Original Article
Analysis of risk factors for lymph node metastasis in 241 patients with thyroid carcinoma and establishment of a prediction model

Wanzhi Chen, Jichun Yu, Kunlin Lei, Rong Xie, Haiyan Wang, Meijun Zhong

Department of Thyroid Surgery, The Second Affiliated Hospital of Nanchang University, Nanchang 330006, Jiangxi, P. R. China

Abstract: This study aimed to identify risk factors for cervical lymph node metastasis (LNM) in papillary thyroid carcinoma (PTC) and develop a clinical prediction model. Retrospectively, data were collected from 348 PTC patients treated at the Second Affiliated Hospital of Nanchang University between January 2019 and December 2022, with 241 patients included in the final analyses. Patients with lateral cervical LNM were categorized into a metastasis group, and those without were in a non-metastasis group. The patients were divided into a training set (n=169) and a validation set (n=72) in a 7:3 ratio. Logistic and least absolute shrinkage and selection operator (LASSO) regression models were used to identify key factors associated with lateral cervical LNM and prognosis, enabling the construction of a predictive model. The model's validity was assessed via the Hosmer-Lemeshow Test, calibration curves, ROC curves, and decision curve analysis. The metastasis group exhibited higher proportions of males, multiple lesions, bilateral involvement, tumor diameter ≥1 cm, and elevated levels of PLR, LMR, and NLR (P<0.05). Logistic regression analysis revealed that gender, multiple lesions, affected side, and tumor diameter were associated with lateral cervical LNM (P<0.05). The predictive Nomogram model, which included factors like affected side, tumor diameter, capsular invasion, central LNM, PLR, and NLR, demonstrated strong predictive accuracy and clinical utility. Thus, this study provides a practical clinical tool through an accurate Nomogram model to assess lateral cervical LNM risk in PTC patients using logistic and LASSO regression analyses.

Keywords: Papillary thyroid carcinoma, lymph node metastasis, risk factors, prediction model

Introduction

Thyroid carcinoma (TC) is a prevalent malignancy, with papillary thyroid carcinoma (PTC) being the most prevalent type, accounting for 85 to 90 percent of all thyroid malignancies [1]. Predominantly affecting middle-aged and older women, PTC is relatively rare in men [2]. Cervical lymph nodes are the most common metastatic sites of PTC, and in some patients, cancer cells can spread to distant organs, such as the lungs and bones [3]. Cervical lymph node metastasis (LNM) can be classified as either central or lateral cervical metastasis [4]. Surgery is the primary treatment for PTC, and assessing LNM preoperatively is crucial in determining the scope and mode of operation. Preoperative identification of LNM allows clinicians to tailor the surgical approach and plan

lymph node dissection more precisely, ensuring comprehensive treatment while minimizing unnecessary procedures [5]. Therefore, accurate evaluation of cervical LNM before surgery is essential for optimal surgical planning.

LNM of PTC may occur in the central or lateral cervical regions. Most guidelines recommend lateral neck lymph node dissection for patients with positive clinical and radiographic findings; however, for those with clinically node-negative (cN0) PTC, this prophylactic surgery does not significantly improve survival or reduce recurrence rates, but may increase postoperative complications and affect patients' quality of life [6]. Therefore, it is controversial whether to perform lateral neck lymph node dissection for cN0 patients. LNM of TC usually occurs in sequential, starting with the central region of

the affected side, then the ipsilateral cervical region, and possibly spreading to the contralateral cervical region or upper mediastinal lymph nodes [7]. However, there are also special cases called jumping metastasis, in which cancer cells metastasize directly from the thyroid to the cervical lymph nodes on the affected side, without passing through the central region [8]. The size and location of tumors, especially those in the upper pole, are considered risk factors for jumping metastasis, but no definitive conclusions can be drawn due to the limited number of cases [9].

Nomograms, using concise and intuitive charts to present the results of regression analysis in the form of lines and scales, are commonly used and highly regarded in medical research [10]. Based on multivariate regression analysis, Nomograms comprehensively take into account a variety of predictors and assigns corresponding values to different states of each factor to indicate their influence on the result variable (i.e. regression coefficient), which is visually represented by the length of the line segment [11]. Using a specific mathematical function, the length of these line segments can be combined to calculate the probability of a specific outcome. Nomograms also offer several advantages over other analytical methods: it can handle multiple types of variables simultaneously, without the need to distinguish between continuous and categorical variables, and can consider multiple potential risk factors at the same time.

A preoperative LNM prediction model is crucial for optimizing surgical planning, allowing for tailored lymph node dissection plans when necessary. It reduces unnecessary intraoperative pathology tests, minimizing surgery duration and resource wastage. Additionally, accurately identifying LNM risk can prevent overtreatment of low-risk patients and reduce postoperative complications. Furthermore, a prediction model can aid in early identification of high-risk cases, facilitating more aggressive intervention where appropriate. Finally, this model is economically advantageous, reducing reliance on costly diagnostic procedures and leading to a more efficient and cost-effective patient care strategy.

Therefore, the aim of this study is to clarify the risk factors for LNM in TC patients by constructing a multifactorial-based prediction model to

assess the risk factors for LNM in the preoperative period and to optimize surgical decision-making. We employed multiple statistical methods to screen out the most relevant features to LNM, integrated clinical and laboratory data, and developed a visualized prediction model. This model is expected to assist physicians to better plan the scope of surgery, reduce unnecessary surgical risks and healthcare costs, and improve overall patient outcomes and quality of life.

Methods and materials

Ethical statement

This study was approved by the Medical Ethics Committee of The Second Affiliated Hospital of Nanchang University.

Sample collection

Data from 348 patients with PTC who were treated in The Second Affiliated Hospital of Nanchang University between January 2019 and December 2022 were retrospectively collected.

Eligibility and exclusion criteria

Inclusion criteria: The patients (1) underwent cervical ultrasonography and thyroid function test before surgery [12, 13], (2) were confirmed as PTC by histopathological examination after surgery, (3) underwent radical surgery for TC, and (4) had complete clinical and follow-up data.

