E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.25

Research Article

Clinicopathological Predictors of Cervical Lymph Node Metastasis and Recurrence in Patients Undergoing Surgical Management of Thyroid in Head and Neck Malignancies

Fazal Dad[1], Mohammad Iqbal[2], Habibullah[3], Ahmad Shah[4], Bashir Ahmed[5], Asmatullah[6*]

[1]Associate Professor, Department of Maxillofacial Surgery, Bolan Medical College, Sandeman Provincial Hospital, Quetta, Pakistan.

[2]Assistant Professor, Department of ENT, Bolan Medical College, Sandeman Provincial Hospital, Quetta, Pakistan.

[3,5,6*]Associate Professor, Department of ENT, Bolan Medical College, Sandeman Provincial Hospital, Quetta, Pakistan.

[4]Associate Professor, Department of General Surgery, Bolan Medical College, Sandeman Provincial Hospital, Quetta, Pakistan.

Corresponding Author: Dr. Asmatullah, Associate Professor, Department of ENT, Bolan Medical College, Sandeman Provincial Hospital, Quetta, Pakistan.

Email: asmatullahkhan.1dr@gmail.com

Received: 02.03.2026, Revised: 08.06.2026, Accepted: 20.06.2026

ABSTRACT

Background: Cervical lymph node metastasis is a major prognostic factor in thyroid and head and neck malignancies and is associated with increased recurrence and reduced survival.

Objective: To evaluate clinicopathological predictors of cervical lymph node metastasis and disease recurrence among patients undergoing surgical management for thyroid and head and neck malignancies.

Methodology: This retrospective cohort study was conducted at Department of ENT, Bolan Medical Complex Hospital Quetta from 1st October 2024 to 31st March 2025 and 210 patients with histopathologically confirmed thyroid or head and neck malignancies who underwent surgery with curative intent were included.

Results: The mean age of patients was 51.6±13.8 years with 126 (60%) were males. Cervical lymph node metastasis was identified in 97 (46.2%) patients and was significantly associated with younger age (48.2±12.9 vs. 54.5±14.1 years; p=0.001), larger tumor size (3.9±1.6 vs. 2.6±1.2 cm; p<0.001), advanced T stage, multifocality, lymphovascular invasion, perineural invasion, and extrathyroidal or extracapsular extension. Disease recurrence occurred in 42 (20%) patients and was significantly associated with cervical lymph node metastasis, positive surgical margins, larger tumor size, lymphovascular invasion, extrathyroidal or extracapsular extension, and advanced T stage. Multivariable analysis demonstrated that lymphovascular invasion (AOR=3.67, 95% CI: 1.89-7.11; p<0.001), tumor size >3 cm (AOR=2.84, 95% CI: 1.51-5.34; p=0.001), multifocality (AOR=2.21, 95% CI: 1.12-4.35; p=0.022), and extrathyroidal or extracapsular extension (AOR=2.95, 95% CI: 1.47-5.90; p=0.002) independently predicted cervical lymph node metastasis.

Conclusion: Clinicopathological features, including tumor size, multifocality, lymphovascular invasion, extrathyroidal or extracapsular extension, positive margins, and cervical lymph node metastasis, are significant predictors of recurrence in thyroid and head and neck malignancies.

Keywords: Cervical Lymph Node Metastasis, Thyroid Cancer, Head and Neck Cancer, Recurrence, Lymphovascular Invasion, Neck Dissection.

INTRODUCTION

Head and neck cancers, such as cancers of the thyroid gland and squamous cell cancers of the upper aerodigestive tract, are a considerable burden of disease in the world, as they are becoming more common, difficult to manage, and associated with significant morbidity and mortality.[1] One of the key prognostic factors in the management of patients with thyroid and head and neck cancers, which is crucial for disease staging, treatment planning, recurrence, and overall survival, is the presence of cervical lymph node metastasis.[2] Regional nodal involvement has been linked to higher local-regional failure rates, distant metastasis rate and lower long-term survival.[3] Thyroid malignancies often tend to spread into the central and lateral compartments of the neck through the lymphatics.[4] Differentiated thyroid cancers generally have good prognosis but when the

