moreover, 29% of that group consisted of patients with papillary microcarcinoma (T1a) who did not have any RAI ablation indication when there was no central lymph node metastasis. Another important finding was the significance in mean tumor dimension and capsule invasion rates of patients with and without central lymph node metastasis. These data support the results of previous studies (3,12). Although the difference between mean tumor dimensions was determined to be statistically significant, in clinical practice it is not significant as the mean values were close (1.72 vs. 1.38 cm). However, thyroidal capsule invasion might be more significant.

Preoperative detailed evaluation by an experienced hand of the thyroid gland and central/lateral lymph node compartments is of great importance, especially the careful inspection of the primary tumor and its contact with the thyroid capsule and the integrity of the capsule.

In this study, an analysis was made of the effect of the application of PCLND on RAI decision and dose. However, no evaluation could be made of the long-term effect of the presence of lymph node metastasis or the application of RAI ablation treatment. We preferred to report the early results of this series as we think that they could be of greater importance, but we also plan to analyze long-term follow-up data.

In conclusion, the application of PCLND affects the RAI ablation dose in approximately half of patients. This effect becomes more prominent in T1 stage tumors.

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