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Original Research

Risk Factors for Right Paratracheal Posterolateral Lymph Node Metastasis in Papillary Thyroid Cancer

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Abstract

Objectives: The incidence of papillary thyroid cancer (PTC) is increasing, and due to the favorable postoperative survival rates, the extent of surgery should be carefully determined, and complications during the operation should be avoided. The recurrent laryngeal nerve (RLN) divides the right paratracheal lymph node (RPTLN) into anteromedial and posterolateral compartments due to its anatomical course on the right and left sides of the neck, and the posterolateral lymph nodes are in close proximity to the RLN. Due to the risk of this complication, in this study, we aimed to determine the risk factors for the development of right paratracheal posterolateral lymph node (RPTPLLN) metastasis in PTC.

Methods: Between 2013 and 2022, patients who underwent central neck dissection (CLND) or central and lateral neck dissection due to the presence of PTC in the right lobe of the thyroid gland were included in the study. Descriptive data, along with preoperative imaging findings and postoperative pathology findings, were retrospectively evaluated.

Results: The data of 55 patients who met the criteria were statistically analyzed. Of these patients, 24 (43.6%) were male and 31 (56.4%) were female. The mean age was 47.9±17.5 years (range: 16-81). The mean tumor size was 2.17±1.43 cm (range: 0.4-7.0). RPTPLLN was observed in 13 patients (23.6%). Univariate analysis revealed that extrathyroidal extension (p=0.008), lymphovascular invasion (p=0.044), presence of right paratracheal anteromedial (RPTAMLN) metastasis (p=0.001), and presence of left paratracheal metastasis (p=0.049) were statistically significant factors. However, in the multivariate analysis, only the presence of RPTAMLN was determined to be a significant variable (p=0.035).

Conclusion: In patients undergoing surgery for PTC, the risk of metastasis in the RPTPLLN should be considered higher when there is metastasis in the RPTAMLN. We believe that formal dissection of the RPTLN should be considered for optimal evaluation in patients with tumors in the right lobe where central dissection is planned. Posterolateral dissection (PLD) should be routinely performed in the presence of clinical lymph nodes in the RPTAMLN. When a decision cannot be made, PLD may not be performed if the anteromedial tissue is examined with frozen pathology and the result is negative.

Keywords: Central right paratracheal posterolateral lymph node, metastasis, papillary thyroid cancer

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Papillary thyroid carcinoma (PTC) is the most frequent kind of thyroid cancer.[1] In the analysis of the SEER (Surveillance, Epidemiology, and End Results) database in the United States, an increasing number of thyroid cancer incidence was 4.9/100,000 in 1975, while it was reported as 15/100,000 in 2015.[2] Lymph node metastasis (LNM) is seen in 30% to 85% of PTC cases, with the most common sites being the central neck lymph nodes.[3-5] The central lymph nodes consist of the prelaryngeal (Delphian), pretracheal, and the right and left paratracheal lymph nodes. The anatomical differences distinguish the right paratracheal lymph nodes (RPTLN) from those on the left side. The right recurrent laryngeal nerve (RLN) separates the RPTLNs into two subcompartments: posterolateral (PL) and anteromedial (AM) lymph nodes. Most guidelines recommend preoperative or intraoperative examination for central lymph node metastasis and advocate performing central lymph node dissection (CLND) either unilaterally or bilaterally. To conduct a complete unilateral or bilateral CLND, both the AM and PL compartments of the paratracheal region need to be dissected.[2,6,7]

The RPTPLLNs are located deep within a long, narrow, and constricted region. This unique and complicated anatomical position makes surgical exposure and dissection challenging. Therefore, the dissection of the RPTPLLNs continues to be a topic of debate in the literature.[8] Additionally, dissection of this region can lead to many complications, such as RLN injury, parathyroid gland injury, and chyle fistula. Some researchers suggest that due to the complex anatomical structure, the increased risk of complications, and the excellent prognosis of the disease, many surgeons may not consider it necessary to remove the RPTPLLNs.[9,10]

However, it has been reported that the rate of RPTPLLNs metastasis in patients with PTC is as high as 9.4% to 32%.[11-13] In the presence of RPTPLLNs metastasis, the surgical strategy is critical for the patient's prognosis. Some studies have stated that 60% of the recurrence in the central lymph node region occurs most frequently in the RPTPLLNs region.[14] In patients where the RPTPLLNs compartment has not been completely removed during the initial surgery, it may be difficult or even impossible to completely dissect the lymph nodes in the secondary surgery.[10] Therefore, the assessment of the presence of right paratracheal posterolateral lymph node metastasis is crucial for the treatment planning in patients with PTC.

