

Risk Factors for Cervical Lymph Node Metastasis and a Predictive Model for Lateral Cervical Lymph Node Metastasis in Papillary Thyroid Carcinoma

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Abstract

Background: Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy. Although the overall prognosis is favorable, cervical lymph node metastasis (LNM) occurs in a substantial proportion of patients and affects both surgical planning and clinical outcomes. Preoperative ultrasonography remains limited in sensitivity, particularly for occult metastases, and existing predictive tools rarely distinguish between central and lateral compartments. A dedicated model for lateral cervical lymph node metastasis (LC-LNM) is therefore needed.

Methods: This single-center retrospective study enrolled 450 patients with newly diagnosed PTC who underwent thyroid surgery between January 2022 and December 2024. Clinicopathological characteristics, BRAF V600E mutation status, preoperative ultrasound features, and surgical data were collected. Variables associated with central lymph node metastasis (CLNM) and LC-LNM were identified by univariate analysis and entered into multivariable binary logistic regression. Model performance was assessed by receiver operating characteristic (ROC) curve analysis, Hosmer–Lemeshow goodness-of-fit testing, calibration curves, and decision curve analysis (DCA).

Results: Tumor maximum diameter, BRAF V600E mutation, calcification, and male sex were significantly associated with CLNM. For LC-LNM, tumor diameter, BRAF V600E mutation, calcification, a taller-than-wide shape (aspect ratio >1), tumor laterality (unilateral vs. bilateral), and an indistinct tumor margin were identified as independent correlates. In the resulting LC-LNM model, tumor diameter, BRAF V600E mutation, calcification, and aspect ratio >1 were positive predictors, whereas unilateral lesions and a clear tumor margin were negative predictors. The model showed good fit (Hosmer–Lemeshow $P = 0.526$) and an AUC of 0.863. Calibration was high (MAE = 0.016; MSE < 0.001; 90th percentile absolute error = 0.055), and DCA indicated net clinical benefit across a threshold probability range of 0.05–0.65.

Conclusion: LNM in PTC is associated with a distinct set of clinicopathological factors in the central and lateral compartments. The proposed LC-LNM model integrates readily available preoperative clinical, ultrasound, and molecular variables and may serve as a quantitative adjunct to guide individualized decision-making regarding lateral neck dissection.

Introduction

Thyroid cancer is the most common endocrine malignancy and one of the most frequently diagnosed head and neck cancers, with papillary thyroid carcinoma (PTC) accounting for the majority of cases. Its global incidence has risen markedly over the past three decades^[1], an increase largely attributable to the widespread use of high-resolution ultrasound and fine-needle aspiration biopsy (FNAB), together with expanded health screening, which together facilitate the detection of small, low-risk tumors^[2].

Although PTC typically follows an indolent course, a considerable proportion of patients develop lymph node metastasis (LNM), most often involving the central and lateral cervical compartments^[2–4]. Accurate compartment-specific assessment of nodal involvement is essential for prognostic

stratification and for tailoring surgical extent^[5, 6]. While the increased detection rate of small thyroid nodules on high-resolution ultrasound has raised global concerns regarding overdiagnosis and overtreatment—such as unnecessary total thyroidectomy and prophylactic lymph node dissection^[2]—current imaging modalities remain imperfect in detecting occult metastases preoperatively^[4, 7].

Multiple clinicopathological features, including age, BRAF V600E mutation status, tumor location, and tumor size, have been linked to LNM in PTC^[8, 9]. While preoperative ultrasound can capture many of these features, the diagnostic performance of any single variable is insufficient to reliably predict LNM. Integrated multivariable models that combine imaging, clinical, and molecular variables are therefore required.

Previous predictive models for LNM in PTC^[10] have most often targeted overall nodal status and rarely distinguish between the central and lateral compartments. Models specifically addressing LC-LNM are scarce and have often omitted integration of preoperative ultrasound features with clinical and molecular parameters, which limits their practical utility for compartment-specific surgical planning. The aims of the present study were therefore twofold: (i) to identify independent risk factors associated with CLNM and LC-LNM in PTC; and (ii) to develop a compartment-specific predictive model for LC-LNM that combines preoperative ultrasound features, clinical variables, and BRAF V600E status, in order to support individualized decision-making regarding lateral neck dissection.

Methods

Study design

This was a single-center retrospective study. Data were collected from patients treated at the Department of Thyroid and Breast Surgery of Shenzhen Second People's Hospital, where the corresponding author and co-authors were conducting clinical work and postgraduate training during the study period. Both Shenzhen Second People's Hospital and Shenzhen University General Hospital are affiliated teaching hospitals of Shenzhen University, and this study was conducted as part of a collaborative clinical research program between the two institutions. The study protocol was reviewed and approved by the Ethics Committee of Shenzhen Second People's Hospital (Approval No. 2025-581-01PJ), which served as the data custodian. Given the retrospective design and the use of de-identified data, the Ethics Committee waived the requirement for informed consent. The study period spanned 1 January 2022 to 31 December 2024, during which eligible patients underwent thyroid surgery. Following ethics approval, the authors accessed the de-identified clinical data from the hospital electronic medical record system for research purposes between 1 November 2025 and 31 December 2025. The authors did not have access to information that could identify individual participants during or after data collection. Enrolled patients were categorized according to the presence or absence of central and lateral cervical lymph node metastases.

Patient selection

Patients with newly diagnosed PTC who underwent thyroid surgery at the Department of Thyroid and Breast Surgery of Shenzhen Second People's Hospital between 1 January 2022 and 31 December 2024 were screened. Of 3,380 patients initially assessed, 450 met the eligibility criteria and were included in the final analysis. Inclusion criteria: (i) age 18–70 years, first diagnosis of PTC, and definitive surgical treatment in accordance with the 2025 China Integrated Oncology Guidelines for Thyroid Cancer; (ii) clearly defined and standardized central and/or lateral lymph node dissection; and (iii) complete preoperative ultrasound and postoperative pathology data, including reliable BRAF V600E mutation testing. Exclusion criteria: (i) severe comorbidity of other major organs, a history of other malignancies, or a family history of PTC in first-degree relatives at diagnosis; (ii) more than two primary tumor foci; (iii) poor-quality or missing imaging data; (iv) postoperative lymph node specimens without identifiable lymphoid tissue; (v) discordant BRAF V600E results between preoperative FNAB and postoperative pathology; (vi) actual treatment inconsistent with guideline recommendations; and (vii) missing key clinical data (Fig. 1).

Histopathology

All surgical specimens were independently reviewed by two or more pathologists with at least 10 years of experience in thyroid pathology to confirm the diagnosis of PTC and to determine BRAF V600E mutation status. The BRAF V600E mutation was detected using a commercial assay kit (Amoy Diagnostics, Xiamen, China).

Clinical data

Demographic information, including sex and age, was extracted from the hospital electronic medical record system. The surgical strategy for each patient was independently determined by two senior thyroid surgeons (associate chief physician or above) in accordance with the 2025 China Integrated Oncology Guidelines for Thyroid Cancer. Patients whose actual treatment deviated from guideline recommendations were excluded to ensure that all included patients received guideline-concordant surgery.

