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ORIGINAL ARTICLE

Clinicopathologic Predictors and Nodal Burden Pattern of Skip Metastasis in Papillary Thyroid Carcinoma: A Multicenter Study

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Received: 4 December 2025 | **Revised:** 23 March 2026 | **Accepted:** 25 March 2026

Keywords: lateral neck metastasis | multicenter study | papillary carcinoma | risk assessment | skip metastasis

ABSTRACT

Background: Skip metastasis (SM), defined as lateral lymph node metastasis without central involvement, is an important but unpredictable spread pattern in papillary thyroid carcinoma (PTC). This study aimed to determine its prevalence, identify clinicopathologic predictors, and develop a preoperative risk model.

Methods: We retrospectively analyzed 130 PTC patients with histologically confirmed lateral metastasis who underwent total thyroidectomy, bilateral central neck dissection, and unilateral or bilateral lateral dissection at three tertiary centers between 2019 and 2025. Clinicopathologic and nodal variables were compared between the SM and non-skip metastasis (NSM) groups. Independent predictors were evaluated using multivariable logistic regression, and model performance was assessed with ROC AUC.

Results: SM occurred in 12.3% of patients. SM was associated with older age, upper-pole tumor location, solitary intrathyroidal focus, and lower nodal burden. Independent predictors were age ≥ 39.5 years and upper-pole location, while same-lobe multifocality was inversely associated. The model showed good discrimination with an AUC of 0.841.

Conclusion: Older patients with solitary upper-pole PTC warrant meticulous preoperative lateral-neck assessment. A simplified preoperative model incorporating age, tumor topography, and multifocality may support risk-based surgical planning.

1 | Introduction

Papillary thyroid carcinoma (PTC) is the most common differentiated thyroid malignancy, representing over 90% of all thyroid cancers [1]. Its incidence has risen steadily over recent decades, reflecting both improved detection through ultrasonography and fine-needle aspiration and a true rise in disease burden [2]. Despite its favorable prognosis, with 5-year disease-specific

Abbreviations: ATA, American Thyroid Association; AUC, area under the curve; CI, confidence interval; CLND, central lymph node dissection; ETE, extrathyroidal extension; IQR, interquartile range; LLND, lateral lymph node dissection; LN, lymph node; LNR, lymph node ratio; LVI, lymphovascular invasion; NSM, non-skip metastasis; OR, odds ratio; PTC, papillary thyroid carcinoma; ROC, receiver operating characteristic; SM, skip metastasis.

A portion of this study was presented as an abstract at the World Congress of Thyroid Cancer 2025.

survival rates exceeding 95%–99% [3–5], cervical lymph node metastases remain common, affecting 30%–60% of patients [6]. While lymph node involvement has only a modest impact on overall survival [5], it increases the risk of locoregional recurrence and persistent disease, complicating long-term management [7].

The regional lymphatic spread of PTC usually occurs in a stepwise pattern, beginning with the central compartment, progressing to the ipsilateral lateral cervical levels (II–V), and, later, to contralateral or mediastinal nodes [8]. An atypical metastatic pattern known as skip metastasis (SM), defined as lateral lymph node metastasis without central compartment involvement [1, 9], challenges this conventional "central-then-lateral" model and has been reported across a broad range in the literature, reflecting differences in populations, tumor features, and pathological assessment [6–9]. These metastatic patterns carry important surgical implications. Similar to the 2014 American Thyroid Association (ATA) guidelines, the 2025 update continues to discourage prophylactic lateral lymph node dissection (LLND; Levels II–V) in the absence of proven metastasis, whereas therapeutic CLND is recommended in patients with cN1b disease [10]. Collectively, these recommendations underscore the delicate balance between maximizing oncologic benefit and minimizing surgical morbidity, while highlighting the persistent uncertainty in preoperative risk stratification that arises from imaging limitations, heterogeneous tumor behavior, and atypical metastatic patterns such as SM. Different from the 2014 ATA guideline, the 2025 update specifically emphasizes that upper-pole PTCs may have a greater tendency to metastasize directly to lateral neck levels, particularly II and III, even when the central compartment appears uninvolved, underscoring the importance of individualized and anatomy-based evaluation of the lateral neck in such patients [10].