Exclusion criteria: Patients were excluded if they had (1) a history of head and neck tumors, (2) recurrent TC, (3) other types of thyroid malignancies, (4) distant organ metastases, or (5) defective clinical and follow-up data (**Figure 1**).

Sample screening

A total of 318 cases were included according to the inclusion criteria, and 241 eligible samples were finally included after further screening with the exclusion criteria. Next, they were randomized into a training set (n=169) and a validation set (n=72) according to a ratio of 7:3, in which the training set was used for feature screening and prediction of lateral cervical LNM in TC, while the validation group was used
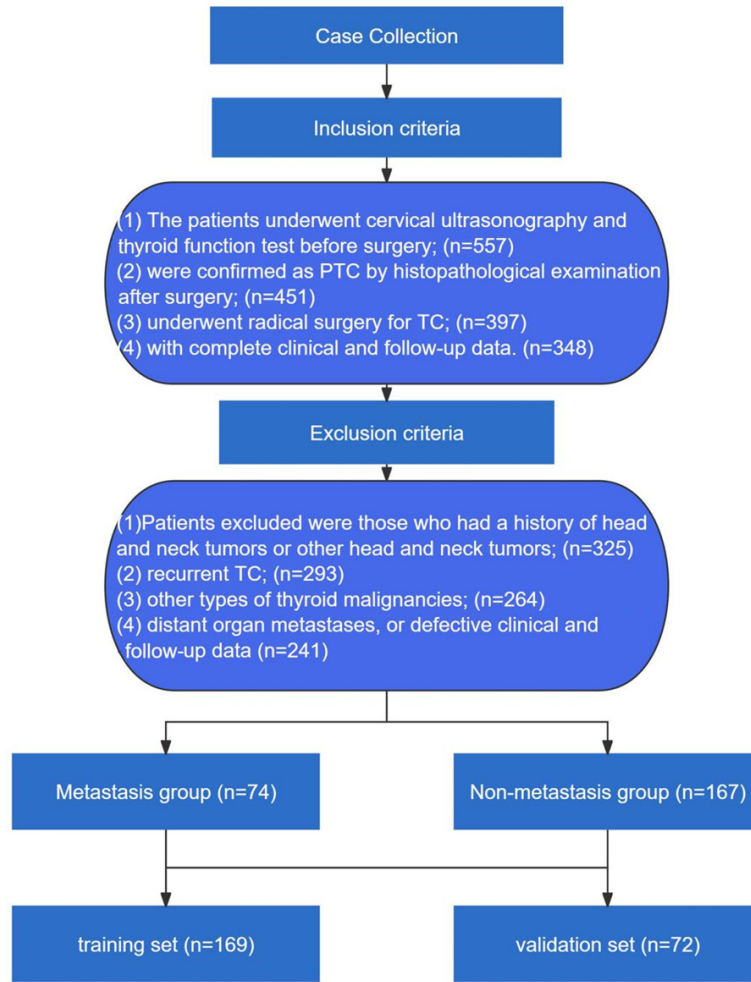
Figure 1. Flow chart of case screening.

for model validation. According to postoperative pathological features, patients with lateral cervical LNM were divided into a metastasis group and those without were included in a non-metastasis group.

Clinical data collection

We collected clinical and laboratory data from the two groups of patients. Clinical data included age, gender, multiple lesions, affected side, tumor diameter, capsular invasion, calcification, combined Hashimoto's thyroiditis, and central LNM. The laboratory indicators detected were free triiodothyronine (FT3), free thyroxine (FT4), thyroid stimulating hormone (TSH), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and neutrophil-to-lymphocyte ratio (NLR). All the laboratory indicators were obtained at the initial examination.

LASSO regression analysis

LASSO regression is an algorithm for variable screening. It controls the complexity of the model by adjusting the complexity adjustment factor λ. As λ increases, the penalty for the parameters increases. When λ reaches a certain value, the unimportant variables will be compressed to 0 and removed from the model, so as to find the variables that have the most significant influence on the outcome events. This method can not only solve multicollinearity problems, but also avoid data overfitting. To screen out potential predictors with non-zero coefficients, R Studio software was used to incorporate statistically significant factors ($P < 0.05$) identified by univariate analysis into the LASSO regression model. Analyses were performed using the "glmnet" package of R 4.3.2.

Evaluation and validation of the prediction model

Calibration evaluation: The consistency between the predicted values of the model and the actual observed values was evaluated by using the Hosmer-Lemeshow (H-L) test and calibration plot, with the calibration plot being the visualization of the H-L goodness-of-fit test.

Differentiation evaluation: The receiver operating characteristic (ROC) was used to evaluate the model's differentiation ability by calculating the area under the curve (AUC). An AUC value between 0.5 and 0.6 indicates poor differentiation, while an AUC value above 0.75 suggests good differentiation performance.

Clinical practicability evaluation: The decision curve analysis (DCA) was used to evaluate the clinical value of the model by comparing the benefits under different decision thresholds. A decision curve at the top right of a particular reference line indicates favorable clinical utility of the model.

Table 1. Comparison of baseline data of patients

Factors	Metastasis group (n=74)	Non-metastasis group (n=167)	χ^2	P
Age (years old)				
≥45	44	90	0.644	0.422
<45	30	77		
Gender				
Male	15	70	10.524	0.001
Female	59	97		
Multiple lesions				
With	17	94	22.907	<0.001
Without	57	73		
Affected side				
Unilateral	39	145	33.066	<0.001
Bilateral	35	22		
Tumor diameter (cm)				
≥1	45	52	18.774	<0.001
<1	29	115		
Calcification				
With	17	47	0.703	0.402
Without	57	120		
Combined Hashimoto's thyroiditis				
With	45	117	1.991	0.158
Without	29	50		
TSH (uUl/ml)				
<4.2	21	117	0.06	0.806
≥4.2	53	50		

Note: TSH, thyroid stimulating hormone.