Ultrasound data

All preoperative ultrasound findings were independently re-evaluated by two senior sonographers (associate chief physician or above) to ensure accuracy and consistency. The ultrasound variables assessed included maximum tumor diameter, lesion distribution (unilateral vs. bilateral), margin characteristics (clear vs. indistinct), presence of calcifications, a taller-than-wide shape defined as an aspect ratio > 1 (longitudinal/transverse diameter on a transverse plane), and coexisting thyroiditis.

Statistical analysis

Statistical analyses were performed separately for CLNM and LC-LNM. Continuous variables were compared using the Mann–Whitney U test and categorical variables using the chi-square test. Variables with statistical significance in univariate analysis were entered into multivariable binary logistic regression. Model fit was evaluated by the Hosmer–Lemeshow test, and diagnostic performance was quantified by ROC curve analysis and area under the curve (AUC). Calibration curves and decision curve analysis (DCA) were generated to assess calibration and clinical utility. Coefficients of significant predictors were extracted using the R functions `coef`, `cat`, and `sprintf` to construct the LC-LNM prediction formula, and curves depicting sensitivity and specificity across threshold values were plotted. All analyses were conducted in R version 4.5.0, and figures were produced in R version 4.5.0 and GraphPad Prism version 10.4.2. A two-sided $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics

Baseline characteristics of the study population are summarized in Table 1. In the non-CLNM group ($n = 209$), median age was 40 years (IQR 34–51), and 32 patients (15.3%) were male; in the CLNM group ($n = 241$), median age was 36 years (IQR 30–45), and 80 patients (33.1%) were male. In the non-LC-LNM group ($n = 389$), median age was 38 years (IQR 32–49), and 88 patients (22.6%) were male; in the LC-LNM group ($n = 61$), median age was 35 years (IQR 32–40), and 24 patients (39.3%) were male.

Table 1
Baseline characteristics of the study population.

Classify	non-CLNM (n = 209)	CLNM (n = 241)	P	non-LC- LNM (n = 389)	LC-LNM (n = 61)	P
Male, n (%)	32 (15.3)	80 (33.1)	< 0.001*	88 (22.6)	24 (39.3)	0.007*
Age (years)	40 (34–51)	36 (30–45)	< 0.001*	38 (32–49)	35 (32–40)	0.015*
Diameter (mm)	7 (5–9)	11 (7–15)	< 0.001*	8 (6–12)	15 (11–20)	< 0.001*
Clear tumor boundary, n (%)	75 (35.9)	72 (29.9)	0.191	135 (34.7)	12 (19.7)	0.019*
Coexistent thyroiditis, n (%)	62 (29.7)	61 (25.3)	0.340	103 (26.5)	20 (32.8)	0.354
BRAF V600E mutation, n (%)	149 (71.3)	214 (88.8)	< 0.001*	307 (78.9)	56 (91.8)	< 0.001*
Calcification present, n (%)	104 (49.8)	179 (74.3)	< 0.001*	233 (59.9)	50 (82.0)	< 0.001*
Aspect ratio > 1, n (%)	132 (63.2)	149 (61.8)	0.845	234 (60.2)	47 (77.0)	0.011*
Unilateral lesion, n (%)	195 (93.3)	196 (81.3)	< 0.001*	352 (90.5)	39 (63.9)	< 0.001*
<i>Data are presented as n (%) for categorical variables and median (Q1–Q3) for continuous variables (non-normal distribution). Mann–Whitney U test for continuous variables; chi-square test for categorical variables. CLNM, central lymph node metastasis; LC-LNM, lateral cervical lymph node metastasis. *P < 0.05.</i>						

Association of BRAF V600E and clinicopathological factors with CLNM

Univariate analysis

Kolmogorov–Smirnov testing indicated that age and tumor maximum diameter were non-normally distributed, and the Mann–Whitney U test was therefore used. Compared with the non-CLNM group, patients with CLNM were younger (median 36 vs. 40 years, $P < 0.001$) and had larger tumors (median 11 vs. 7 mm, $P < 0.001$). Chi-square analysis showed higher proportions of males (33.1% vs. 15.3%, $P < 0.001$), bilateral lesions (18.7% vs. 6.7%, $P < 0.001$), BRAF V600E mutation (88.8% vs. 71.3%, $P < 0.001$), and calcification (74.3% vs. 49.8%, $P < 0.001$) in the CLNM group. Tumor margin clarity ($P = 0.191$), aspect ratio > 1 ($P = 0.845$), and coexisting thyroiditis ($P = 0.340$) did not differ significantly between groups (Table 1).

Multivariable logistic regression

Variables identified in univariate analysis (age, tumor diameter, male sex, tumor laterality, BRAF V600E, and calcification) were entered into multivariable logistic regression (Table 2; Fig. 2). Male sex ($P = 0.006$), larger tumor diameter ($P < 0.001$), BRAF V600E mutation ($P < 0.001$), and calcification ($P < 0.001$) were independently associated with CLNM. Although age ($P = 0.027$) and tumor laterality ($P = 0.011$) reached statistical significance, age showed an OR close to unity ($OR = 0.978$), indicating a minimal per-year effect, and tumor laterality contributed only marginally to ROC performance in preliminary modelling; these two variables were therefore excluded from the final predictive model. The resulting four-variable model showed acceptable fit (Hosmer–Lemeshow $P = 0.260$).

Table 2
Multivariable logistic regression of factors associated with CLNM in PTC.

<i>Classify</i>	<i>B</i>	<i>SE</i>	<i>Wald</i>	<i>P</i>	<i>OR</i>	<i>95% CI</i>
Male sex	0.723	0.264	7.477	0.006*	2.060	1.227–3.457
Age	−0.022	0.010	4.868	0.027*	0.978	0.959–0.998
Diameter	1.408	0.242	33.762	< 0.001*	4.087	2.542–6.572
Unilateral lesion	−0.896	0.352	6.480	0.011*	0.408	0.205–0.814
BRAF V600E	1.433	0.299	23.024	< 0.001*	4.191	2.334–7.524
Calcification	0.913	0.233	15.310	< 0.001*	2.491	1.577–3.935
<i>B, regression coefficient; SE, standard error; Wald, Wald statistic. *$P < 0.05$.</i>						

Diagnostic performance and combined model

Individual ROC analysis of the four predictors (Table 3) showed that tumor diameter had the highest discriminative ability ($AUC = 0.700$; 95% CI, 0.625–0.748), followed by calcification ($AUC = 0.623$; 95% CI, 0.570–0.675), male sex ($AUC = 0.589$), and BRAF V600E ($AUC = 0.588$), all with $P < 0.01$. The combined four-variable model (Fig. 3) yielded an AUC of 0.758 (95% CI, 0.701–0.815), indicating moderate predictive capacity.

Table 3
Diagnostic performance of individual predictors for CLNM by ROC analysis.