In the present study, we aimed to determine the risk factors for the RPTPLLNs metastasis in PTC, considering the risks of complications and challenges in determining the surgical extent.

Methods

The study was approved by the Local Ethics Committee on 10.10.2023 with decision number 4118. Fifty-five patients who underwent CND or central and lateral neck dissection due to PTC in the right lobe of the thyroid gland between 2013 and 2022, were included in the study. Informed consents were obtained from all the patients. Demographic profile, as well as data regarding their disease and treatment, were obtained retrospectively from the hospital records.

The inclusion criteria were as follows: (1) patients diagnosed as PTC pathologically; (2) presence of a tumoral lesion in the right thyroid lobe; (3) all patients with at least unilateral CLND, including the right side, and bilateral CLND and/or lateral LND. Preoperatively, all lymphatic compartments were evaluated in detail by an experienced radiologist via ultrasound.

The anatomical and dissection definitions of the central region were made according to the American Thyroid Association, Surgical Affairs Committee consensus report.[7] The central region was defined as the area above the hyoid bone, laterally to the carotid arteries, and inferiorly to the intersection point of the innominate artery and trachea on the right inferior and the symmetry of this point on the left in the axial plane.[2] The central region was divided into four separate regions; prelaryngeal, pretracheal, left paratracheal, right paratracheal. If the paratracheal tissue on one side, along with the prelaryngeal and pretracheal compartments, was dissected, it was defined as unilateral CLND. If the paratracheal tissues on both sides were dissected, it was defined as bilateral CLND (Fig. 1).[2]

Therapeutic CLND is defined as the removal of the metastatic lymph nodes detected clinically or by preoperative/intraoperative imaging techniques. Prophylactic CLND, on the other hand, is defined as dissection performed when there is no metastasis detected clinically or by imaging methods.[6,15]

The LND was completed simultaneously with thyroidectomy. The right paratracheal lymph nodes were divided into two compartments as anterior and posterior to the right RLN (Fig. 1). After the right RLN has been fully exposed till its laringeal entry, the lymphatic fat tissue located medially and laterally to the right RLN was removed.

The data was collected from the patient's medical record regarding the gender, age, tumor size, bilaterality, multifocality, lymphovascular invasion, extrathyroidal invasion, presence of Hashimoto's thyroiditis, prelaryngeal, pretracheal, left paratracheal, and right paratracheal AM and PL LNM. Postoperative follow-up was conducted for at least 6