Statistical analysis

SPSS 26.0 was used for data processing and analyses. The comparison of counting data adopted the χ^2 test. Logistic and LASSO regression models were used to determine the characteristic factors for lateral cervical LNM in TC. The LASSO regression was conducted using the "glmnet" package in R (4.3.2) for drawing and analysis. Common characteristic factors were screened by Venn diagram. ROC curves were drawn to analyze the implications of the risk score and the value of the characteristic factors in predicting lateral cervical LNM in TC patients. The calibration degree and clinical practicability of the model were evaluated by DCA, calibration curves, and H-L test. The Nomogram was plotted using the rms package of R software. The differences between the AUC of the validation set and the training set model were compared using Delong test. All analyses relied upon a P<0.05 statistical significance criterion.

Results

Comparison of baseline data

Comparing the clinical data between the metastasis and non-metastasis groups, it was found that the proportions of males and those with multiple lesions, bilateral lesions, and tumor diameter ≥1 cm were significantly higher in the metastasis group than in the non-metastasis group, with statistical differences (P<0.05, **Table 1**). Subsequently, we divided the clinical data of patients into a validation set and a training set according to a 7:3 ratio. The inter-group comparison revealed no statistical difference in clinical data between the two sets (P>0.05, **Table 2**).

Comparison of laboratory indicators

Comparing the laboratory indicators of the two groups, it was found that the two groups were

Table 2. Comparison of baseline data between training and validation groups

Factors	Training group (n=169)	Validation group (n=72)	χ^2	*P*
Age (years old)				
≥45	100	34	2.920	0.084
<45	69	38		
Gender				
Male	59	26	0.032	0.858
Female	110	46		
Multiple lesions				
With	76	35	0.269	0.604
Without	93	37		
Affected side				
Unilateral	131	53	0.426	0.514
Bilateral	38	19		
Tumor diameter (cm)				
≥1	71	26	0.731	0.393
<1	98	46		
Calcification				
With	47	17	0.457	0.499
Without	122	55		
Combined Hashimoto's thyroiditis				
With	113	49	0.033	0.857
Without	56	23		
TSH (uUl/ml)				
<4.2	120	50	0.059	0.808
≥4.2	49	22		
Central lymph node metastasis				
With	118	45	1.237	0.266
Without	51	27		

Note: TSH, thyroid stimulating hormone.

not statistically significant in FT3, FT4, and TSH, (P>0.05), but the PLR, LMR and NLR were higher in the metastasis group than in the non-metastasis group (P<0.001, **Table 3**). In addition, the differences in laboratory indicators between the validation and training datasets were also compared, and no statistically significant differences were identified (P>0.05, **Table 4**).

Determination of the optimal cut-offs for laboratory indicators

ROC curves were plotted to determine binary cut-offs for laboratory indicators with statistical significance. Through analysis, we found that the optimal cut-offs for PLR, LMR, and NLR were 161.13, 4.15, and 9.49, respectively, and the AUCs were 0.663, 0.592, and 0.830, respectively (**Figure 2**).

Logistic regression screening for characteristic factors affecting lateral cervical LNM in TC

Logistic regression was carried out to screen the characteristic factors affecting lateral cervical LNM in TC. All these factors were assigned (**Table 5**). Univariate analysis showed that gender, multiple lesions, affected side, tumor diameter, PLR, and NLR were correlated with lateral cervical LNM (**Table 6**, P<0.05). Subsequently, through multivariate logistic regression analysis, we identified a strong correlation of multiple lesions, affected side, tumor diameter, PLR, LMR, and NLR with lateral cervical LNM in TC (**Table 7**, P<0.05).

LASSO regression screening for characteristic factors

LASSO regression was used to screen the characteristic factors affecting lateral cervical LNM

Table 3. Comparison of laboratory indicators between the metastasis and non-metastasis groups

Indicators	Metastasis group (n=74)	Non-metastasis group (n=167)	t	P
FT3 (pmol/L)	4.43±1.66	4.13±1.87	1.225	0.222
FT4 (pmol/L)	15.89±3.29	16.25±3.08	-0.797	0.427
TSH (mU/L)	2.47±0.72	2.45±0.81	0.216	0.829
PLR	144.26±59.93	113.98±39.03	3.988	<0.001
LMR	4.77±1.17	4.40±1.28	2.214	0.028
NLR	10.31±2.58	7.15±1.99	10.346	<0.001

Note: FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio.

Table 4. Comparison of laboratory indicators between the validation and training groups

Indicators	Training group (n=169)	Validation group (n=72)	t	P
FT3 (pmol/L)	4.24±1.88	4.19±1.65	-0.199	0.842
FT4 (pmol/L)	16.22±3.12	15.96±3.21	-0.592	0.555
TSH (mU/L)	2.48±0.79	2.38±0.75	-0.957	0.340
PLR	119.79±47.94	131.14±48.82	1.673	0.097
LMR	4.53±1.28	4.47±1.21	-0.371	0.711
NLR	7.90±2.70	8.62±2.41	1.955	0.052

Note: FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio.
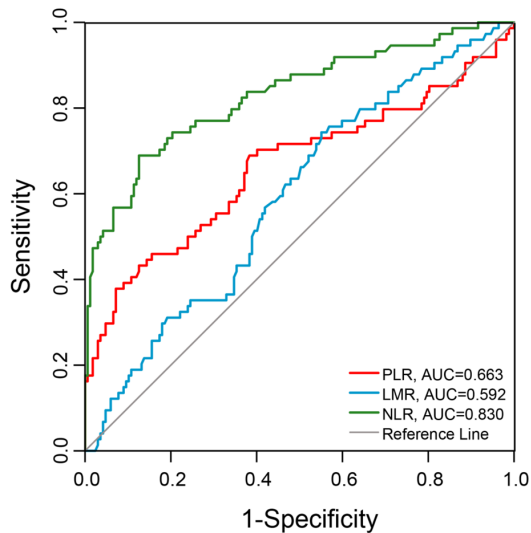
Figure 2. Receiver operating characteristic curves of laboratory indicators with statistical significance.

in TC. When λ=0.013424(.1se), 7 characteristic factors for lateral cervical LNM were screened out, namely, gender, multiple lesions, affected side, tumor diameter, combined Hashimoto's thyroiditis, PLR, and NLR (**Figure 3A**, **3B**).