SM raises questions about PTC tumor biology and lymphatic anatomy. It is most often attributed to upper-pole tumors with drainage along the superior thyroid vessels to lateral nodes [11]; alternative explanations include occult central micrometastases and host factors (e.g., Hashimoto's thyroiditis) [12]. Although lateral lymph node involvement is staged as N1b, indicating a higher recurrence risk than N1a, the prognostic behavior of SM remains controversial. While some reports suggest a more favorable prognosis [13], the majority of studies demonstrate similar outcomes to other lateral node-positive cases when managed with appropriate therapy [8].

Multiple clinicopathological factors have been linked to SM, including upper-pole location, small tumors, extrathyroidal extension (ETE), Hashimoto's thyroiditis, absence of BRAFV600E, and older age [14, 15]. Evidence is heterogeneous across studies, but recognizing these features preoperatively may heighten suspicion and may justify a more meticulous lateral-neck assessment. Recent studies have also explored preoperative prediction models for nodal metastasis, particularly in PTC, highlighting the value of integrating clinical and ultrasonographic parameters to optimize surgical planning [16].

Within this context, SM challenges the conventional stepwise model of lymphatic dissemination and further complicates surgical decision-making in PTC. Therefore, the present study aims to investigate the predictors and prevalence of SM in PTC to improve risk stratification and guide surgical decision-making.

2 | Materials and Methods

2.1 | Study Design and Ethical Approval

This multicenter retrospective cohort study was conducted at three tertiary endocrine surgery centers in Istanbul, Turkey (Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Basaksehir Cam and Sakura City Hospital, and Istinye University LIV Hospital). All operations were performed by high-volume endocrine surgeons. The study protocol was approved by the Bakırkoy Dr. Sadi Konuk Institutional Ethics Committee (No. 2025-15-35). Informed consent was waived due to the retrospective design. The study was conducted and reported in accordance with the Declaration of Helsinki.

2.2 | Patient Selection

Medical records from the three institutions were reviewed for all consecutive patients who underwent thyroidectomy with cervical lymph node dissection between January 2019 and January 2025. Eligibility requires age ≥18 years; primary total thyroidectomy with bilateral CLND (Levels VI–VII) and unilateral or bilateral LLND (at least Levels IIa–Vb); histopathologic confirmation of PTC; and histologically proven lateral cervical lymph node metastasis in the surgical specimen. Patients were excluded for non-PTC histology, absence of histologically proven lateral metastasis, incomplete records, prior thyroid or neck surgery, prior head-and-neck irradiation, or synchronous extrathyroidal malignancies.

2.3 | Preoperative Evaluation

Preoperative work-up included high-resolution cervical ultrasonography performed by experienced radiologists to assess thyroid nodules and cervical lymph nodes. Suspicious nodules underwent ultrasound-guided fine-needle aspiration biopsy, and inconclusive cytology of lymph nodes was further evaluated by thyroglobulin washout.

2.4 | Surgical Procedures

All patients underwent total thyroidectomy with bilateral CLND (Level VI–VII). LLND was performed unilaterally or bilaterally based on preoperative radiological and/or cytological confirmation of metastasis. The extent of LLND included Levels IIa–Vb. Lymph node packets were labeled by level (IIa, III, IV, Vb, and VI).

2.5 | Histopathological Evaluation

All resection specimens were examined by dedicated thyroid pathologists at the participating institutions. Extracted variables comprised tumor histological subtype; maximal diameter (mm) recorded as a continuous measure and additionally categorized as >10 versus ≤ 10 mm; and intrathyroidal topography (upper, middle, lower pole, or isthmus). Invasion parameters encompassed lymphovascular invasion (LVI) and ETE. Tumor multiplicity was defined as follows: multifocality, ≥ 2 discrete foci within the same lobe; and multicentricity, tumor foci present in different lobes (bilateral involvement). Nodal metrics included the number of harvested and metastatic lymph nodes in the central (Level VI) and lateral (levels IIa–III–IV–Vb) compartments; the lymph node ratio (LNR) (metastatic/harvested) for each compartment and overall; and the level-specific distribution of metastatic lateral nodes.

2.6 | Definition of SM

SM was defined as pathologically confirmed lateral metastasis (Levels II–V) without any positive nodes in the central compartment (Level VI; including Delphian, pretracheal, and paratracheal nodes). Patients were classified as (1) the SM group or (2) the non-skip metastasis (NSM) group (both central and lateral metastasis).

2.7 | Data Collection

Demographic variables (age and gender), clinical and imaging findings, tumor characteristics (size, location, focality, subtype, and invasion features), and lymph node data (counts, LNR, distribution by level) were extracted from medical and pathology records.