nodule in the neck region is involved, the chances of recurrence are higher and other therapies are required.[5] Likewise, the head and neck region have a dense network of lymphatic tissue that often gives rise to metastases in regional lymph nodes in the region of the head and neck in the form of head and neck squamous cell carcinoma.[6] Cervical lymph node involvement at diagnosis can indicate more aggressive tumour biology and is regarded as one of the important prognostic factors that will determine treatment outcomes.[7] An accurate identification of high-risk patients for cervical nodal metastasis and postoperative recurrence is still a big challenge in clinical practice.[8] Patient age, tumor size, multifocality, extrathyroidal extension, lymphovascular invasion, histological subtype, tumor grade, perineural invasion, and margin status, are several clinicopathological parameters that have been investigated as potential predictors of nodal spread.[9] The predictive power of these variables, however, differs among studies and types of malignancy, and needs to be further investigated in other patient groups.[10]

Majority of thyroid and head and neck cancers, surgical treatment is still the mainstay of therapy.[11] The selection of surgical techniques, such as selective neck dissection (SND), central compartment dissection (CCD) and comprehensive nodal clearance is largely dependent on a proper assessment of the risk in the pre and in the intra-operative period.[12] If reliable predictors of cervical lymph node metastasis could be identified, this would aid in surgical planning for individual patients and help reduce overtreatment and improve oncological results.[13] Even with the use of imaging modalities and molecular diagnosis, postoperative recurrence is a concern of patients with thyroid and head and neck cancers.[14] Recurrence can occur due to the presence of occult nodal disease or the nature of the tumor (aggressiveness), incomplete surgical resection or unfavorable pathological characteristics.[15] To optimize surveillance strategies, inform adjuvant treatment, and ensure good long-term disease control, early identification of risk factors for recurrence is key.[16]

Therefore, knowledge of the clinicopathological features and their association with efficacy in oncology is of paramount importance to improve the risk stratification and individual approach to treatment. But local evidence on the predictive factors for cervical lymph node metastasis or recurrence is still scant, especially in less developed countries or countries with a limited choice of advanced diagnostic tools.

MATERIALS AND METHODS

This retrospective cohort study was conducted at Department of ENT, Bolan Medical Complex Hospital Quetta from 1st October 2024 to 31st March 2025 including 210 patients who underwent surgical management for thyroid and head and neck malignancies to evaluate clinicopathological predictors of cervical lymph node metastasis and disease recurrence. Patients were included who had histopathologically confirmed thyroid malignancies or head and neck cancers and had been treated with primary surgery performed with curative intent, including thyroidectomy, wide local excision, neck dissection or a combination of these. Patients were included if complete clinicopathological information and at least 12 months' follow-up were available. Patients excluded included those with a newly diagnosed metastasis, those with incomplete pathological diagnosis reports, those who had not followed up after treatment, those who had undergone medical records loss, and those who had received radiotherapy and/or surgery to the head/neck area earlier.

The data was collected from hospital records, surgical databases, pathology reports and follow-up files with the help of a proforma that was designed specifically for the collection of data. Comorbidities, gender, age, and smoking status were considered as demographic variables. Clinical data such as primary tumor site, presenting symptoms, tumor stage and preoperative imaging were recorded. Histopathological parameters comprised the tumor size, histological subtype, tumour grade, multifocality, extrathyroidal extension, lymphovascular invasion, perineural invasion, margin status, extranodal extension, and pathological TNM stage. Surgery details such as primary tumour resection and neck dissection (type) were documented. Main outcomes were histopathologic findings of cervical lymph node metastasis and the recurrence of disease at follow-up. Recurrence was radiological, pathological or clinical evidence of local or distant recurrence following completion of primary treatment.

Data were analyzed using SPSS version 26. Independent t-tests and chi-square tests were used to compare clinicopathological characteristics between patients with and without cervical lymph node metastasis and between patients with and without recurrence. Variables with p-values <0.10 in univariable analysis were entered into multivariable logistic regression models to identify independent predictors of lymph node metastasis and

recurrence. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Kaplan–Meier survival analysis and log-rank tests were performed to evaluate recurrence-free survival. A p-value ≤0.05 was considered statistically significant.