Screening of common characteristic factors and construction of a Nomogram model

Using the Venn diagram for screening, it was found that multiple lesions, affected side, PLR, and NLR were predictive factors of lateral cervical LNM in TC (**Figure 4A**). Model calculation formula: -1.549 + Multiple lesions Without * -1.118 + Affected side Bilateral * -2.498 + PLR < 161.13 * 2.030 + NLR < 9.49 * 3.202. We then built a Nomogram prediction model based on these four factors. In the Nomogram, the affected side had the strongest influence on lateral cervical LNM in TC, while gender, multiple lesions, and tumor diameter, had strong impacts. Among them, males, multiple lesions, bilateral lesions, and tumor diameter ≥1 cm were the risk factors for lateral cervical LNM in TC (**Figure 4B**).

Evaluation of the performance of the prediction model in the training dataset

DCA, calibration curves, ROC curves and H-L test were used to evaluate the differentiation, calibration, and clinical practicability of the model. The DCA showed that in the training group, the net benefit of the risk prediction model was relatively high, with the red line corresponding to the threshold probability located at the upper right of the None line and the All line, indicating good clinical practicability of the model (**Figure 5A**). The calibration curve obtained by 1000 bootstrap iterations revealed that the red line coincided with the black diagonal dotted line, indicating the stable performance of the model (**Figure 5B**). According to ROC curve analysis, the AUC of the risk score in predicting lateral cervical LNM in patients with TC was 0.907, which indicates that this model has high accuracy in predicting lateral cervical LNM in TC (**Figure 5C**). Finally, through the H-L test analysis, it was found that

Table 5. Assignment

Factors	Assignment
Age (years old)	≥45 = 1, <45 = 0
Gender	Male = 1, female = 0
Multiple lesions	With = 1, without = 0
Affected side	Unilateral = 1, bilateral = 0
Tumor diameter (cm)	≥1 = 1, <1 = 0
Calcification	With = 1, without = 0
Combined Hashimoto's thyroiditis	With = 1, without = 0
TSH (μUl/ml)	≥4.2 = 0, <4.2 = 1
PLR	<161.13 = 0, ≥161.13 = 1
LMR	<4.15 = 0, ≥4.15 = 1
NLR	<9.49 = 0, ≥9.49 = 1

Note: TSH, thyroid stimulating hormone; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio.

the chi-square value of the model in the training set was 2.993 (P=0.934).

Effectiveness evaluation of the predictive model in the validation dataset

Based on the coefficients of the Nomogram characteristic factors, we calculated the risk score of each patient in the validation group. Subsequently, the discrimination, calibration, and clinical utility of the model were also assessed using DCA, calibration and ROC curves, as well as the H-L test. According to DCA, the model had a high net benefit in the validation set, indicating its favorable clinical practicability (**Figure 6A**). Furthermore, as shown by the calibration curve obtained by 1000 bootstrap iterations, the red line overlapped with the black diagonal dotted line, indicating stable model performance (**Figure 6B**). Moreover, as indicated by ROC curve analysis, the AUC of the risk score in predicting lateral cervical LNM in patients with TC was 0.868, indicating good accuracy of the model in predicting lateral cervical LNM in TC (**Figure 6C**). In addition, no statistical difference in the AUC was found by the Delong test (D=0.778, P=0.438). Finally, the H-L test analysis found that the chi-square value of the model in the training set was 4.347 (P=0.824).

Discussion

TC, especially PTC, is the most common endocrine tumor worldwide [14]. Notably, it is prone to LNM, especially in the neck region [15].

Understanding the metastatic propensity is very important to determine the treatment strategy and can help accurately assess prognosis. Predicting lateral cervical LNM is of great significance to patients, as patients with occult cervical LNM are at higher risk of disease recurrence and distant metastasis [16]. Therefore, preoperative evaluation of lateral cervical LNM is crucial in the surgical planning and management of patients.

In this study, logistic regression was used to screen the characteristics of lateral neck LNM in TC patients. Six factors (multiple lesions, affected side, tumor diameter, PLR, LMR, and NLR) were found to be predictors of cervical side LNM in TC patients, following the selection from seven risk factors. Kim et al. [17] performed a retrospective analysis and found that male was an independent predictor of LNM. Furthermore, Ito et al. [18] recommended prophylactic lymph node dissection in male patients with PTC. In addition, a meta-analysis by So et al. [19], which included 16 studies, also noted a higher incidence of LNM in male PTC patients. The present study found that males were also an independent risk factor for developing lateral neck LNM in patients with TC, which is consistent with previous studies. These studies suggest that male patients may be at high risk for TC LNM. However, Zhao et al. [20] analyzed data from 215 patients with PTMC and concluded that there was no significant correlation between gender and LNM. We speculate that the reason for this discrepancy may be gender differences due to biological mechanisms, differences in study design and methodology, and other influencing factors such as tumor diameter and multiple lesions. Despite these differences, the majority of evidence supports a higher risk of lateral neck LNM in male TC patients, which has important implications for understanding disease mechanisms and developing treatment strategies.

Multiple lesions PTC is relatively common in patients, but its incidence varies widely across studies [21]. Multiple PTC is more likely to occur with central and lateral cervical LNM [22, 23]. These studies, as well as ours, emphasize the importance of considering the number of cancer foci when planning treatment, especially

Table 6. Univariate analysis

Factors	β	Standard error	P	OR	95% confidence interval	
					Lower bound	Upper bound
Age	0.227	0.286	0.423	1.225	0.720	2.186
Gender	-1.043	0.329	0.002	0.352	0.185	0.671
Multiple lesions	-1.463	0.317	0.000	0.232	0.124	0.431
Affected side	-1.777	0.326	0.000	0.169	0.089	0.321
Tumor diameter	1.233	0.291	0.000	3.432	1.940	6.069
Calcification	-2.727	0.326	0.403	0.761	0.402	1.441
Combined Hashimoto's thyroiditis	-0.411	0.292	0.159	0.663	0.374	1.175
TSH	-0.076	0.308	0.806	0.927	0.507	1.697
PLR	1.612	0.332	0.000	5.012	2.617	9.601
LMR	0.859	0.308	0.005	2.360	1.290	4.318
NLR	2.735	0.343	0.000	15.416	7.873	30.187

Note: TSH, thyroid stimulating hormone; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio.