<i>Classify</i>	<i>AUC</i>	<i>SE</i>	<i>P</i>	<i>95% CI</i>
Male sex	0.589	0.027	0.001*	0.537–0.642
Diameter	0.700	0.025	< 0.001*	0.625–0.748
BRAF V600E	0.588	0.027	0.001*	0.534–0.641
Calcification	0.623	0.027	< 0.001*	0.570–0.675
* <i>P</i> < 0.05.				

Although the CLNM model remains open to further optimization, routine prophylactic central neck dissection is widely performed in clinical practice, and current guidelines set stringent criteria for omitting this procedure^[11]. In contrast, there is no equivalent standard indication for prophylactic lateral neck dissection, making accurate preoperative prediction of LC-LNM of greater direct clinical value. Subsequent analyses therefore focus on developing a compartment-specific predictive model for LC-LNM.

LC-LNM: associated factors and predictive model development

Univariate analysis

Age and tumor diameter again deviated from normality and were analyzed by the Mann–Whitney U test. Compared with the non-LC-LNM group, the LC-LNM group was younger (median 35 vs. 38 years, $P = 0.015$) and had larger tumors (median 15 vs. 8 mm, $P < 0.001$). In chi-square analysis, the LC-LNM group showed higher proportions of males (39.3% vs. 22.6%, $P = 0.007$), indistinct tumor margins (correspondingly, clear margins were less frequent: 19.7% vs. 34.7%, $P = 0.019$), BRAF V600E mutation (91.8% vs. 78.9%, $P < 0.001$), calcification (82.0% vs. 59.9%, $P < 0.001$), aspect ratio > 1 (77.0% vs. 60.2%, $P = 0.011$), and bilateral lesions (36.1% vs. 9.5%, $P < 0.001$). Coexisting thyroiditis did not differ significantly ($P = 0.354$). Age, tumor diameter, male sex, tumor margin, BRAF V600E, calcification, aspect ratio, and tumor laterality were therefore entered into multivariable analysis (Table 1).

Multivariable logistic regression

In multivariable binary logistic regression, tumor diameter (OR = 3.103; 95% CI, 1.983–4.858; $P < 0.001$) and tumor laterality, with unilateral lesions being protective (OR = 0.202; 95% CI, 0.099–0.413; $P < 0.001$), were the strongest predictors. BRAF V600E mutation (OR = 3.397; 95% CI, 1.187–9.728; $P = 0.023$), calcification (OR = 2.668; 95% CI, 1.197–5.948; $P = 0.016$), aspect ratio > 1 (OR = 2.833; 95% CI, 1.344–5.972; $P = 0.006$), and a clear tumor margin, which was associated with lower risk (OR = 0.452; 95% CI, 0.206–0.993; $P = 0.048$), were also independently predictive. Sex ($P = 0.176$) and age ($P = 0.208$) did not

reach significance and were excluded from the final model (Table 4). The resulting six-variable model demonstrated good fit (Hosmer–Lemeshow $P = 0.526$).

Table 4
Multivariable logistic regression of factors associated with LC-LNM in PTC.

<i>Classify</i>	<i>B</i>	<i>SE</i>	<i>Wald</i>	<i>P</i>	<i>OR</i>	<i>95% CI</i>
Male sex	0.454	0.336	1.828	0.176	1.575	0.805–3.045
Age	−0.021	0.017	1.587	0.208	0.979	0.947–1.012
Diameter	1.133	0.229	24.539	< 0.001**	3.103	1.983–4.858
Unilateral lesion	−1.598	0.363	19.322	< 0.001**	0.202	0.099–0.413
BRAF V600E	1.223	0.537	5.192	0.023*	3.397	1.187–9.728
Calcification	0.981	0.409	5.758	0.016*	2.668	1.197–5.948
Aspect ratio > 1	1.041	0.380	7.491	0.006**	2.833	1.344–5.972
Clear tumor boundary	−0.793	0.401	3.909	0.048*	0.452	0.206–0.993
<i>LC-LNM, lateral cervical lymph node metastasis; PTC, papillary thyroid carcinoma; B, regression coefficient; SE, standard error. *P < 0.05; **P < 0.01.</i>						

Model performance and clinical utility

ROC curve analysis of the LC-LNM model (Fig. 4) yielded an AUC of 0.863, indicating good discrimination. The calibration curve (Fig. 5) closely approximated the ideal reference line, suggesting strong agreement between predicted and observed probabilities. Quantitative calibration metrics (Table 5) were MAE = 0.016, MSE < 0.001, and 90th percentile absolute error = 0.055. DCA (Fig. 6) showed that the model produced greater net clinical benefit than the "treat-all" and "treat-none" strategies across threshold probabilities ranging from 0.05 to 0.65.

Table 5
Quantitative calibration metrics of the LC-LNM predictive model.

<i>Metric</i>	<i>Value</i>	<i>Interpretation</i>
MAE	0.016	Mean deviation between predicted and observed probabilities ≈ 1.6%
MSE	< 0.001	Low MSE indicates high predictive accuracy
90th percentile absolute error	0.055	90% of prediction errors ≤ 5.5%
<i>MAE, mean absolute error; MSE, mean squared error.</i>		

LC-LNM prediction formula and optimal threshold

Coefficients of significant predictors were extracted to construct the following logit equation:

$$\text{logit}(p) = 0.167 \times \text{Diameter} + 1.041 \times \text{Calcification} + 1.392 \times \text{BRAF mutation} + 1.063 \times \text{Aspect ratio} + (-1.650) \times \text{Unilateral lesion} + (-0.884) \times \text{Clear tumor boundary} - 5.059$$

The individual predicted probability was calculated as $P = 1 / (1 + e^{-\text{logit}(p)})$. The Youden index identified 0.14 as the optimal threshold, at which sensitivity was 0.80 and specificity 0.81, corresponding to a false-negative rate of 20% and a false-positive rate of 19% (Fig. 7). At this threshold, the model achieves balanced discrimination and is suitable for standardized decision-making in concordance with current clinical guidelines. Probabilities below 0.14 favor specificity (reducing false positives), whereas probabilities above 0.14 favor sensitivity (reducing false negatives) (Table 6).

Table 6
Sensitivity, specificity, and clinical decision-making across threshold values.

Region	Sensitivity	Specificity	Clinical decision
Left of optimal threshold	↑	↓	Screening (reduce missed diagnoses)
Right of optimal threshold	↓	↑	Confirmation (reduce false positives)
Optimal threshold (P = 0.14)	Balanced (0.80)	Balanced (0.81)	Standardized guideline-based decision

Discussion

In this single-center study of 450 patients with PTC, we identified distinct sets of clinicopathological factors associated with CLNM and LC-LNM and developed an LC-LNM predictive model combining routinely available clinical, ultrasound, and molecular variables. Tumor diameter, BRAF V600E mutation, calcification, and male sex were associated with CLNM, whereas LC-LNM was additionally related to an aspect ratio > 1, bilateral lesions, and an indistinct tumor margin. The six-variable LC-LNM model demonstrated good calibration (Hosmer–Lemeshow P = 0.526), strong discrimination (AUC = 0.863), and net clinical benefit across threshold probabilities of 0.05–0.65 by DCA.