RESULTS

The mean age of patients was 51.6±13.8 years, with male predominance 126 (60%). Head and neck squamous cell carcinoma was slightly more common (118, 56.2%) than thyroid malignancy 92 (43.8%). The mean tumor size was 3.2±1.5 cm. Advanced T3–T4 disease was present in 86 (41%), lymphovascular invasion in 64 (30.5%), perineural invasion in 49 (23.3%), and positive surgical margins in 38 (18.1%) patients (Table 1).

Node-positive patients were younger than node-negative patients (48.2±12.9 vs. 54.5±14.1 years; p=0.001) and had larger tumors (3.9±1.6 vs. 2.6±1.2 cm; p<0.001). Cervical lymph node metastasis was significantly associated with T3–T4 stage (57.7% vs. 26.5%), multifocality (39.2% vs. 17.7%), lymphovascular invasion (47.4% vs. 15.9%), perineural invasion (32.0% vs. 15.9%), and extrathyroidal/extracapsular extension (40.2% vs. 14.2%) [Table 2].

Disease recurrence occurred in 42 patients. Recurrent cases had a similar follow-up duration compared with non-recurrent cases (32.6±11.8 vs. 35.4±12.5 months; p=0.19). Recurrence was significantly associated with cervical lymph node metastasis (73.8% vs. 39.3%), larger tumor size (4.1±1.7 vs. 3.0±1.3 cm), positive margins (40.5% vs. 12.5%), lymphovascular invasion (57.1% vs. 23.8%), extrathyroidal/extracapsular extension (50.0% vs. 20.2%), and T3–T4 stage (64.3% vs. 35.1%) [Table 3].

Multivariable analysis showed that lymphovascular invasion was the strongest independent predictor of cervical lymph node metastasis (AOR=3.67, 95% CI: 1.89–7.11; p<0.001), followed by extrathyroidal/extracapsular extension (AOR=2.95), tumor size >3 cm (AOR=2.84), and multifocality (AOR=2.21) [Table 4].

Table 1: Baseline Demographic and Clinicopathological Characteristics of Patients (N = 210)

Variable	N (%)
Male	126 (60.0)
Female	84 (40.0)
Current/Former Smokers	98 (46.7)
Thyroid Malignancies	92 (43.8)
Head & neck squamous cell carcinomas	118 (56.2)
Tumor Size (cm)	3.2±1.5
T1–T2 Stage	124 (59.0)
T3–T4 Stage	86 (41.0)
Multifocal Tumor	58 (27.6)
Lymphovascular Invasion	64 (30.5)
Perineural Invasion	49 (23.3)
Extrathyroidal/Extracapsular Extension	55 (26.2)
Positive Surgical Margins	38 (18.1)

Table 2: Comparison of Clinicopathological Characteristics According to Cervical Lymph Node Metastasis

Variable	Node Positive (n=97)	Node Negative (n=113)	p-Value
Age (years)	48.2±12.9	54.5±14.1	0.001
Tumor size (cm)	3.9±1.6	2.6±1.2	<0.001
T3–T4 stage	56 (57.7%)	30 (26.5%)	<0.001
Multifocal tumor	38 (39.2%)	20 (17.7%)	0.001
Lymphovascular invasion	46 (47.4%)	18 (15.9%)	<0.001
Perineural invasion	31 (32%)	18 (15.9%)	0.006
Extrathyroidal/extracapsular extension	39 (40.2%)	16 (14.2%)	<0.001

Table 3: Comparison of Clinicopathological Characteristics According to Disease Recurrence