Table 7. Multivariate analysis

Factors	β	Standard error	P	OR	95% confidence interval	
					Lower bound	Upper bound
Gender	-0.867	0.472	0.066	0.420	0.161	1.038
Multiple lesions	-1.443	0.438	0.001	0.236	0.096	0.543
Affected side	-2.299	0.516	0.000	0.100	0.035	0.265
Tumor diameter	1.445	0.429	0.001	4.242	1.873	10.172
PLR	1.522	0.476	0.001	4.581	1.828	11.983
LMR	0.929	0.442	0.036	2.531	1.084	6.200
NLR	2.562	0.439	0.000	12.956	5.661	32.013

Note: PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio.

when assessing the risk of cervical LNM in patients with PTC. Bilateral lobar involvement is relatively common, accounting for approximately 20% of patients [24]. Compared with unilateral multifocal PTC, bilateral PTC is characterized by a larger tumor size, which makes it more likely to develop extrathyroidal invasion and cervical LNM [25]. A study [26] identified a significant correlation between bilateral PTC and cervical LNM, which is consistent with our findings. Thus, PTC with bilateral involvement is at higher risk of developing cervical LNM, which emphasizes the need to pay special attention to the characteristics of bilateral cancers when evaluating and treating PTC. Tumor diameter has also been shown to be an important predictor of lateral cervical LNM. Thresholds for tumor size have varied among studies, generally ranging from 0.5 to 3.0 cm. The risk of lateral cervical metastasis was found to be significantly increased and the percentage of positive cervical nodes was significantly higher when the tumor diameter exceeds 1 cm, especially with a diameter ≥4 cm [3, 19]. These findings are consistent with ours, where multivariate analysis showed that tumor diameter ≥1 cm was an independent risk factor for cervical LNM, which highlights the importance of considering tumor diameter when assessing the risk of cervical LNM in patients with PTC.

Elevated PLR implies increased platelet activity, which enhances angiogenesis and promotes tumor growth; low LMR suggests impaired immunosurveillance due to decreased lymphocyte counts, while elevated monocyte levels indicate increased pro-tumorigenic activity [27]. Elevated NLR reflects an imbalance between neutrophils and lymphocytes leading to a pro-tumorigenic environment through increased cytokine secretion and impaired immune response [28]. Together, these ratios
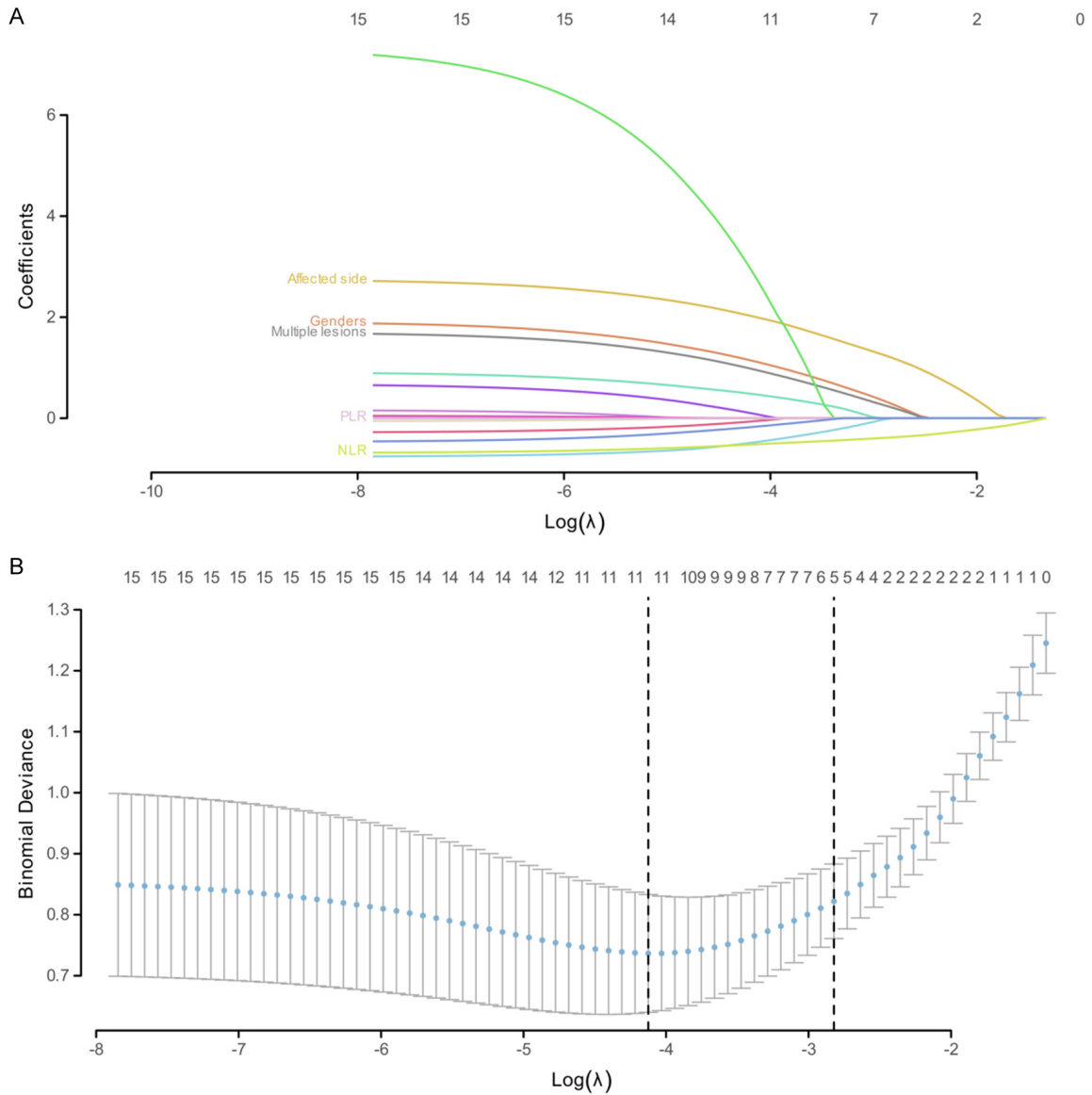
Figure 3. LASSO regression screening for characteristic factors for lateral cervical lymph node metastasis in thyroid carcinoma. A. The number of features selected for different regularization strengths (λ values). B. The coefficient paths of the final 7 selected characteristic factors.