At the optimal probability threshold of 0.14, sensitivity and specificity were balanced (0.80 and 0.81, respectively). In clinical practice, the model is intended to complement—rather than replace—preoperative ultrasound and FNAB. When the predicted probability exceeds 0.14, aggressive evaluation of suspicious lateral cervical nodes, including FNAB, is warranted to minimize missed metastases; when the predicted probability is 0.14 or below, close observation with selective reassessment may be appropriate, particularly when imaging and clinical findings are not overtly suspicious. In both scenarios, the final surgical decision should incorporate physician judgment and patient preference after disclosure of the individual risk estimate (Fig. 8).

Our findings are broadly consistent with prior work. BRAF V600E has been repeatedly linked to LNM in PTC, with reported interactions with obesity, hypertension, tumor size, and calcification^[12]. Zhang et al. identified tumor maximum diameter, extrathyroidal extension, and CLNM as independent risk factors for LC-LNM, with tumor diameter alone achieving an AUC of 0.639^[13]. Our model, which integrates multiple variables, achieved substantially higher discrimination (AUC = 0.863) without requiring advanced imaging. We did not, however, include variables such as hypertension, smoking history, or CLNM status, and these may further refine future compartment-specific models.

More sophisticated approaches have also shown promise. Contrast-enhanced ultrasound improves the characterization of suspicious lymph nodes compared with conventional ultrasound^[14], and radiomics-based models combining multimodal ultrasound features with clinical variables have achieved AUCs of 0.841–0.883^[15]. Deep learning integrated with ultrasound features—such as nodal multifocality, location, and microcalcifications—has yielded AUCs of 0.812–0.829^[16], and artificial intelligence applied to ultrasound image analysis has further supported these findings^[17]. However, most such models do not distinguish between central and lateral compartments. Our model offers comparable discrimination for LC-LNM while relying on variables that are routinely obtained in standard preoperative workup, which favors generalizability and ease of clinical deployment.

Current guidelines recommend therapeutic lateral neck dissection for biopsy-confirmed N1b disease^[11, 18]; however, preoperative assessment relies heavily on ultrasound and FNAB, both of which may yield false negatives, particularly for small or partially cystic nodes. By integrating BRAF V600E status, tumor size, calcification, and aspect ratio with laterality and margin characteristics, the present model provides a quantitative adjunct that may reduce both under- and over-treatment. Importantly, the model uses data that are available at the point of preoperative decision-making and does not require advanced imaging or artificial intelligence infrastructure.

This study has several limitations. First, it is a single-center retrospective analysis, which introduces potential selection and information bias and limits generalizability; external validation in multicenter prospective cohorts is required. Second, although ultrasound images were independently reviewed and BRAF V600E testing followed standardized protocols, interpretation of small or borderline lesions remains challenging, and some diagnostic uncertainty cannot be fully excluded. Third, postoperative follow-up data were not included, precluding evaluation of the model's prognostic performance in terms of recurrence and survival. Future work incorporating longitudinal outcomes, additional variables such as CLNM status, and advanced imaging or deep learning features may further improve predictive performance.

In conclusion, we developed and internally evaluated a six-variable predictive model for LC-LNM in PTC that demonstrated good calibration and discrimination. By providing an individualized quantitative estimate of LC-LNM risk based on routinely available preoperative variables, the model may serve as a useful adjunct to existing risk stratification and inform decisions regarding selective lateral neck dissection, pending external validation.

Abbreviations

Thyroid carcinoma (PTC)

Lymph node metastasis (LNM)

Lateral cervical lymph node metastasis (LC-LNM)

Central lymph node metastasis (CLNM)

Receiver operating characteristic (ROC)

Decision curve analysis (DCA).

Fine-needle aspiration biopsy (FNAB)

Declarations

Ethics approval and consent to participate

This retrospective case-control study used only archived medical records from previous clinical practice and did not involve any prospective intervention on human participants. No personally identifiable information was collected. The study protocol was approved by the Ethics Committee of The Second People's Hospital of Shenzhen (Approval No. 2025-581-01PJ), which granted a waiver of informed consent.

All patient data were strictly confidential and accessible only to the research team. The results may be presented at academic conferences or published in journals, but no commercial interests are involved, and personal privacy is fully protected. This study did not use medical records or specimens that patients had previously explicitly refused to allow for research purposes.

This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and the relevant regulations of China.

Consent for publication

Not applicable. This manuscript does not contain any individual person's data in any form (including individual details, images, or videos). All authors have reviewed the final manuscript and approve its submission and publication.

Availability of data and materials

Due to ethical and privacy restrictions, the data that support the findings of this study are not publicly available. Data may be available from the corresponding author upon reasonable request and with institutional ethics approval.

Competing interests

The authors declare no competing interests.

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Author contributions

Peng Gong and Peng Liu was involved in funding acquisition and research supervision. Jinhui Zha and Yonghao Zhong were responsible for sample collection , drafted the manuscript and experiment execution. Shun Zeng and Yunqiu Dong carried out data analysis and visualization. All authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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Figures