2.8 | Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test. As most continuous data were not normally distributed, results were expressed as medians with interquartile ranges (IQRs) and compared between groups using the Mann–Whitney *U* test. Categorical variables were summarized as frequencies and percentages, and group comparisons were performed using the chi-square test or Fisher's exact test when appropriate. Given the exploratory nature of the study, variables identified as potential predictors ($p<0.05$ in univariate analyses) were included in the multivariable model. To minimize overfitting (SM events, $n=16$), a parsimonious model including only preoperative variables (age, tumor topography, and multifocality) was used. Multifocality was included because ultrasonography can reliably identify multiple intrathyroidal foci in most cases and therefore serves as a preoperative surrogate for pathological multifocality. Model calibration was evaluated using the Hosmer–Lemeshow test, and discriminatory ability was assessed by the area under the receiver operating characteristic (ROC) curve (AUC). To assess the internal validity and stability of the multivariable logistic-regression model, a bootstrapping procedure with 1000 resamples was performed. Bias-corrected accelerated (BCa) 95% confidence intervals (CIs) were calculated for the independent predictors. Optimal cut-off values were determined using Youden's index. A two-tailed $p<0.05$ was considered statistically significant.

3 | Results

3.1 | Patient and Tumor Characteristics

A total of 130 patients with PTC and pathologically confirmed lateral lymph node metastasis were included in the study. The median age of the cohort was 39 (26–50) years, and 63.8% were female ($n=83$). SM was identified in 16 patients (12.3%), whereas 114 patients (87.7%) had concurrent central and lateral lymph node metastasis.

Patients with SM were significantly older than those without SM (median: 47 [40–62] vs. 36.5 [25–49] years; $p=0.011$). ROC analysis identified 39.5 years as the Youden-optimal cutoff for age (AUC = 0.697, 95% CI: 0.56–0.83; $p=0.011$), with a sensitivity of 0.813 and a specificity of 0.561. Accordingly, age ≥ 39.5 years was more frequent in the SM group (81.25% vs. 43.86%; $p=0.007$). SM tumors tended to be smaller (median: 12.5 vs. 20 mm; $p=0.051$) and more often microcarcinomas (≤ 10 mm; 43.75% vs. 14.91%; $p=0.011$).

SM occurred predominantly in upper-pole tumors (62.50% vs. 21.05%; $p=0.001$), whereas middle, lower, and isthmus locations did not differ significantly ($p>0.05$). Multifocal tumors were less frequent among SM cases compared with NSM cases (18.75% vs. 49.12%; $p=0.044$), and lymphatic invasion was observed less often in the SM group (37.50% vs. 68.42%; $p=0.032$).

Table 1 summarizes the clinicopathological differences between the two groups.

3.2 | Lymph Node Metastasis Patterns

Patients with SM had fewer metastatic lateral lymph nodes (median: 2.00 [1.00–3.75] vs. 5.00 [2.75–9.00]; $p=0.002$) and a lower lateral LNR (0.06 [0.02–0.13] vs. 0.13 [0.08–0.20]; $p=0.010$), whereas the total number of dissected lateral nodes did not differ significantly ($p=0.826$).

The total number of positive lymph nodes was markedly lower in SM patients (2.00 [1.00–3.75] vs. 11.50 [6.00–18.00]; $p<0.001$), while the total number of retrieved nodes was comparable ($p=0.366$). Similarly, the total LNR was significantly lower in the SM group (0.05 [0.02–0.09] vs. 0.19 [0.12–0.31]; $p<0.001$). Although level-specific involvement rates did not differ significantly, single-level metastasis was markedly more common in SM cases (50.00% vs. 13.16%; $p=0.002$) (Figure 1).

Table 2 summarizes the lymph node metastasis pattern between the SM and NSM groups.

The median number of central lymph nodes retrieved was 11.50 (IQR: 7.50–17.75) in the SM group and 19.00 (IQR: 10.75–25.00) in the NSM group ($p=0.041$). Despite the statistically lower central yield in the SM group, the median number of

TABLE 1 | Baseline demographic and tumor characteristics of patients with and without skip metastasis in papillary thyroid carcinoma.