reflect the state of systemic inflammation and immune surveillance, providing valuable prognostic information for predicting cervical LNM in PTC. For example, Song et al. [29] found an interaction between NLR and PLR, and suggested that NLR and PLR could be used as independent predictors of central LNM. In addition, Huang et al. [30] reported that higher NLR and PLR values were indicative of higher risk of recurrence in PTC patients.

Nomogram models are widely used to predict risk and prognosis of diseases [31]. The model can display the weights of various factors by the lengths of the line segments, and the risk of an outcome event can be obtained by simple summation and calculation without complex function transformations [32, 33], which is of great simplicity thus facilitates its application in clinical practice. In this study, we screened four predictors, namely multiple lesions, affected side, PLR, and NLR, by taking the intersection of LASSO and logistic regression. Subsequently, we demonstrated the model's superiority in terms of discrimination, calibration, and clinical utility. In particular, in the ROC curve analysis,
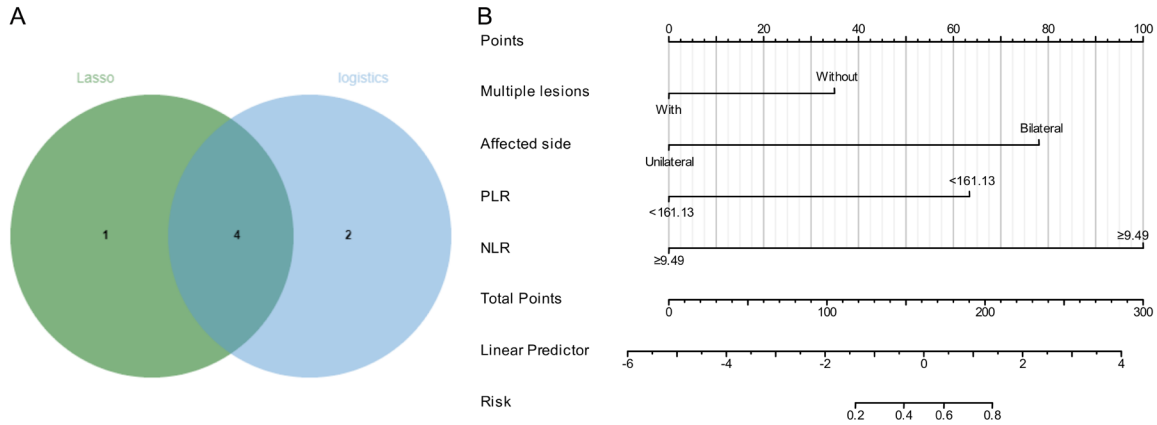
Figure 4. Common factor screening and Nomogram model establishment. A. Wayne diagram screening for common characteristic factors between logistic and LASSO regression; B. Construction of a Nomogram model.
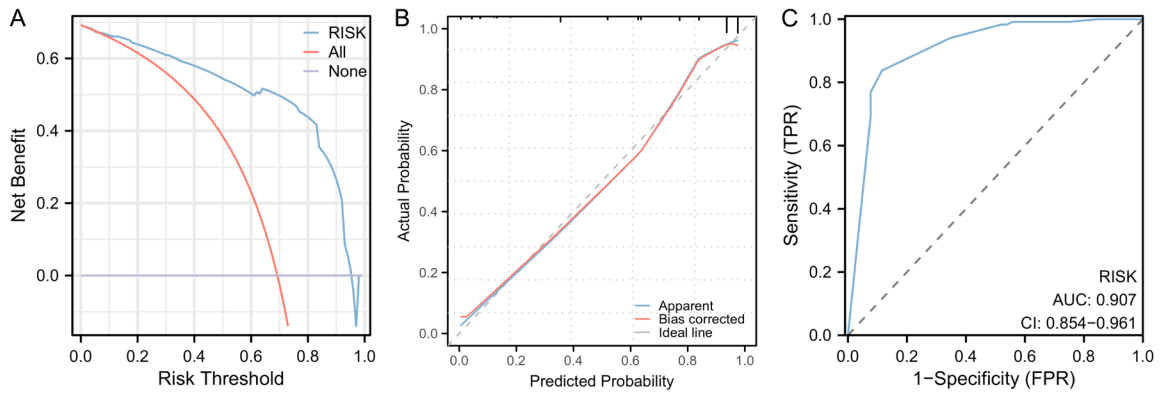

Figure 5. Evaluation of the performance of the predictive model in the training group. A. DCA of the risk of lateral cervical lymph node metastasis (LNM) in patients with thyroid carcinoma (TC); B. Calibration curve of the risk of lateral cervical LNM in patients with TC; C. ROC curve analysis of the risk of lateral cervical LNM in patients with TC.
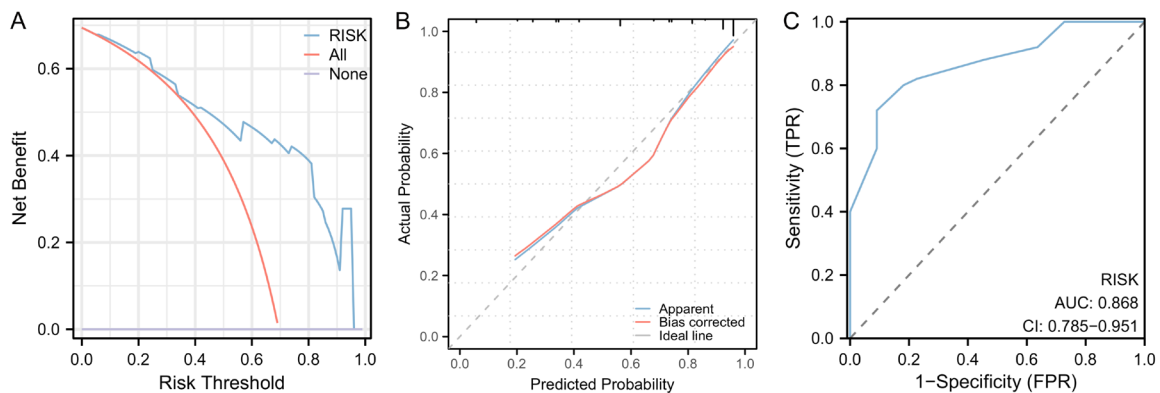