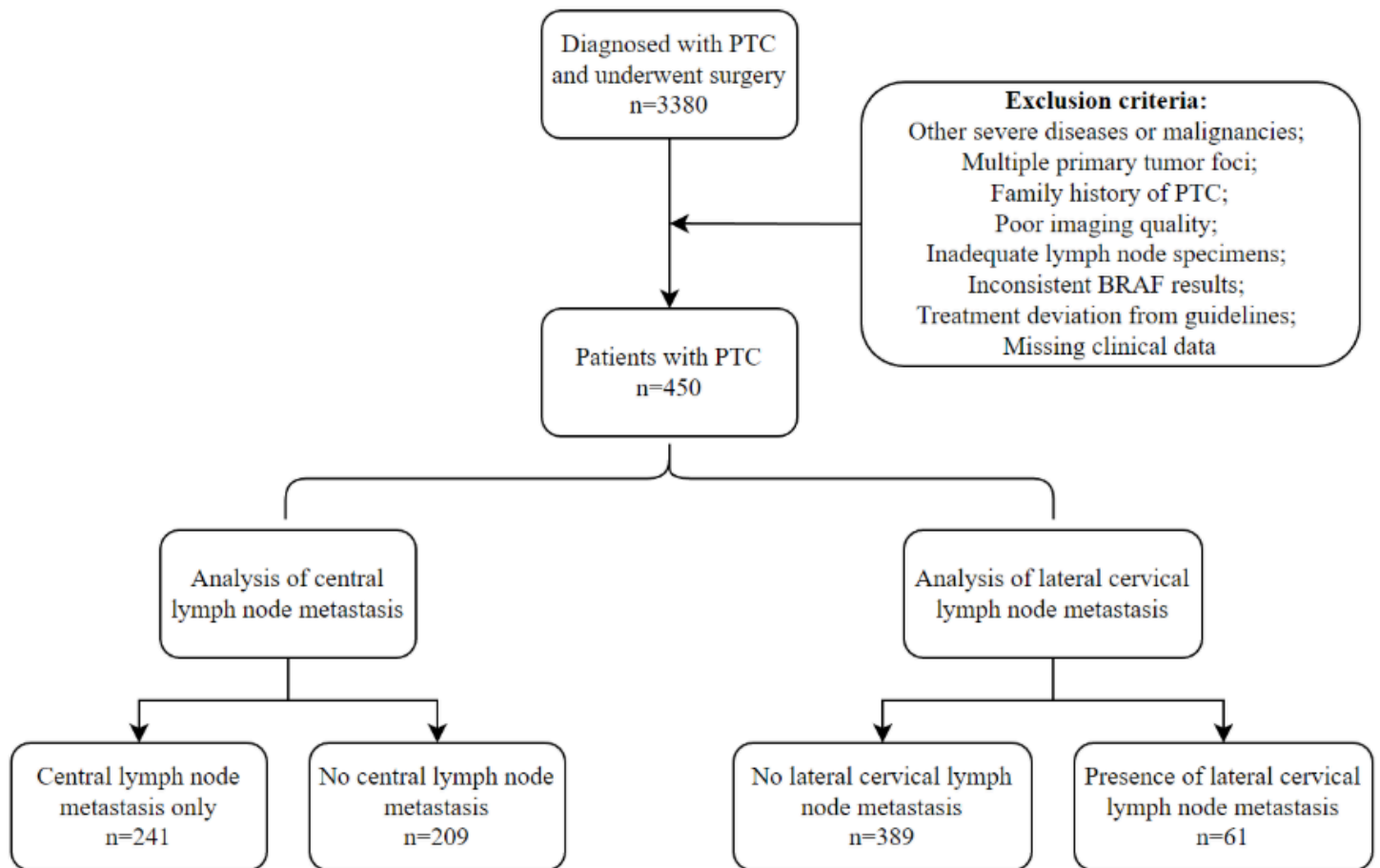


Figure 1

Flowchart of patient enrollment and exclusion.

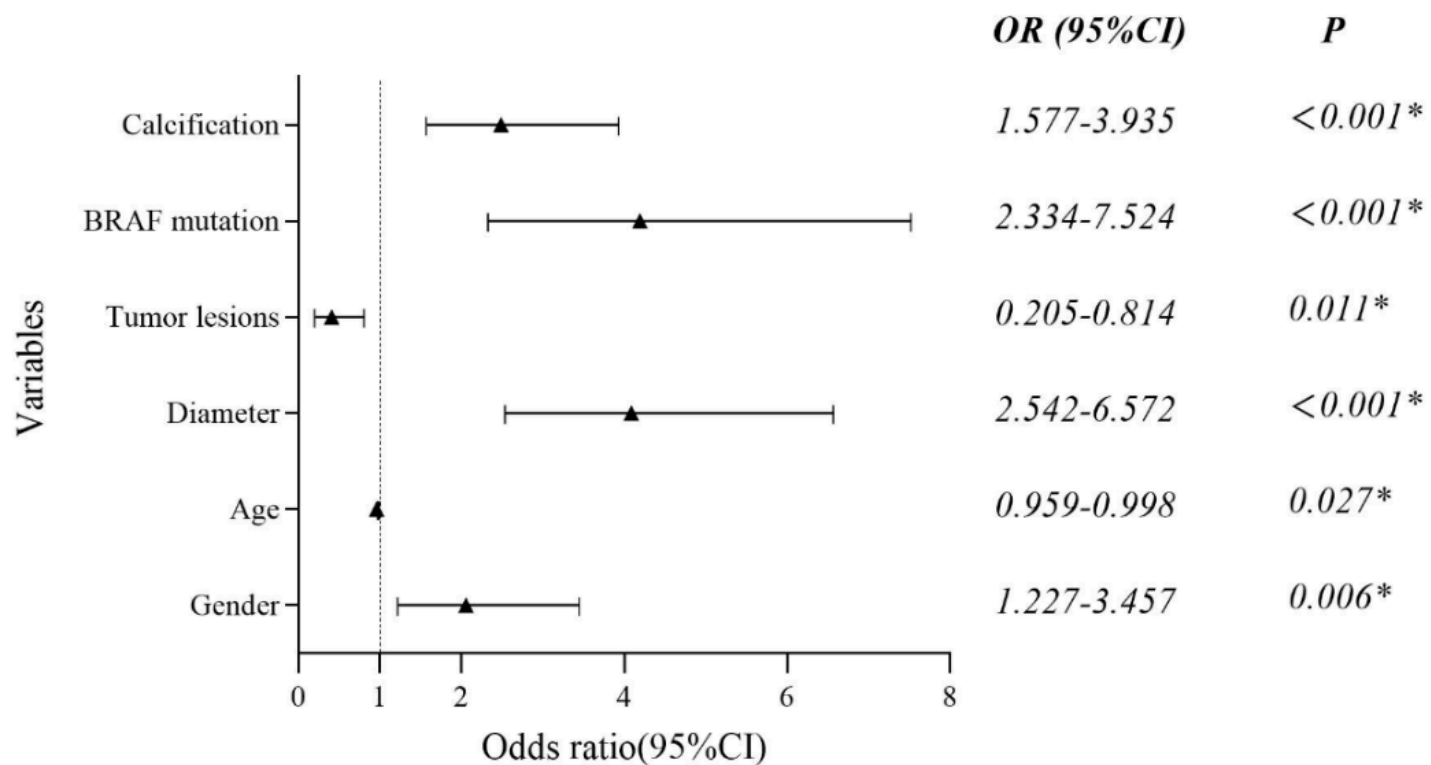


Figure 2

Forest plot of the association between BRAF V600E mutation, tumor diameter, male sex, and calcification with CLNM. *Indicates statistical significance.