Variable	SM ($n=16$)	NSM ($n=114$)	p
Age (years), median (IQR)	47 (40.25–62.00)	36.5 (25.00–49.00)	**0.011**
Age ≥ 39.5 years, n (%)	13 (81.25)	50 (43.86)	**0.007**
Gender (female), n (%)	12 (75.00)	71 (62.28)	0.475
Tumor size (mm), median (IQR)	12.5 [9.25–24.50]	20 [13.00–32.00]	0.051
Microcarcinoma (≤ 10 mm), n (%)	7 (43.75)	17 (14.91)	**0.011**
Tumor location[a]			**0.005**
Upper, n (%)	10 (62.50)	24 (21.05)	
Middle, n (%)	5 (31.25)	61 (53.51)	
Lower, n (%)	1 (6.25)	18 (15.79)	
Isthmus, n (%)	0 (0)	11 (9.65)	
Multifocality, n (%)	3 (18.75)	56 (49.12)	**0.044**
Multicentricity, n (%)	7 (43.75)	57 (50.00)	0.840
Lymphatic invasion, n (%)	6 (37.50)	78 (68.42)	**0.032**
Vascular invasion, n (%)	3 (18.75)	31 (27.19)	0.560
Extrathyroidal extension, n (%)	1 (6.25)	27 (23.68)	0.191
Histological subtype[a]			0.633
Classical, n (%)	11 (68.75)	82 (71.93)	
Tall cell, n (%)	3 (18.75)	11 (9.65)	
Oncocytic, n (%)	1 (6.25)	2 (1.75)	
Diffuse sclerosing, n (%)	1 (6.25)	4 (3.51)	
The others[b]	0 (0)	15 (13.16)	

Note: Bold values indicate statistically significant results ($p < 0.05$).
Abbreviations: IQR, interquartile range; NSM, non-skip metastasis; SM, skip metastasis.
[a] p values represent overall comparisons among subcategories (chi-square or Fisher's exact test). Pairwise subgroup analyses were not performed due to small sample sizes.
[b] "The others" include rare subtypes, solid/trabecular, hobnail, and clear cell, infiltrative follicular subtype (< 5%).

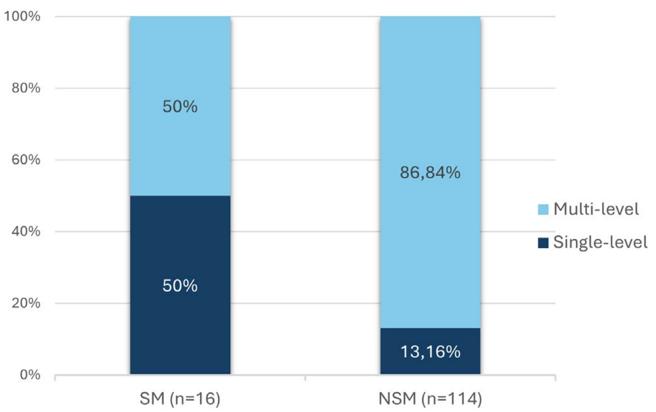

FIGURE 1 | Distribution of metastatic lymph node levels in the skip metastasis (SM) group and non-skip metastasis (NSM) group. [Color figure can be viewed at wileyonlinelibrary.com]

harvested nodes remained above six in all cases. Postoperative follow-up data were available for all 16 SM patients over a median of 46.5 months (range: 30–66). No central compartment recurrence was detected on surveillance ultrasonography, and serum thyroglobulin levels remained low (median: 0.04 ng/mL).

3.3 | Multivariate Analysis of SM Predictors

In the parsimonious multivariable logistic-regression model, age ≥ 39.5 years (odds ratio [OR]: 8.305, 95% CI: 1.913–36.048; $p=0.005$) and upper-pole location (OR: 11.395, 95% CI: 3.044–42.662; $p<0.001$) were independently associated with SM, whereas multifocality demonstrated an inverse association (OR: 0.173, 95% CI: 0.040–0.747; $p=0.019$) (Table 3).

The ROC analysis of the preoperative three-variable model yielded an AUC of 0.841 (95% CI: 0.74–0.93), indicating good discriminatory performance, with a sensitivity of 81.3% and a specificity of 71.1% (Figure 2). Furthermore, internal validation through bootstrapping was performed to ensure the stability of the model. The bootstrap-corrected p values for age ($p=0.003$), tumor location ($p=0.002$), and multifocality ($p=0.018$)

TABLE 2 | Nodal characteristics and level-specific distribution of patients with and without skip metastasis.