Figure 6. Effectiveness evaluation of the predictive model in the validation group. A. DCA of the risk of lateral cervical lymph node metastasis (LNM) in patients with thyroid carcinoma (TC); B. Calibration curve of the risk of lateral cervical LNM in patients with TC; C. ROC curve analysis of the risk of lateral cervical LNM in patients with TC.

the AUC values demonstrated a high accuracy of the model in predicting TC lateral neck LNM, which was subsequently confirmed in both the training and validation sets. In addition, it was

determined by Delong's test that there was no difference in the AUC between the validation set and the training set, further illustrating the predictive value of the model.

Despite the study's progress in predicting the risk of TC lateral neck LNM, several limitations remain. First, the retrospective design may lead to selection bias and information bias. Second, the small sample size limits the broad applicability of the conclusions. Third, the study was based on a single center, which diminishes the generalizability of the results. Last, the limited timeframe of the data collection does not allow for the full capture of long-term trends. To improve the accuracy, reliability, and applicability, further studies should consider a prospective design and expanded sample size from multiple centers, with extended time frame for data collection. These improvements would enable the comprehensive evaluation of long-term trends and outcomes.

Conclusion

Through comprehensive application of logistic regression and LASSO regression models, this study effectively identified key characteristic factors affecting lateral cervical LNM in TC patients, including gender, multiple lesions, affected side, and tumor diameter. These findings are not only consistent with previous research results, but also have great application value in clinical practice, especially in developing treatment strategies and surgical planning for TC. In addition, the Nomogram model we constructed demonstrates high accuracy and reliability, providing clinicians with an intuitive and simple tool to assess the risk of lateral cervical LNM in TC patients.

Acknowledgements

Disclosure of conflict of interest

None.

Address correspondence to: Haiyan Wang and Meijun Zhong, Department of Thyroid Surgery, The Second Affiliated Hospital of Nanchang University, Nanchang 330006, Jiangxi, P. R. China. Tel: +86-0791-87357518; E-mail: jzx13970010377@163.com (HYW); Zhongmeijun0523@163.com (MJZ)

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[1] Abraham PJ, Wang R, Bahl D, Bhambhvani P, Ho S, Fazendin JM, Chen H and Lindeman BM. Virtual tumor board: papillary thyroid carcinoma with nodal disease. CA Cancer J Clin 2023; 73: 555-561.

[2] Liu Q, Ma B, Song M, Sun W and Zhang H. Age-dependent changes in the prognostic advantage of papillary thyroid cancer in women: a SEER-based study. Clin Endocrinol (Oxf) 2023; 99: 342-349.

[3] Kim CA, An HR, Yoo J, Lee YM, Sung TY, Kim WG and Song DE. Morphometric analysis of lateral cervical lymph node metastasis in papillary thyroid carcinoma using digital pathology. Endocr Pathol 2024; 35: 113-121.

[4] Zhou LQ, Zeng SE, Xu JW, Lv WZ, Mei D, Tu JJ, Jiang F, Cui XW and Dietrich CF. Deep learning predicts cervical lymph node metastasis in clinically node-negative papillary thyroid carcinoma. Insights Imaging 2023; 14: 222.

[5] Kwon HK, Cheon YI, Shin SC, Sung ES, Lee JC, Kim IJ and Lee BJ. Risk factors of suprasternal lymph node metastasis in papillary thyroid carcinoma with clinical lateral cervical lymph node metastasis. Gland Surg 2021; 10: 512-520.

[6] Zhao BH, Huang ZH, Huang YC, Zhang XW, An CM, Niu LJ and Li ZJ. Preliminary study of superselective lymph node dissection in regional lateral cervical lymph node metastasis of papillary thyroid carcinoma. Zhonghua Zhong Liu Za Zhi 2021; 43: 484-489.

[7] Zhang ML, Guo LM, Li PC, Zhang JK and Guo CX. An effective method to reduce lymphatic drainage post-lateral cervical lymph node dissection of differentiated thyroid cancer: a retrospective analysis. World J Surg Oncol 2022; 20: 294.

[8] Gao J, Xin Y, Yang L, Liu Y, Tian Z and Shang X. Risk factors of skip lateral cervical lymph node metastasis in papillary thyroid carcinoma. Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 2022; 36: 528-532; 539.

[9] Feng JW, Qin AC, Ye J, Pan H, Jiang Y and Qu Z. Predictive factors for lateral lymph node metastasis and skip metastasis in papillary thyroid carcinoma. Endocr Pathol 2020; 31: 67-76.

[10] Zhao L, Wu F, Zhou T, Lu K, Jiang K, Zhang Y and Luo D. Risk factors of skip lateral cervical lymph node metastasis in papillary thyroid carcinoma: a systematic review and meta-analysis. Endocrine 2022; 75: 351-359.

[11] Tang VW. Role of pathologists in nomogram development. Pathology 2023; 55: 1048-1049.

[12] Perrier ND, Brierley JD and Tuttle RM. Differentiated and anaplastic thyroid carcinoma: major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer J Clin 2018; 68: 55-63.