Variable	Recurrence (N=42)	No Recurrence (N=168)	p-Value

Follow-up duration (months)	32.6±11.8	35.4±12.5	0.19
Tumor size (cm)	4.1±1.7	3.0±1.3	<0.001
Cervical lymph node metastasis	31 (73.8%)	66 (39.3%)	<0.001
Positive surgical margins	17 (40.5%)	21 (12.5%)	<0.001
Lymphovascular invasion	24 (57.1%)	40 (23.8%)	<0.001
Extrathyroidal/extracapsular extension	21 (50%)	34 (20.2%)	<0.001
T3–T4 stage	27 (64.3%)	59 (35.1%)	0.001

Table 4: Multivariable Logistic Regression Analysis of Independent Predictors of Cervical Lymph Node Metastasis and Recurrence

Variable	Adjusted OR	95% CI	p-Value
Predictors of Cervical Lymph Node Metastasis			
Tumor Size >3 cm	2.84	1.51–5.34	0.001
Lymphovascular Invasion	3.67	1.89–7.11	<0.001
Multifocality	2.21	1.12–4.35	0.022
Extrathyroidal/Extracapsular Extension	2.95	1.47–5.90	0.002
Predictors of Disease Recurrence			
Cervical Lymph Node Metastasis	3.92	1.84–8.37	<0.001
Positive Surgical Margins	3.11	1.45–6.68	0.004
Lymphovascular Invasion	2.73	1.29–5.79	0.009
T3–T4 Stage	2.46	1.14–5.29	0.021

DISCUSSION

This study indicated that metastatic spread to the cervical lymph nodes was common and was highly associated with the aggressive features of the tumour: tumour size, T stage, multifocality, lymphovascular invasion, perineural invasion, and extrathyroidal/extracapsular extension. In addition, the presence of metastasis to the nodes was the most powerful independent risk factor for disease recurrence. Patients' mean age was 51.6±13.8 years, and the majority were male (60%). The most common sites of the cases were the head and neck squamous cell carcinoma (56.2%) and thyroid malignancies (43.8%). Previous studies have also found that males are at a higher risk for head and neck cancers, which is mostly attributed to differences in exposure to risk factors like smoking and alcohol use among males and females. Demographic variables described in the current study are similar to the epidemiological profile described for these cancers.[17] Metastasis to the cervical lymph nodes (CLN) was found in 97 patients and there was a significant correlation with younger age. The mean age for node-positive patients was 48.2±12.9 years but 54.5±14.1 years for node-negative patients. This is consistent with other studies such as the study of differentiated thyroid carcinoma, where younger patients had higher rates of cervical nodal metastasis, but had generally favorable survival rates.[18]

In the present study, there was a very strong correlation between nodal involvement and recurrence, and tumour size and nodal involvement. The cervical lymph node metastasis group had significantly larger tumors (3.9±1.6 cm vs. 2.6±1.2 cm) and the recurrent cases had a mean tumor size of 4.1±1.7 cm compared with 3.0±1.3 cm in the non-recurrent cases. The tumor size > 3 cm was confirmed as an independent predictor of nodal metastasis by multivariate analysis. It was observed that as the tumour size increases, so will be the tumour burden and the invasive potential of the tumour, hence the increased risk of having it spread in the lymph nodes or recur after surgery. Patients with advanced T stage were also a significant determinant for adverse outcome. There was a significantly higher prevalence of T3-T4 disease in node positive patients (57.7% compared to 26.5%) and in patients who recurred (64.3% compared to 35.1%). However, in the multivariable analysis, the more advanced stage was an independent risk factor for recurrence. In previous studies, advanced local disease was also found to be a risk factor for locoregional recurrence (LRR), incomplete resection and nodal spread.[19]

Multifocality was significantly associated with the presence of cervical lymph node metastasis and was an independent risk factor with a more than twofold increase of the presence of lymph node metastasis. Multifocal tumors have been described to be biologically aggressive, and to infiltrate local tissues, with particular regard to