Variable	SM ($n=16$)	NSM ($n=114$)	p
Lateral positive LN, median (IQR)	2.00 (1.00–3.75)	5.00 (2.75–9.00)	**0.002**
Lateral total LN, median (IQR)	40.00 (24.25–61.00)	36.00 (26.00–59.25)	0.826
Lateral LNR, median (IQR)	0.06 (0.02–0.13)	0.13 (0.08–0.20)	**0.010**
Central total LN retrieved (IQR)	11.50 (7.50–17.75)	19.00 (10.75–25.00)	**0.041**
Total positive LN, median (IQR)	2.00 (1.00–3.75)	11.50 (6.00–18.00)	**< 0.001**
Total retrieved LN, median (IQR)	55.50 (35.5–79.75)	56.00 (40.00–84.00)	0.366
Total LNR, median (IQR)	0.05 (0.02–0.09)	0.19 (0.12–0.31)	**< 0.001**
Level IIa involvement, *n* (%)	9 (56.25)	73 (64.04)	0.743
Level III involvement, *n* (%)	11 (68.75)	92 (80.70)	0.323
Level IV involvement, *n* (%)	8 (50.00)	82 (71.93)	0.088
Level Vb involvement, *n* (%)	2 (12.50)	25 (21.93)	0.521
Single-level lateral involvement, *n* (%)	8 (50.00)	15 (13.16)	**0.002**
All levels (IIa–III–IV–Vb) involved, *n* (%)	1 (6.25)	16 (14.04)	0.447

Note: Bold values indicate statistically significant results ($p < 0.05$).
Abbreviations: IQR, interquartile range; LN, lymph node; LNR, lymph node ratio; NSM, non-skip metastasis; SM, skip metastasis.

TABLE 3 | Multivariate logistic-regression analysis showing independent preoperative predictors of skip metastasis.

Variable	OR	CI_low	CI_high	p	Bootstrap 95% CI	Bootstrap p
Age ≥ 39.5	8.305	1.913	36.048	**0.005**	3.384–38.735	**0.003**
Tumor location (upper)	11.395	3.044	42.662	**< 0.001**	4.204–54.598	**0.002**
Multifocality	0.173	0.040	0.747	**0.019**	< 0.001–0.521	**0.018**

Note: Bold values indicate statistically significant results ($p < 0.05$).
Abbreviations: CI, confidence interval; OR, odds ratio.

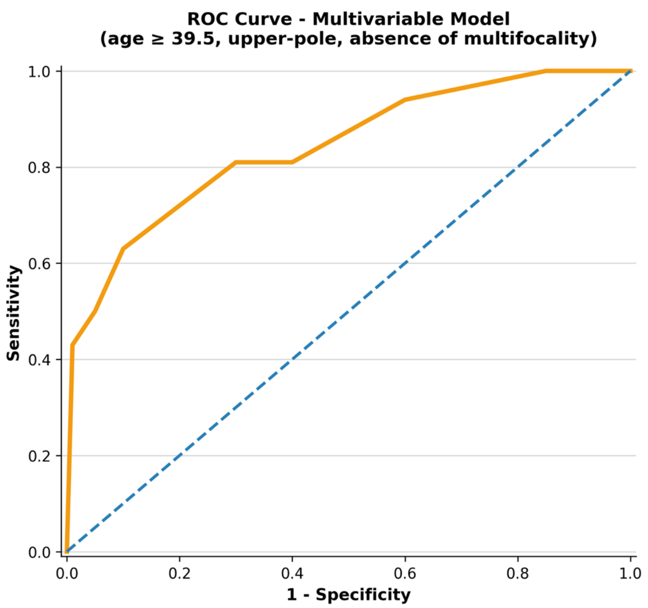

FIGURE 2 | Receiver operating characteristic (ROC) curve for the multivariable model predicting skip metastasis. [Color figure can be viewed at wileyonlinelibrary.com]

remained significant, further validating the reliability of these predictors for SM.

4 | Discussion

In this retrospective multicenter cohort, SM was detected in 12.3% of PTC patients, aligning with reported rates of approximately 2%–38% across the literature [14]. Such variability among studies likely reflects differences in cohort selection, tumor characteristics, and the extent of nodal dissection. A recent meta-analysis of 18 studies ($n=2165$) similarly reported a pooled prevalence of around 12% (5%–25%), reinforcing that SM is not uncommon in PTC [17]. This atypical spread pattern challenges the conventional stepwise model of PTC dissemination and underscores the importance of meticulous preoperative evaluation of the lateral neck, even when central nodes appear disease-free.