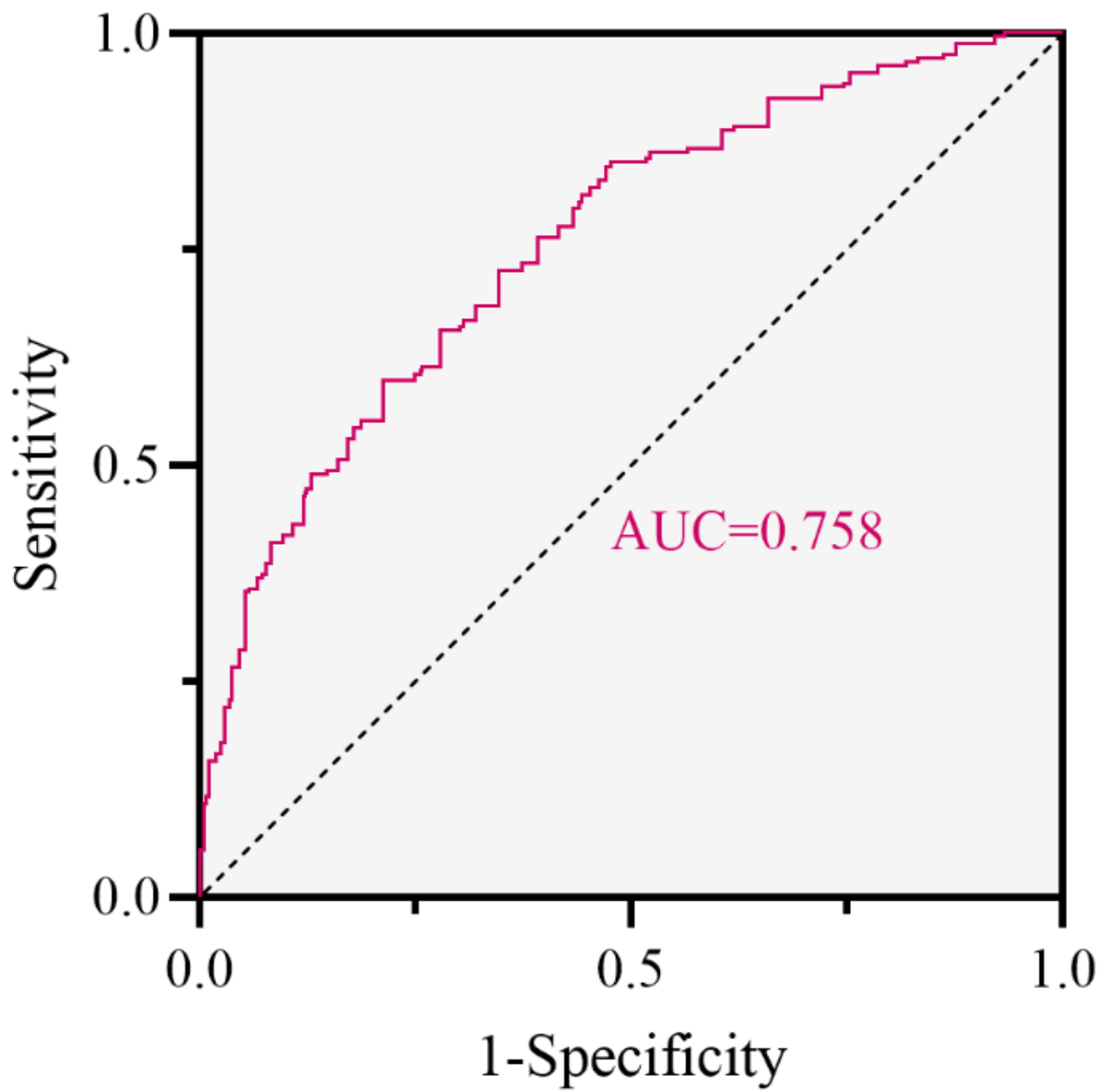


Figure 3

ROC curve of the combined multivariable predictive model for CLNM constructed using multivariate logistic regression.

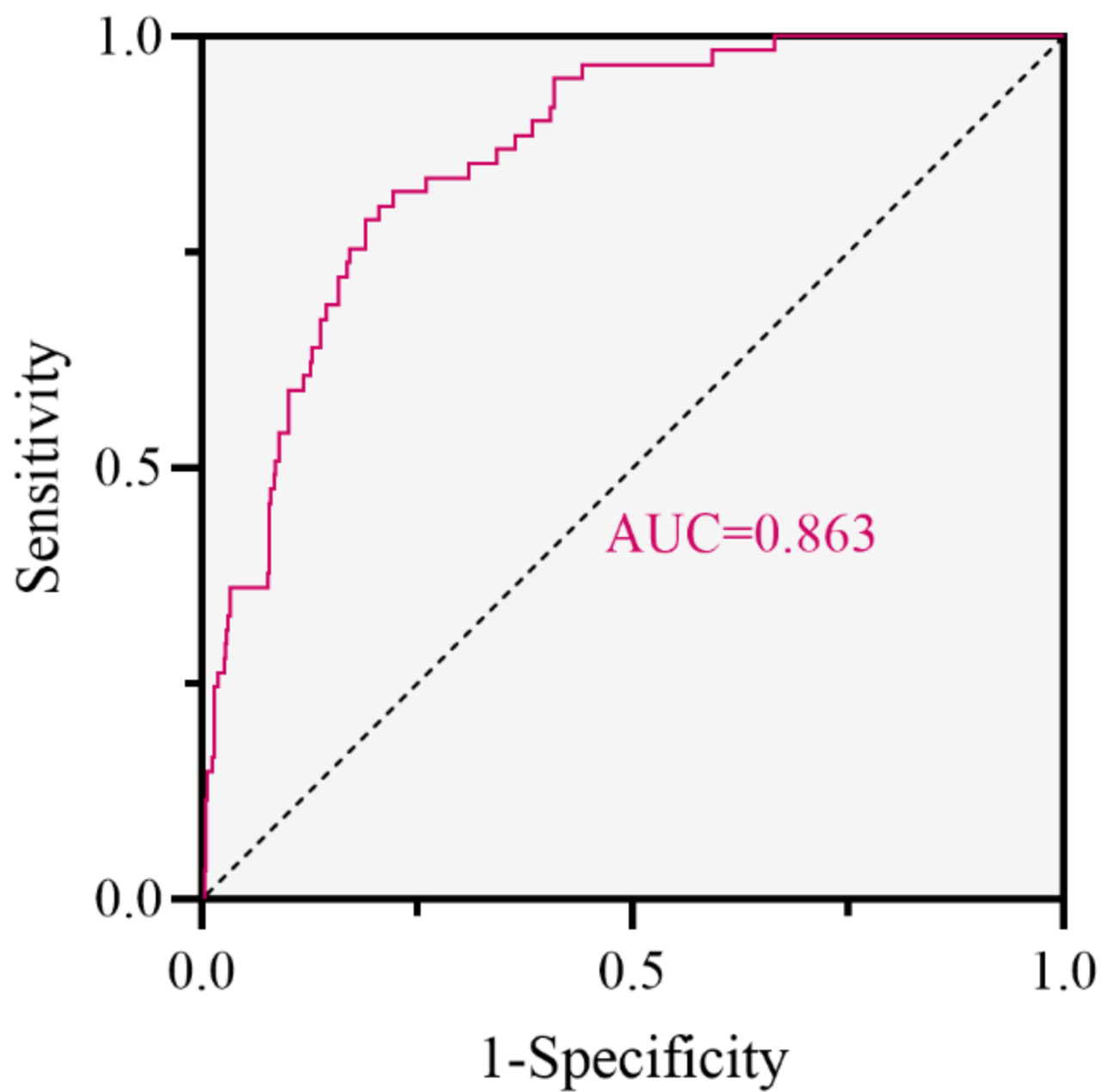


Figure 4

ROC curve of the predictive model for lateral cervical lymph node metastasis in PTC patients (AUC = 0.863).