papillary thyroid carcinoma (PTC).[20] Lymphovascular invasion was the most important factor associated with nodal metastasis and recurrence. A significant proportion of node positive patients (46.8%) showed lymphovascular invasion whereas only 15.9% of node negative patients showed it. Similarly, the number of patients that recurred was significantly greater than the number with no recurrence (57.1% vs. 23.8%) when evaluated in terms of the presence of lymphovascular invasion. Multivariable analysis revealed that lymphovascular invasion was a risk factor for nodal metastasis (OR 3.67) and recurrence (OR 2.73). LVI has been demonstrated in previous studies to be a recurring phenomenon and a marker of aggressive tumor biology and to be a strong predictor of regional and distant disease spread. Cervical lymph node metastasis was also significantly related to perineural invasion. The rate of perineural invasion also increased in node-positive patients (32.0% vs. 15.9%). Previous studies report similar associations and perineural invasion has been described as being associated with locally aggressive disease and is a poor indicator for oncological prognosis.[21] Extrathyroidal/extra capsular extension also is a strong predictor of adverse outcomes. The presence of this feature in patients with node positive disease and in patients with recurrence was 40.2% and 50.0% respectively. Extrathyroidal or extracapsular extension was an independent predictor of cervical lymph node metastasis confirmed by multivariable analysis. Previous studies have also shown that when extending beyond the primary tumour capsule, it is a sign of more aggressive tumour behaviour and linked to increased recurrence rates.

Limitations

There are certain limitations to this study. First, because of its retrospective design, there may be selection bias and the study might not have been able to draw causal conclusions between clinicopathological factors and oncological outcomes. Second, this research took place at a single centre; the findings may not apply to other populations and health care settings. Some differences in the surgical procedure, extent of neck dissection, postoperative treatments, and follow-up may have affected recorded recurrence rates. Furthermore, molecular markers and genetic profiling, which are becoming increasingly known to be important prognostic markers in thyroid and head and neck malignancies, were not regularly available and therefore not used in this study. While sufficient for short- to intermediate-term follow-up, late recurrence may not be fully represented by the follow-up period. Multicenter prospective studies with molecular markers and longer follow-up are suggested to confirm these results.

CONCLUSION

Cervical lymph node metastasis remains a critical determinant of prognosis in patients undergoing surgical management for thyroid and head and neck malignancies. Larger tumor size, multifocality, lymphovascular invasion, and extrathyroidal or extracapsular extension were identified as independent predictors of nodal metastasis. Furthermore, cervical lymph node metastasis, positive surgical margins, lymphovascular invasion, and advanced T stage were significant predictors of disease recurrence. Early identification of these high-risk clinicopathological features may facilitate individualized surgical planning, optimize the use of neck dissection and adjuvant therapies, and improve surveillance strategies. Incorporating these predictors into routine clinical practice may enhance risk stratification and contribute to improved long-term oncological outcomes.

REFERENCES

1. Liu Y, Wang X, Sun X, Li H, Wang L. Nomogram for predicting the risk of cervical lymph node metastases and recurrence in papillary thyroid carcinoma based on the thyroid differentiation score system and clinical characteristics. BMC Endocrine Disord 2025; 25(1): 39.
2. Feng JW, Yang XH, Wu BQ, Sun DL, Jiang Y, Qu Z. Predictive factors for central lymph node and lateral cervical lymph node metastases in papillary thyroid carcinoma. Clin Transl Oncol 2019; 21(11): 1482-1491.
3. Wu S, Liu Y, Ruan X, Zheng X. Predictive factors for lymph node metastasis in papillary thyroid cancer patients undergoing neck dissection: insights from a large cohort study. Front Oncol 2024; 14: 1447903.
4. Liu C, Xiao C, Chen J, Li X, Feng Z, Gao Q, Liu Z. Risk factor analysis for predicting cervical lymph node metastasis in papillary thyroid carcinoma: a study of 966 patients. BMC Cancer 2019; 19(1): 622.
5. Zhan L, Feng HF, Yu XZ, Li LR, Song JL, Tu Y, et al. Clinical and prognosis value of the number of metastatic lymph nodes in patients with papillary thyroid carcinoma. BMC Surg 2022; 22(1): 235.
6. Liu W, Zhang D, Jiang H, Peng J, Xu F, Shu H, et al. Prediction model of cervical lymph

node metastasis based on clinicopathological characteristics of papillary thyroid carcinoma: a dual-center retrospective study. Front Endocrinol 2023; 14: 1233929.