SM in this cohort was significantly associated with upper-pole tumor location and older age, whereas multifocality showed an inverse relationship. Upper-pole predominance (62.5% in SM vs. 21.1% in NSM; $p=0.001$) and its strong independent association (OR: 11.4, 95% CI: 3.0–42.6) support the anatomic hypothesis that superior thyroid lymphatics may drain directly to lateral compartments, bypassing the central basin [9, 14, 15, 17, 18]. Thus, upper-pole PTC should raise suspicion for lateral node involvement even in the absence of central disease. Preoperative ultrasonography should carefully evaluate the lateral neck levels in these patients, as reliance on the central-first spread model may lead to missed metastases [14].

Tumor size appears inversely related to SM risk. In this cohort, skip cases had smaller primaries (median 12.5 vs. 20.0 mm; $p = 0.051$), and microcarcinomas (≤ 10 mm) were more frequent (43.8% vs. 14.9%; $p = 0.011$). Although tumor size did not reach statistical significance in univariate or multivariate analysis, this borderline finding carries notable clinical relevance. In the current era of active surveillance and de-escalated surgical approaches for low-risk PTC, microcarcinomas may be increasingly managed without upfront surgery. However, our findings suggest that these tumors may harbor a propensity for isolated lateral spread via alternative lymphatic routes, potentially bypassing the central compartment. This raises an important consideration: patients with small, upper-pole, solitary PTCs under active surveillance protocols may warrant more vigilant preoperative lateral neck ultrasonography to avoid delayed recognition of occult lateral metastases. This pattern mirrors prior reports noting overrepresentation of microcarcinomas among skip cases [17, 18]. Nie et al. similarly found the highest skip frequency in tumors ≤ 0.5 cm ($p = 0.001$) [9]. Smaller tumors may metastasize laterally through alternative lymphatic pathways before central involvement develops, whereas larger tumors more commonly follow the traditional stepwise route.

Patients with SM were significantly older than those with NSM (median: 47.0 vs. 36.5 years; $p = 0.011$), and age ≥ 39.5 years remained an independent predictor in multivariate analysis. This finding agrees with several studies identifying older age as a risk factor [13, 14, 19], while others have found no significant association [17, 18]. Bahcecioglu et al. proposed an ROC-derived cutoff around 45 years for SM, and Hou et al. reported 44.5 years, supporting the relevance of the mid-40s in preoperative risk stratification [14, 19]. The biological explanation may relate to age-related changes in lymphatic architecture or immune surveillance that facilitate alternative drainage pathways.

In this cohort, aggressive features such as ETE and LVI were less frequent among SM patients. Lymphatic invasion was significantly lower in SM (37.5%) than in NSM (68.4%; $p = 0.032$). Gross ETE occurred in 6.3% of SM cases compared with 23.7% of NSM cases, showing a trend toward lower frequency without statistical significance ($p = 0.191$). Although earlier studies have reported inconsistent findings for LVI and ETE [14, 18, 20, 21], our results align with meta-analytic data indicating a possible inverse association between LVI and SM [17]. Differences in pathological definitions and variable reporting across studies limit definitive conclusions. Future research incorporating standardized pathology criteria and molecular markers may help elucidate these relationships.

Multifocality was significantly less common in the SM group compared with the NSM group (18.8% vs. 49.1%; $p = 0.044$) in this study. Moreover, in multivariate analysis, same-lobe multifocality remained an independent negative predictor of SM (OR: 0.173, 95% CI: 0.040–0.747; $p = 0.019$), indicating that solitary tumors are more likely to develop isolated lateral spread. Similar findings have been reported in previous studies, where the incidence of SM was lower among multifocal PTCs [22]. This relationship may be anatomically explained, as the presence of multiple tumor foci within the same lobe increases the likelihood that at least one drains through the central compartment, thereby reducing the probability of isolated lateral spread.

In our cohort, SM was characterized by a markedly lower nodal burden in the lateral neck. SM cases had fewer positive lateral nodes (median: 2 vs. 5; $p = 0.002$) and more localized disease, with 50% showing metastasis confined to a single lateral level (usually Level II or III). These findings suggest that SM may be associated with a more limited and focused pattern of nodal spread. Prior studies have reported similar observations [22, 23]. Lei et al. found that patients with SM had significantly fewer metastatic lateral nodes and were more likely to have metastasis confined to one cervical level (typically Level II) [23].