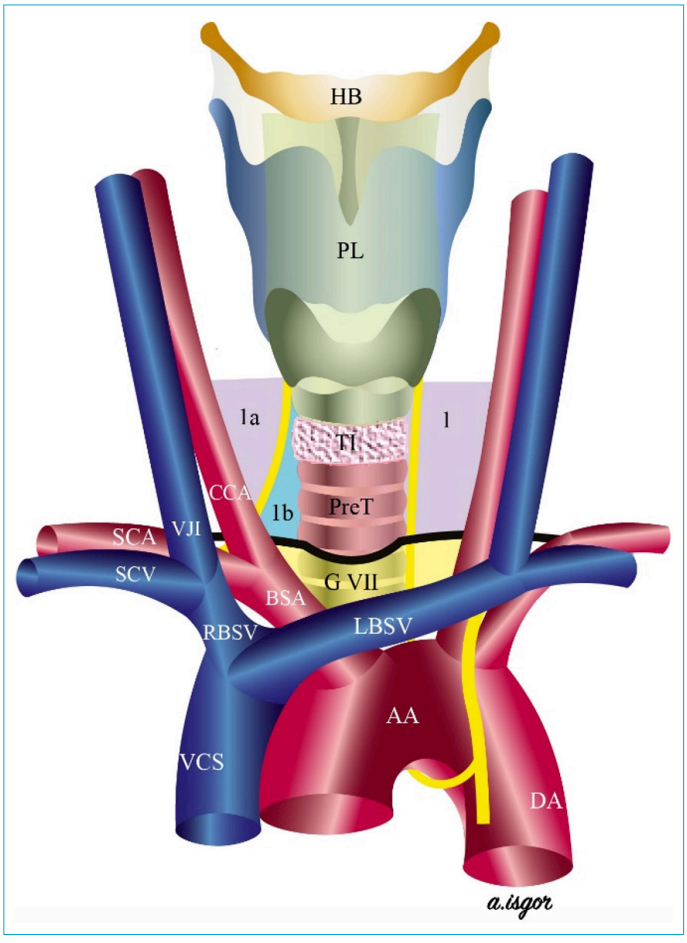

Figure 1. The distribution of central lymph node compartments.

HB: Hyoid Bone; PL: Prelaryngeal Group, 1a: Right Paratracheal Posterolateral Group. 1b: Right Paratracheal Anteromedial Group; PreT: Pretracheal Group. 1: Left Paratracheal Group; RLN: Recurrent Laryngeal Nerve; V: Vagus Nerve; TI: Thyroid Isthmus; AA: Aortic Arch; DA: Descending Aorta; BSA: Brachiocephalic Artery; SCA: Subclavian Artery; CCA: Common Carotid Artery; SVC: Superior Vena Cava; RBCV: Right Brachiocephalic Vein; LBCV: Left Brachiocephalic Vein; SCV: Subclavian Vein; VJI: Internal Jugular Vein; G VII: Seventh Cervical Lymphatic Group; Dark Black Line: Sternal Notch. n: Number; SD: Standart Deviation.

months. The patients were divided into two groups based on their pathological reports: those with RPTPLLNs metastasis (Group 1) and those without right paratracheal metastasis (Group 2). Demographic and clinicopathological data were compared between the two groups.

Intraoperative nerve monitoring was applied to all patients. Preoperative and postoperative vocal cord examinations were performed by an otolaryngologist via fiberoptic laryngoscopy for all patients.

Statistical Analysis

Statistical Analysis SPSS (Statistical Packages for the Social Sciences, software, edition 21, SPSS Inc., Chicago, USA) was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, percentage, minimum, and maximum) were used to evaluate the study data. The "Mann–Whitney U"-test was used to compare the quantitative variables that did not show normal distribution between the two groups. "Pearson Chi-square test" and "Fisher's Precision Test" were used to compare the qualitative data. A formula was created based on the significant factors for RPTPLLN metastasis identified in the univariate analysis results. Logistic regression analysis was performed to determine the independent variables associated with the risk of RPTPLLN metastasis. The statistical significance was accepted as $p<0.05$.

Results

The data of 55 patients with PTC in the right lobe of the thyroid who underwent CLND or central and lateral LND at our clinic were retrospectively evaluated. In our study, 2 out of 55 patients underwent therapeutic CLND, while 28 patients underwent total thyroidectomy with prophylactic CLND and lateral selective LND, and 25 patients underwent total thyroidectomy with prophylactic CLND.

Of the patients, 24 (43.6%) were male and 31 (56.4%) were female, with a mean age of 47.9±17.5 years (range: 16-81). The mean tumor size determined using the pathological examinations of the patients was 2.17±1.43 cm (range: 0.4-7.0). Of the 55 patients in the study, 13 (23.6%) had right paratracheal metastasis (Group 1), while 42 patients (76.4%) were without metastasis. No significant difference was detected comparing the two groups in terms of gender (p=0.217) (Table 1).

Among the histopathological characteristics of the tumor, the rate of lymphovascular invasion was significantly higher in Group 1 compared to Group 2 (84.6% vs. 63.8%; p=0.037, respectively). Similarly, the rate of extrathyroidal extension was significantly higher in patients with metastasis in the right paratracheal lymph node region compared to those without metastasis (84.6% vs. 42.9%, p=0.008, respectively). The rate of metastasis in the central left paratracheal lymph node region was also significantly higher in patients with metastasis in the right paratracheal lymph node compared to those without metastasis (69.2% vs. 38.1%; p=0.049, respectively). Additionally, the rate of metastasis in the RPTAMLN was significantly higher in patients with metastasis in the right paratracheal lymph node compared to those without metastasis (92.3 % vs. 38.1%; p=0.001, respectively) (Table 1).