[13] Koca CF, Yıldırım IO, Cicek MT and Aslan M. Successful localization of abnormal parathyroid tissue with ultrasound-guided methylene blue dye injection before surgery for metastatic or recurrent thyroid cancers and parathyroid adenomas. Am J Otolaryngol 2023; 44: 103678.

[14] Zhang B, Wu W, Liu J, Liang Z and Zong L. Comparison of treatment and prognosis between follicular variant papillary thyroid carcinoma and classical papillary thyroid carcinoma. Horm Metab Res 2023; 55: 855-868.

[15] Seo DH, Lee SG, Lee HY, Jeong S, Park S, Lee J and Jo YS. Lymph node metastasis-dependent molecular classification in papillary thyroid carcinoma defines aggressive metastatic outgrowth. Clin Transl Med 2023; 13: e1211.

[16] Li X and Cheng R. TPO as an indicator of lymph node metastasis and recurrence in papillary thyroid carcinoma. Sci Rep 2023; 13: 10848.

[17] Kim SK, Park I, Woo JW, Lee JH, Choe JH, Kim JH and Kim JS. Predictive factors for lymph node metastasis in papillary thyroid microcarcinoma. Ann Surg Oncol 2016; 23: 2866-2873.

[18] Ito Y, Higashiyama T, Takamura Y, Miya A, Kobayashi K, Matsuzuka F, Kuma K and Miyauchi A. Risk factors for recurrence to the lymph node in papillary thyroid carcinoma patients without preoperatively detectable lateral node metastasis: validity of prophylactic modified radical neck dissection. World J Surg 2007; 31: 2085-2091.

[19] So YK, Kim MJ, Kim S and Son YI. Lateral lymph node metastasis in papillary thyroid carcinoma: a systematic review and meta-analysis for prevalence, risk factors, and location. Int J Surg 2018; 50: 94-103.

[20] Zhao W, Chen S, Hou X, Liao Q, Chen G and Zhao Y. Predictive factors of lateral lymph node metastasis in papillary thyroid microcarcinoma. Pathol Oncol Res 2019; 25: 1245-1251.

[21] Zhao ZL, Dong G, Wang SR, Liu Y, He JF, Shi LL, Guo JQ, Wang ZH, Cong ZB, Liu LH, Yang BB, Qu CP, Wei Y, Peng LL, Li Y, Lu NC, Wu J and Yu MA. Efficacy and safety of microwave ablation for the treatment of multifocal versus unifocal T1N0M0 papillary thyroid carcinoma: a propensity-matched multicentre retrospective study. Eur Radiol 2023; 33: 8727-8735.

[22] Offi C, Misso C, Antonelli G, Esposito MG, Brancaccio U and Spiezia S. Laser ablation treatment of recurrent lymph node metastases from papillary thyroid carcinoma. J Clin Med 2021; 10: 5295.

[23] Wang Z, Chang Q, Zhang H, Du G, Li S, Liu Y, Sun H and Yin D. A clinical predictive model of central lymph node metastases in papillary thyroid carcinoma. Front Endocrinol (Lausanne) 2022; 13: 856278.

[24] Wang W, Su X, He K, Wang Y, Wang H, Wang H, Zhao Y, Zhao W, Zarnegar R, Fahey TJ 3rd, Teng X and Teng L. Comparison of the clinicopathologic features and prognosis of bilateral versus unilateral multifocal papillary thyroid cancer: an updated study with more than 2000 consecutive patients. Cancer 2016; 122: 198-206.

[25] Zhang T, He L, Wang Z, Dong W, Sun W, Zhang P and Zhang H. The differences between multifocal and unifocal papillary thyroid carcinoma in unilateral lobe: a meta-analysis. Front Oncol 2021; 11: 657237.

[26] Patron V, Hitier M, Bedfert C, Métreau A, Dugué A and Jegoux F. Predictive factors for lateral occult lymph node metastasis in papillary thyroid carcinoma. Eur Arch Otorhinolaryngol 2013; 270: 2095-2100.

[27] Li C, Li J, Li S, Zhao Y, Liu G, Du R, Dionigi G, Liang N and Sun H. Prognostic significance of inflammatory markers LMR, PLR, MPV, FIB in intermediate-and high-risk papillary thyroid carcinoma. Front Endocrinol (Lausanne) 2022; 13: 984157.

[28] Ozmen S, Timur O, Calik I, Altinkaynak K, Simsek E, Gozcu H, Arslan A and Carlioglu A. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) may be superior to C-reactive protein (CRP) for predicting the occurrence of differentiated thyroid cancer. Endocr Regul 2017; 51: 131-136.

[29] Song CY, Meng YL, Liu B, Yan L, Shang PZ, Jia ZF, Jiang YB and Meng FY. Correlation analysis of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio and central cervical lymph node metastasis of papillary thyroid microcarcinoma. Zhonghua Zhong Liu Za Zhi 2021; 43: 944-948.

[30] Huang Y, Liu Y, Mo G, Zhou T, Hou Q, Shi C, Jiang Q and Lv Y. Inflammation markers have important value in predicting relapse in patients with papillary thyroid carcinoma: a long-term follow-up retrospective study. Cancer Control 2022; 29: 10732748221115236.

[31] Kang NL, Gao YH, Lin MX, Wu LY, Ye XY, Lin HM, Ruan QF, Lin S, Liu HH, Huang LL, Jiang JJ, Liu YR, Zheng Q, Mao RC and Zeng DW. Development a novel nomogram model for predicting significant hepatic histological changes in chronic hepatitis B virus carriers. J Med Virol 2023; 95: e28943.

[32] Liu WC, Li MP, Hong WY, Zhong YX, Sun BL, Huang SH, Liu ZL and Liu JM. A practical dynamic nomogram model for predicting bone metastasis in patients with thyroid cancer. Front Endocrinol (Lausanne) 2023; 14: 1142796.

[33] Zhao J, Wang L, Zhang Y, He H, Zhao P and Luo Y. Predictors of metastasis in cervical indeterminate lymph nodes after thyroid cancer ablation by long-term ultrasound follow-up. Int J Hyperthermia 2023; 40: 2207792.