An important methodological consideration in SM studies is whether the absence of central metastasis reflects a true biological phenomenon or an artifact of inadequate central compartment dissection. In this cohort, the SM group had a lower median central lymph node yield compared with the NSM group (11.5 vs. 19.0; $p = 0.041$). However, the median yield in the SM group exceeded the commonly recommended threshold of > 6 central lymph nodes for adequate dissection, as proposed by Robinson et al. to rule out occult nodal disease with 90% confidence [24], and all procedures were performed by high-volume endocrine surgeons with standardized bilateral central dissection (Levels VI–VII). The yield difference likely reflects the smaller, solitary, upper-pole tumor profile of this subgroup rather than surgical inadequacy. Importantly, postoperative surveillance over a median of 46.5 months revealed no central compartment recurrence among the 16 SM patients, and serum thyroglobulin levels remained very low (median: 0.04 ng/mL). These observations provide strong evidence that SM in this cohort represents an alternative lymphatic drainage pathway rather than a missed central disease.

The main limitations of this study include its retrospective nature, the relatively small number of SM cases, and the lack of long-term follow-up data. To address the potential for overfitting due to the limited number of events ($n = 16$), we constructed a parsimonious multivariable model and employed a robust internal validation strategy using bootstrapping with 1000 resamples. This computational method allows for stable estimation of confidence intervals by repeatedly sampling from the original dataset with replacement, thereby ensuring that our predictive model is not overly fitted to our specific cohort. Nevertheless, the predictive model we propose for SM risk estimation should be further validated in independent patient populations to ensure its external generalizability. Despite these limitations, the multicenter design and the use of detailed nodal mapping across three tertiary centers strengthen the reliability of our findings.

5 | Conclusion

SM is a noteworthy pattern of lymphatic spread in PTC, observed in about 12% of patients with lateral lymph node involvement in our multicenter series. Older age (≥ 39.5 years) and upper-pole tumor location were independent predictors, while multifocality was inversely associated. These tumors tended to be smaller and demonstrated a lower nodal burden, often confined to a single lateral neck level.

Recognizing these predictors has important implications for surgical planning. In patients with solitary upper-pole PTC, particularly at older age, meticulous preoperative assessment of the lateral neck may reveal occult metastases. Our predictive model showed good discrimination (AUC = 0.841) and, after external validation, could support risk-based surgical decision-making. Integrating clinical, radiologic, and molecular features in future research will refine individualized management strategies. Awareness of SM patterns can ultimately guide optimal initial treatment and improve locoregional control in patients with PTC.

Acknowledgments

The authors thank all clinical and pathology teams at the participating centers for their contributions to data collection and patient care.

Funding

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. Q. Li, C. Huang, H. Zou, J. Zhang, and J. Xin, "Single-Center External Validation and Reconstruction of Multiple Predictive Models for Skip Lateral Lymph Node Metastasis in Papillary Thyroid Carcinoma," *Frontiers in Endocrinology* 15 (2024): 1366679.

2. L. Davies and H. G. Welch, "Current Thyroid Cancer Trends in the United States," *JAMA Otolaryngology. Head & Neck Surgery* 140, no. 4 (2014): 317–322.

3. Y. Ito, A. Miyauchi, M. Kihara, M. Fukushima, T. Higashiyama, and A. Miya, "Overall Survival of Papillary Thyroid Carcinoma Patients: A Single-Institution Long-Term Follow-Up of 5897 Patients," *World Journal of Surgery* 42, no. 3 (2018): 615–622.

4. J. L. Song, L. R. Li, Z. L. Xu, J. J. Li, S. R. Sun, and C. Chen, "Long-Term Survival in Patients With Papillary Thyroid Cancer Who Did Not Undergo Prophylactic Central Lymph Node Dissection: A SEER-Based Study," *World Journal of Oncology* 13, no. 3 (2022): 136–144.

5. D. H. Su, S. H. Chang, and T. C. Chang, "The Impact of Locoregional Recurrences and Distant Metastases on the Survival of Patients With Papillary Thyroid Carcinoma," *Clinical Endocrinology* 82, no. 2 (2015): 286–294.

6. Y. Guo, Y. Liu, W. Teng, et al., "Predictive Risk-Scoring Model for Lateral Lymph Node Metastasis in Papillary Thyroid Carcinoma," *Scientific Reports* 15, no. 1 (2025): 9542.

7. Y. S. Lee, S. C. Shin, Y. S. Lim, et al., "Tumor Location-Dependent Skip Lateral Cervical Lymph Node Metastasis in Papillary Thyroid Cancer," *Head & Neck* 36, no. 6 (2014): 887–891.

8. L. Gao, X. Li, Y. Xia, et al., "The Prognostic Implication of Skip Metastasis to Lateral Neck in Patients With Papillary Thyroid Cancer," *Quantitative Imaging in Medicine and Surgery* 14, no. 12 (2024): 9477–9485.