In our study, a total of 6 RLN paralyses (5.45 %) developed on 110 neck sides. No significant difference was found between Group 1 and Group 2 in terms of paralysis development (p=0.554). In the postoperative period, a total of

Table 1. Factors affecting the development of right paratracheal posterolateral lymph node metastases

Features	Group 1 Right Paratracheal Posterolateral Lymph Node Metastases (+) n=13	Group 2 Right Paratracheal Posterolateral Lymph Node Metastases (-) n=42	p
Age (Mean±SD)	47.31±15.99	48.14±18.12	0.882
Gender (n,%)			
Male	6 (46.2)	18 (42.9)	0.834
Female	7 (53.8)	24 (57.1)	
Tumor Size (cm) (Mean±SD)	2.48±2.00	2.07±1.22	0.375
Tumor Size (cm) (n,%)			
<2 (cm)	7 (53.8)	6 (42.9)	0.922
>2 (cm)	6 (46.2)	24 (57.1)	
Lymphocytic Thyroiditis (n,%)	4 (30.8)	18 (16.7)	0.267
Lymphovascular Invasion (n,%)	11 (91.7)	25 (59.5)	0.044
Multicentricity (n,%)	11 (84.6)	28 (63.8)	0.252
Multifocality (n,%)	10 (76.9)	26 (63.4)	0.368
Extracapsuler Extension (n,%)	8 (61.5)	18 (43.9)	0.267
ETE (Extrathyroidal Extension) (n,%)	11 (84.6)	18 (42.9)	0.008
Prelarengeal Lymph Node Metastases (n,%)	5 (38.5)	9 (21.4)	0.218
Pretracheal Lymph Node Metastases (n,%)	4 (30.8)	17 (40.5)	0.529
Left Paratracheal Lymph Node Metastases (n,%)	9 (69.2)	16 (38.1)	0.049
Right Paratracheal Anteromedial Lymph Node Metastases (n,%)	12 (92.3)	16 (38.1)	0.001
Complications			
RLS paralysis	2 (15.4)	4 (9.5)	0.554
Hypocalcemia	3 (23.1)	5 (11.9)	0.318

n: Number, SD: Standar Deviation.

8 patients (14.5 %) developed transient hypocalcemia in 55 patients. No significant difference was found between Group 1 and Group 2 in terms of hypocalcemia development (p=0.318) (Table 1).

A formula was created that included the features of extrathyroidal extension, lymphovascular invasion, presence of left paratracheal lymph node and RPTAMLN metastasis. Among the factors that were significant in the pairwise comparison regarding the development of RPTPLLN metastasis; the logistic regression analysis revealed the presence of RPTAMLN metastasis as an independent risk factor for the development of RPTPLLN metastasis (p=0.035). Presence of RPTAMLN metastasis increases the risk of RPTPLLN metastasis by approximately 12 times (Table 2).

Discussion

Currently, the primary treatment for PTC is surgery. However, in the literature, there is an ongoing debate about the extent of the surgery. The association between PTC and RPTPLLN metastasis was first reported by Lee et al. in 2009. [16] Since this study, although the RPTPLLN compartment is part of the right paratracheal region, the routine dissection of this compartment remains controversial. The terminology for this compartment is also debated. Some researchers define them as the lymph nodes posterior to the right RLN, while others describe them as right paraesophageal lymph nodes.[9-11]

Table 2. Factors affecting the development of right paratracheal posterolateral lymph node metastases according to logistic regression

	Odds ratio (95% CI Lower-Upper)	p
Extrathyroidal Extension		0.382
Negative	1 (Reference)	
Positive	2.533 (0.315-20.354)	
Lymphovascular Invasion		0.417
Negative	1 (Reference)	
Positive	3.131 (0.199-49.270)	
Left Paratracheal Lymph Node Metastases		0.641
Negative	1 (Reference)	
Positive	1.546 (0.248-9.649)	
Right Paratracheal Anteromedial Lymph Node Metastases		0.035
Negative	1 (Reference)	
Positive	11,805 (1,191-116,976)	