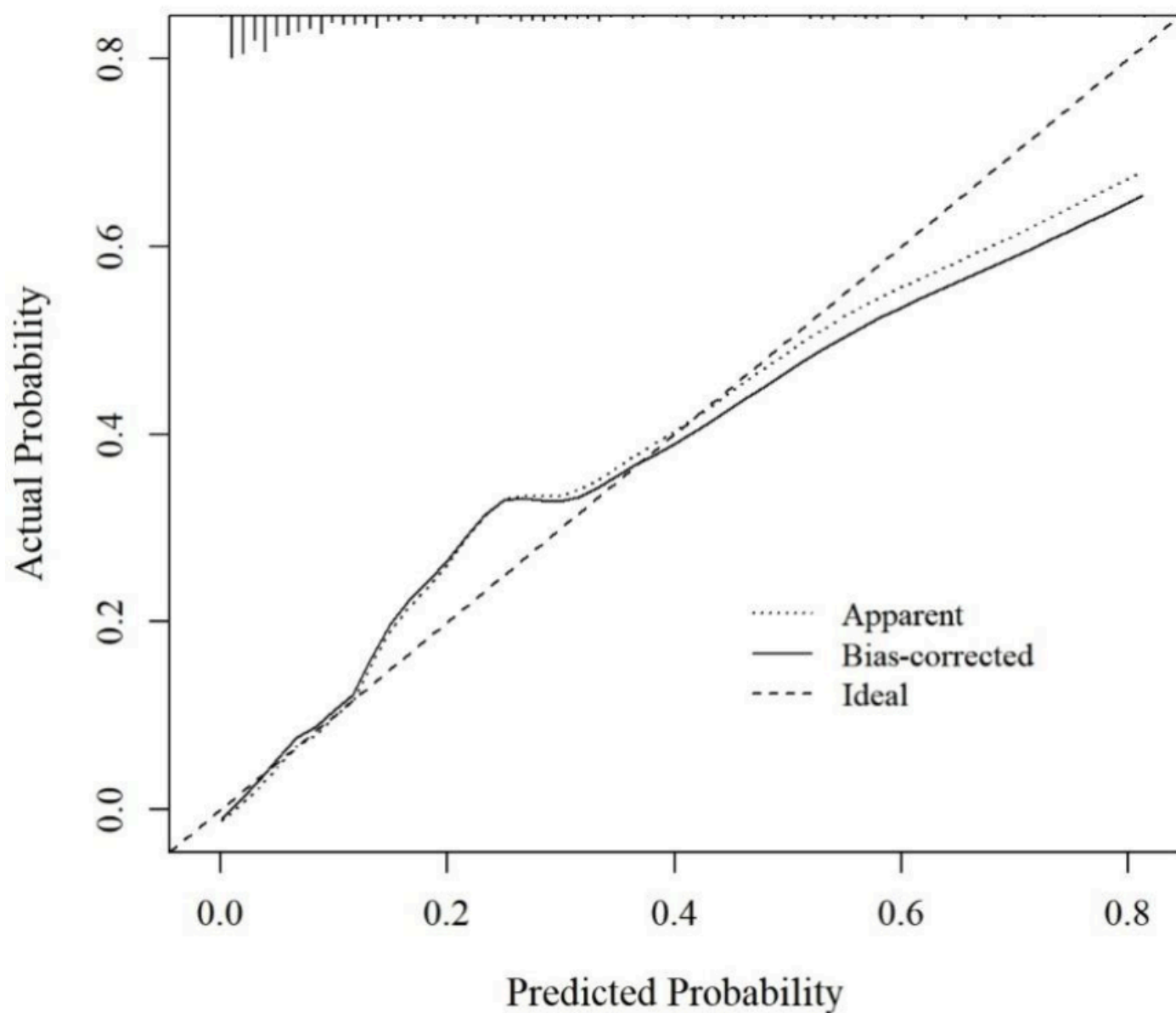


Figure 5

Calibration curve of the predictive model for lateral cervical lymph node metastasis in PTC patients. Apparent: observed calibration curve without bias correction; Bias-corrected: calibration curve adjusted for bias, reflecting the model's true performance; Ideal: reference line ($y = x$), representing perfect prediction.