9. X. Nie, Z. Tan, and M. Ge, "Skip Metastasis in Papillary Thyroid Carcinoma Is Difficult to Predict in Clinical Practice," *BMC Cancer* 17, no. 1 (2017): 702.

10. M. D. Ringel, J. A. Sosa, Z. Baloch, et al., "2025 American Thyroid Association Management Guidelines for Adult Patients With Differentiated Thyroid Cancer," *Thyroid* 35, no. 8 (2025): 841–985.

11. Y. Zhang, X. Ji, Z. Yang, and Y. Wang, "Risk Factors for Cervical Lymph Node Metastasis of Papillary Thyroid Cancer in Elderly Patients Aged 65 and Older," *Frontiers in Endocrinology* 15 (2024): 1418767.

12. J. Fu, J. Liu, Z. Wang, and L. Qian, "Predictive Values of Clinical Features and Multimodal Ultrasound for Central Lymph Node Metastases in Papillary Thyroid Carcinoma," *Diagnostics* 14, no. 16 (2024): 1770.

13. B. Miličić, R. Prstačić, and D. Prgomet, "Skip Metastases in Papillary Thyroid Carcinoma–Prevalence, Predictive and Clinicopathological Factors," *Acta Clinica Croatica* 59, no. S1 (2020): 122–128.

14. I. B. Bahcecioglu, A. B. Bahcecioglu, S. B. Morkavuk, et al., "Predicting the Unexpected: Clinicopathological Insights Into Skip Metastasis in Papillary Thyroid Carcinoma," *Journal of Clinical Medicine* 14, no. 12 (2025): 4255.

15. S. Zhu, Q. Wang, D. Zheng, et al., "A Novel and Effective Model to Predict Skip Metastasis in Papillary Thyroid Carcinoma Based on a Support Vector Machine," *Frontiers in Endocrinology* 13 (2022): 916121.

16. S. Y. Lin, M. Y. Li, C. P. Zhou, et al., "Accurate Preoperative Prediction of Nodal Metastasis in Papillary Thyroid Microcarcinoma: Towards Optimal Management of Patients," *Head & Neck* 46, no. 5 (2024): 1009–1019.

17. Y. Qiu, Y. Fei, J. Liu, et al., "Prevalence, Risk Factors and Location of Skip Metastasis in Papillary Thyroid Carcinoma: A Systematic Review and Meta-Analysis," *Cancer Management and Research* 11 (2019): 8721–8730.

18. Y. Zhao, W. Li, L. Tao, J. Fan, W. Zhan, and W. Zhou, "Risk Factors and Nomogram to Predict Skip Metastasis in Papillary Thyroid Carcinoma," *Gland Surgery* 13, no. 2 (2024): 178–188.

19. J. Hou, Y. Zhang, Y. Fan, and B. Wu, "Risk Factors of Skip Lateral Lymph Node Metastasis in Papillary Thyroid Carcinoma," *European Archives of Oto-Rhino-Laryngology* 278, no. 2 (2021): 493–498.

20. W. X. Jin, Y. X. Jin, D. R. Ye, et al., "Predictive Factors of Skip Metastasis in Papillary Thyroid Cancer," *Medical Science Monitor* 24 (2018): 2744–2749.

21. Z. Huang, M. Song, S. Wang, et al., "Preoperative Serum Thyroglobulin Is a Risk Factor of Skip Metastasis in Papillary Thyroid Carcinoma," *Annals of Translational Medicine* 8, no. 6 (2020): 389.

22. J. H. Park, Y. S. Lee, B. W. Kim, H. S. Chang, and C. S. Park, "Skip Lateral Neck Node Metastases in Papillary Thyroid Carcinoma," *World Journal of Surgery* 36, no. 4 (2012): 743–747.

23. J. Lei, J. Zhong, K. Jiang, Z. Li, R. Gong, and J. Zhu, "Skip Lateral Lymph Node Metastasis Leaping Over the Central Neck Compartment in Papillary Thyroid Carcinoma," *Oncotarget* 8, no. 16 (2017): 27022–27033.

24. T. J. Robinson, S. Thomas, M. A. Dinan, S. Roman, J. A. Sosa, and T. Hyslop, "How Many Lymph Nodes Are Enough? Assessing the Adequacy of Lymph Node Yield for Papillary Thyroid Cancer," *Journal of Clinical Oncology* 34, no. 28 (2016): 3434–3439.