The right paratracheal region is divided into two compartments by the RLN. Since this tissue is located posterolateral to the RLN, we believe it is appropriate to define this area as the RPTPLLN compartment. Although literature reports metastasis rates up to 32% for the RPTPLLN compartment, three different meta-analyses from 2019 to 2022 report an average rate of approximately 9%.[9-11]

In PTC, lymph node metastasis initially occurs in the ipsilateral paratracheal region.[6]

In the present study, the rate of RPTPLLN metastasis in PTCs localized to the right lobe was 23.9%, with approximately ¾ of patients having no metastasis. The univariate analysis showed that patients with metastasis in the RPTPLLN region had significantly higher rates of lymphovascular invasion (84.6% vs. 63.8%; p=0.037), extrathyroidal extension (84.6% vs. 42.9%; p=0.008), metastasis to the RPTAMLN region (92.3% vs. 38.1%; p=0.001), and left central paratracheal metastasis (69.2% vs. 38.1%; p=0.049). However, logistic regression analysis identified only the presence of RPTAMLN metastasis as an independent risk factor.

In the present study, the risk of RPTPLLN metastasis was nearly 12 times higher in patients with metastasis of RPTAMLNs compared to those without, indicating that the presence of RPTAMLNs metastasis is an important intraoperative factor in predicting RPTPLLN metastasis (OR: 11,805 (95% CI: 1,191-116,976).

In the literature, it has been reported that routine posterolateral dissection (PLD) should be performed in the presence of clinical lymph node involvement in the RPTAMLN compartment. When a decision can not be made, RPTPLLN dissection may not be performed if the anteromedial tissue shows negative results on frozen pathology examination. It has been demonstrated that intraoperative frozen section assessment is a solid method for evaluating the central compartments.[8,17,18]

The presence of right paratracheal anteromedial metastasis has been identified in other studies as an independent risk factor and also a significant risk factor for posterolateral metastasis.[8,18-22]

Although our study did not find significant factors among demographic and other clinicopathological features, several risk factors for RPTPLLN metastasis have been reported in other studies. These factors include: Age <45 or <55, male gender, tumor diameter >1 cm, microcalcifications, multifocality, BRAFV600E mutation, centripetal perfusion pattern on preoperative ultrasound, central metastasis detected on preoperative ultrasound, lateral metastasis detected on ultrasound, lymph node status detected on ultrasound, delphian lymph node metastasis, number of metastatic central lymph nodes, number of pretracheal metastatic lymph nodes, central lymph node metastasis on the left, tumor localized in the right lobe, lower pole localization, right lateral neck metastasis. These factors have been identified as risk factors for RPTPLLN metastasis.[8,18-25]

Recent meta-analyses have also found several significant risk factors for predicting RPTPLLN metastasis in PTC. These factors include: male gender, age <45, tumor size >1 cm, extrathyroidal invasion, multifocality, capsule invasion, presence of central metastasis, number of central metastases >3, RPTAMLN metastasis, lateral metastasis. Researchers suggest that RPTPLLN dissection may be considered in selected patients based on these factors. In the presence of one or more of these risk factors, a more proactive approach to the surgery may be warranted.[9-11]

In addition, Zou and colleagues reported the rate of RPTPLLN metastasis as 30.4%, suggesting that RPTPLLN dissection should not be overlooked. The authors noted that, considering the high rate of RPTPLLN metastasis, the challenges and complications associated with reoperations, RPTPLLN dissection should be considered even in clinically node-negative (cN0) patients when central dissection is being planned.[20]

Additionally, some researchers have reported that extensive LND may increase morbidity without any beneficial surgical outcomes and higher survival rates.[26]

Our study is a retrospectively designed single center study that has a limited number of cases. This is expressed in the discussion section.

Conclusion

As a result, we believe that formal right paratracheal dissection would be appropriate for optimal evaluation in patients with PTC in the right lobe when central dissection is planned. In the presence of a RPTAMLN compartment metastasis, posterolateral dissection should be performed routinely. RPTPLLN compartment dissection might not be performed in the absence of RPTAMLN compartment metastasis.

Disclosures

Ethics Committee Approval: The study was approved by the Sisli Hamidiye Etfal Training and Research Hospital Ethics Committee (Number: 4118, Date: 10.10.2023).

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