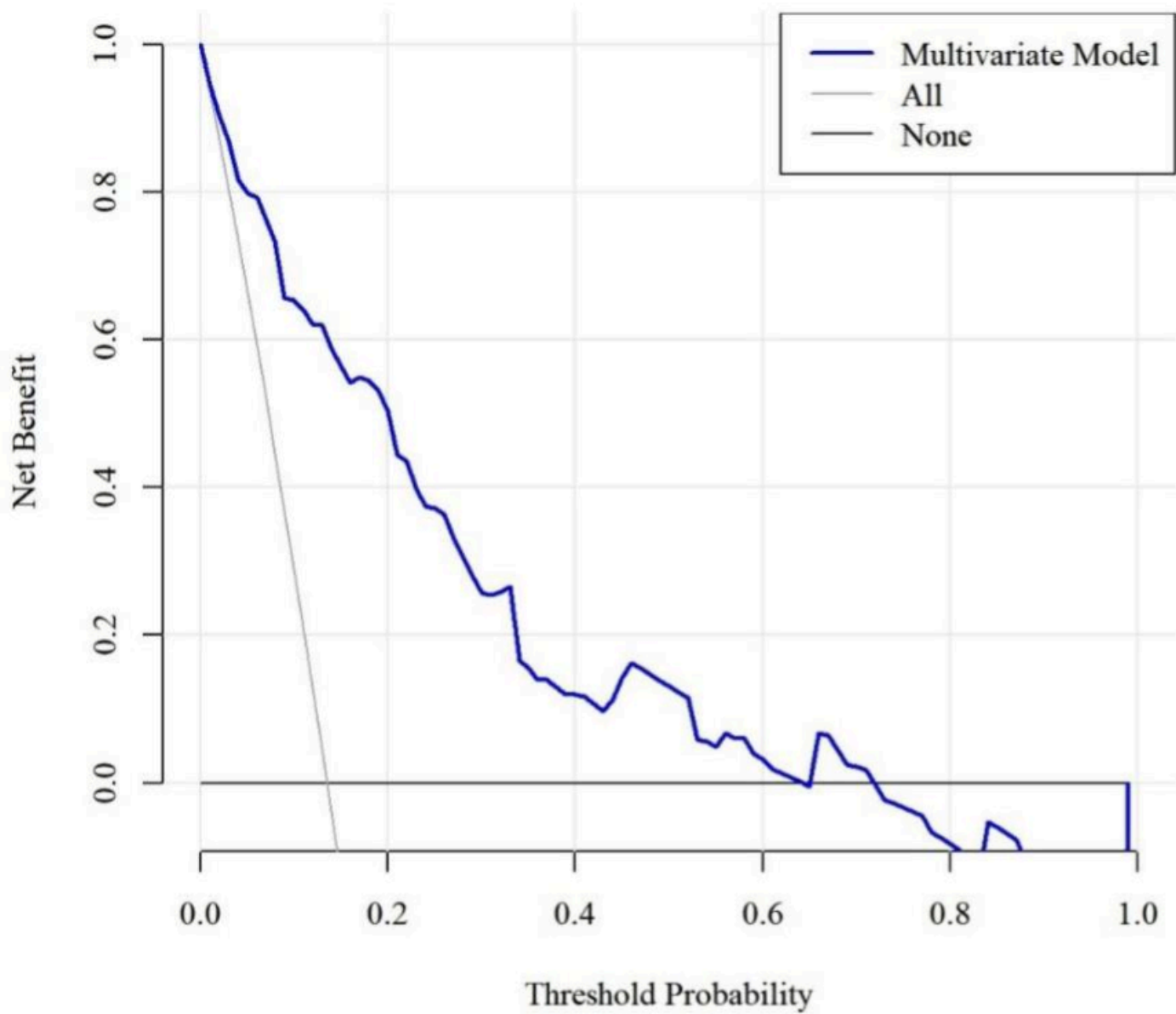


Figure 6

Decision curve analysis of the predictive model for lateral cervical lymph node dissection in PTC patients. All: assumes all patients receive intervention; None: assumes no patients receive intervention.

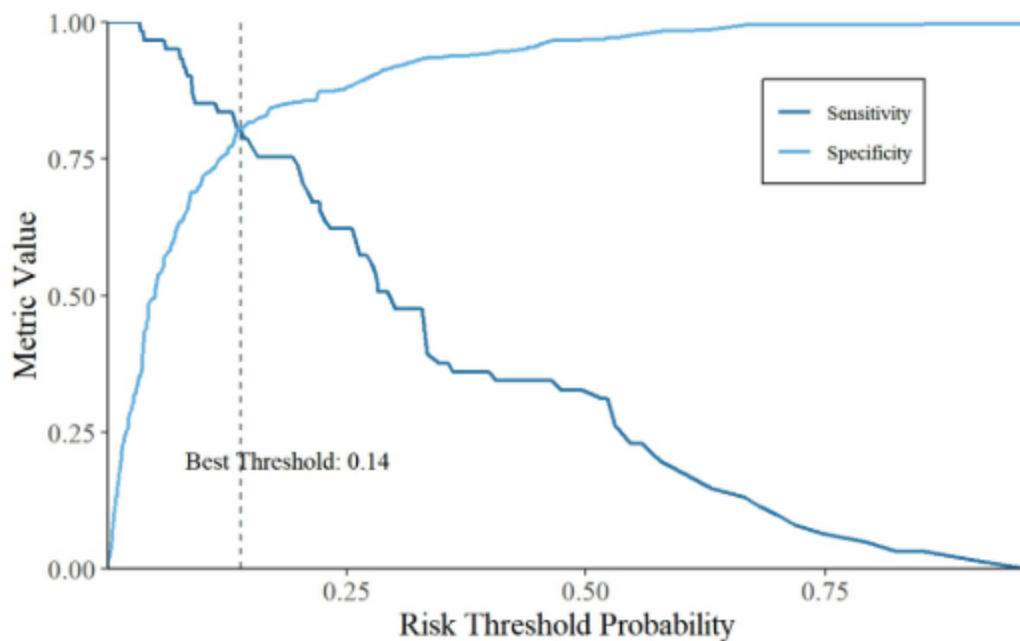


Figure 7

Sensitivity and specificity curves across varying predicted probability thresholds, with the optimal cutoff point ($x = 0.14$) indicated.

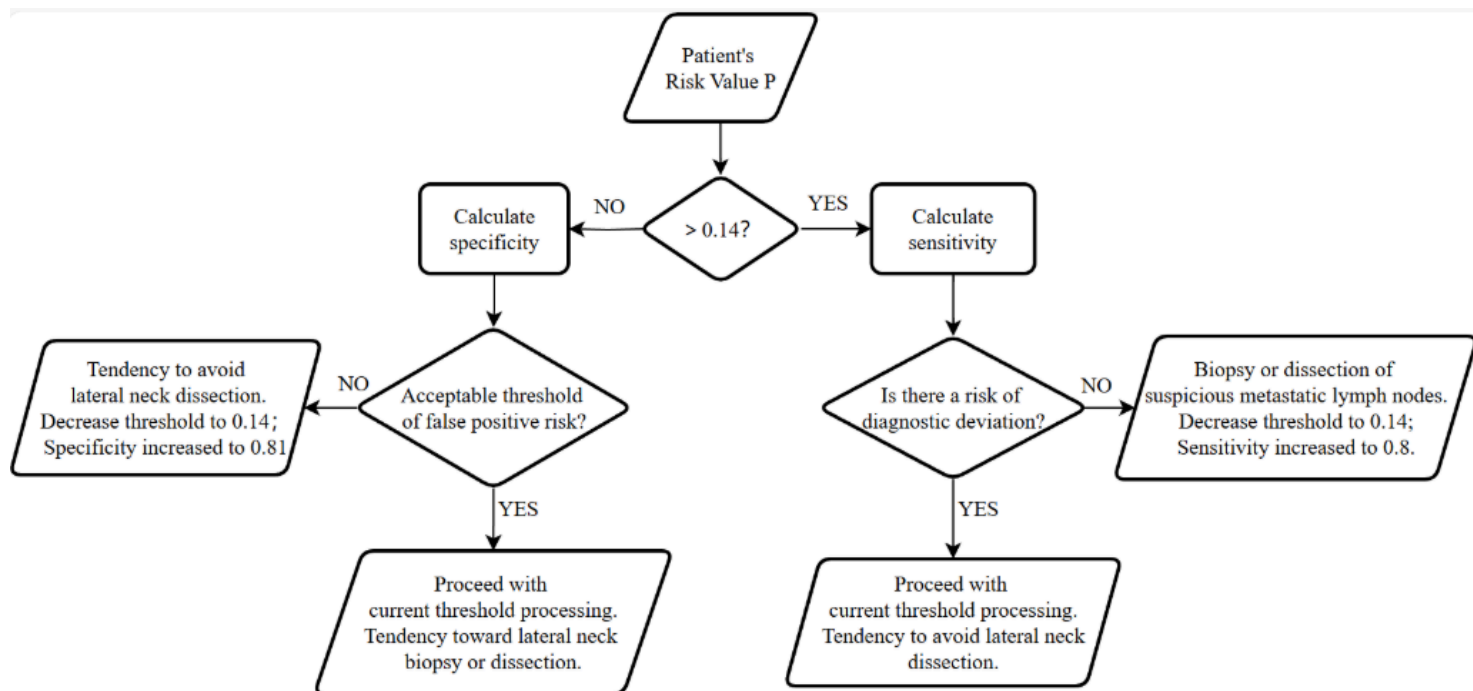


Figure 8

Flowchart illustrating the management of lateral cervical lymph nodes with the support of model-predicted probability P.