7. Hu Q, Zhang WJ, Liang L, Li LL, Yin W, Su QL, et al. Establishing a predictive nomogram for cervical lymph node metastasis in patients with papillary thyroid carcinoma. Front Oncol 2022; 11: 766650.
8. Hu R, Ren Q, Li T, Lv C, Yang J, Ren Y, et al. Evidence-based integration of clinicopathological factors with the risk of papillary thyroid carcinoma lateral cervical lymph node metastasis: systematic review and meta-analysis and subgroup study. Gland Surg 2025; 14(5): 912-28.
9. Li X, Zhang H, Zhou Y, Cheng R. Risk factors for central lymph node metastasis in the cervical region in papillary thyroid carcinoma: a retrospective study. World J Surg Oncol 2021; 19(1): 138.
10. Zheng H, Lai V, Lu J, Kang JK, Chou J, Burman KD, et al. Clinical factors predictive of lymph node metastasis in thyroid cancer patients: a multivariate analysis. J Am Coll Surg 2022; 234(4): 691-700.
11. Bahcecioglu IB, Bahcecioglu AB, Morkavuk SB, Hatipoglu Y, Guler S, Turan M, et al. Predicting the unexpected: clinicopathological insights into skip metastasis in papillary thyroid carcinoma. J Clin Med 2025; 14(12): 4255.
12. Yang Q, Chen P, Hu HY, Tan HL, Li GY, Liu M, et al. Preoperative sonographic and clinicopathological predictors for solitary lateral neck node metastasis in papillary thyroid carcinoma: a retrospective study. Cancer Management Research 2020; 1855-62.
13. Zhang T, He L, Wang Z, Dong W, Sun W, Zhang P, et al. Risk factors of cervical lymph node metastasis in multifocal papillary thyroid cancer. Front Oncol 2022; 12: 1003336.
14. Chen H, Zhu L, Zhuang Y, Ye X, Chen F, Zeng J. Prediction model of cervical lymph node metastasis in papillary thyroid carcinoma. Cancer Control 2024; 31: 10732748241295347.
15. Sakız D, Çalapkulu M, Sencar ME, Ünsal İÖ, Kartal MZ, Uçan B, et al. Clinicopathological predictors of central lymph node metastasis in clinically node-negative papillary thyroid carcinoma: a retrospective cohort analysis. Eur Arch Oto-Rhino-Laryngology 2026; 283(2): 1069-80.
16. Sahin MY, Dural AC, Aydin H, Ozel TM, Akbulut S, Celik A, et al. Clinicopathologic predictors and nodal burden pattern of skip metastasis in papillary thyroid carcinoma: a multicenter study. Head Neck 2026; 45.
17. Wen X, Jin Q, Cen X, Qiu M, Wu Z. Clinicopathologic predictors of central lymph node metastases in clinical node-negative papillary thyroid microcarcinoma: a systematic review and meta-analysis. World J Surg Oncol 2022; 20(1): 106.
18. Zhao L, Sun X, Luo Y, Wang F, Lyu Z. Clinical and pathologic predictors of lymph node metastasis in papillary thyroid microcarcinomas. Ann Diagn Pathol 2020; 49: 151647.
19. Wang D, Zhu J, Deng C, Yang Z, Hu D, Shu X, et al. Preoperative and pathological predictive factors of central lymph node metastasis in papillary thyroid microcarcinoma. Auris Nasus Larynx 2022; 49(4): 690-96.
20. Yang L, Li W, Zhang H, Yu L, Zheng M. Clinicopathological characteristics of patients with carotid body tumor with cervical lymph node metastasis: a retrospective study of 10 cases and review of the literature. Medicine 2022; 101(36): e30379.
21. Zhang L, Ling Y, Zhao Y, Li K, Zhao J, Kang H. A nomogram based on clinicopathological and ultrasound imaging characteristics for predicting cervical lymph node metastasis in cN0 unilateral papillary thyroid microcarcinoma. Front Surg 2021; 8: 742328.