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Development of a Nomogram Based on Hematological Markers and Clinical Pathological Characteristics for Predicting Cervical Lymph Node Metastasis in Oral Squamous Cell Carcinoma

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Abstract

Objective

To investigate the value of preoperative peripheral blood markers combined with clinical pathological features in predicting cervical lymph node metastasis (CLNM) in oral squamous cell carcinoma (OSCC), and to establish and validate a nomogram prediction model.

Methods

A retrospective analysis was conducted on data from 239 OSCC patients who underwent surgery and pathological diagnosis at the Department of Oral Medicine, First Affiliated Hospital of Bengbu Medical College. Among them, 124 patients were included in the training set and 115 in the validation set. Patients were categorized into CLNM-positive and CLNM-negative groups based on postoperative pathological results. Preoperative predictive models for CLNM were constructed based on logistic regression analysis, and the model's performance was validated.

Results

Significant differences were found between the CLNM-positive and -negative groups in gender, tumor differentiation degree, alcohol history, clinical T stage, neutrophil count, neutrophil percentage, lymphocyte count, lymphocyte percentage, C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune inflammation index (SII), systemic inflammatory response index (SIRI), and pan-immune inflammation index (PIV) ($P < 0.05$). Lasso regression identified gender, lymphocyte count, platelet count, globulin, CRP, clinical T stage, and NLR as the most predictive factors. Multivariable logistic regression analysis showed that CRP, clinical T stage, and NLR were independent risk factors for CLNM in OSCC patients ($P < 0.05$). The nomogram prediction model was established and validated. The C-index was 0.864 (95% CI 0.802–0.927) for the training set and 0.832 (95% CI 0.746–0.919) for the validation set. Calibration curves and decision curve analysis (DCA) in both sets indicated good clinical utility of the model.

Conclusions

Clinical T stage, CRP, and NLR are three independent risk factors for predicting CLNM in OSCC patients. The nomogram model based on these markers shows good discriminatory ability, calibration, and clinical applicability, which can help preoperatively assess metastasis risk and improve personalized and precise treatment decisions.

Background

Oral squamous cell carcinoma (OSCC) is one of the most common malignant tumors in the head and neck, with its incidence and mortality rates continuously rising worldwide. OSCC accounts for about 40% of all head and neck cancers and over 95% of oral cancers[1, 2]. OSCC often occurs in the hidden areas of the oral mucosa, where early clinical symptoms are nonspecific. Most patients seek medical attention only after experiencing pain, ulcers, or functional impairments, which leads to a majority of cases being diagnosed at advanced stages[3]. Studies show that approximately 30%–50% of OSCC patients already have cervical lymph node metastasis (CLNM) at the time of diagnosis[4]. CLNM is considered one of the most critical factors influencing the prognosis of OSCC patients. The occurrence of CLNM reduces the 5-year survival rate by about 40%–50% and significantly increases the risks of local recurrence and distant metastasis[5, 6]. Therefore, precise preoperative assessment of CLNM risk is of paramount clinical importance for treatment decisions, especially when determining whether to perform prophylactic neck dissection, and for developing personalized treatment plans to improve long-term survival outcomes[7].

Currently, the evaluation of OSCC cervical lymph node metastasis mainly relies on imaging and pathological methods. 18F-FDG PET/CT is highly sensitive for detecting metabolically active metastases, particularly in advanced or high-risk patients, but it may yield false positives in inflammatory lymph nodes, and its high cost and radiation dose limit its widespread use in routine screening[8, 9]. Cervical ultrasound offers advantages such as being easy to perform, non-invasive, and highly repeatable, but the results are highly dependent on the operator’s experience, and its ability to assess deep or obstructed lymph nodes is limited[10]. Contrast-enhanced CT can quickly assess the size, shape, and enhancement characteristics of lymph nodes for staging but lacks sensitivity for detecting small micro-metastases or hidden metastases[11]. Magnetic Resonance Imaging(MRI), with superior soft tissue resolution compared to CT, can provide a clearer view of tumor infiltration depth and surrounding tissue involvement, though it has a longer scan time and may still produce false positives in distinguishing between inflammation and tumor invasion[12]. Pathological biopsy remains the "gold standard" for diagnosing lymph node metastasis, but it is invasive, prone to sampling errors, and difficult to comprehensively assess cervical and systemic lymph nodes preoperatively[13].

In recent years, tumor-related inflammatory responses have been recognized as key drivers of tumorigenesis, progression, and metastasis. Peripheral blood biomarkers are gaining attention for their non-invasive, cost-effective, easily accessible, and dynamically measurable advantages in predicting cancer metastasis risk[14]. Numerous studies have shown that markers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) are closely related to tumor aggressiveness, biological behavior, and lymph node metastasis in OSCC[15–17]. These inflammatory markers can reflect the immune status and changes in the tumor microenvironment to some extent, providing new biological evidence for preoperative risk stratification. Traditional clinical pathological features such as tumor differentiation, size, and TNM stage have also been confirmed as important predictors of cervical lymph node metastasis in OSCC [18, 19].

However, existing studies mainly focus on single imaging parameters, individual inflammatory markers, or single pathological features, and the integration of multidimensional information is still lacking.

Combining peripheral blood inflammatory markers with clinical pathological features to develop a simple, stable, and highly predictive preoperative risk assessment model remains a gap in current research[20]. No combined prediction tool with practicality, reproducibility, and clinical applicability has been widely used for preoperative assessment of OSCC cervical lymph node metastasis. Therefore, this study aims to integrate peripheral blood inflammation-related markers with clinical pathological characteristics to construct and validate a visual nomogram prediction model for individualized preoperative assessment of CLNM risk in OSCC patients. This model is expected to provide scientific, intuitive decision support for clinicians in treatment strategy selection, surgical scope determination, and follow-up management. Compared to traditional single assessment methods, this combined prediction model has the advantages of low cost, ease of use, and strong reproducibility, making it especially suitable for grassroots and resource-limited areas, with good clinical value and significant translational application prospects.

Methods

Study Subjects

This retrospective study analyzed the medical records of 239 patients with pathologically confirmed oral squamous cell carcinoma (OSCC). Of these, 124 patients treated at the Department of Stomatology, The First Affiliated Hospital of Bengbu Medical College between January 2023 and March 2025 were assigned to the training cohort, while 115 patients treated at the same institution between June 2021 and March 2025 comprised the validation cohort. All patients underwent open surgery with neck dissection performed by an experienced surgical team.Patients were included if they met the following criteria: (1) histologically confirmed OSCC treated surgically; (2) complete clinical and pathological data; (3) no preoperative radiotherapy, chemotherapy, targeted therapy, or immunotherapy; (4) no history of other malignancies; and (5) absence of distant metastasis. Exclusion criteria were: (1) severe systemic diseases, such as significant hepatic, renal, cardiac, or hematologic disorders; (2) active inflammatory conditions, concurrent infections, or acute exacerbations of chronic inflammatory diseases prior to surgery; and (3) metastatic tumors involving the oral cavity.This study was approved by the Ethics Committee of The First Affiliated Hospital of Bengbu Medical College (Ethics Approval Code: No. 2020LK075).

Data collation

Clinical and pathological data were obtained by reviewing the electronic medical records of all enrolled patients. The collected variables included demographic characteristics, hematological parameters, clinical T stage, tumor differentiation, and cervical lymph node metastasis status.Preoperative peripheral blood parameters comprised White Blood Cell (WBC), Neutrophil (NEUT), Monocyte (MONO), Platelet (PLT), Lymphocyte (LYMPH), Hemoglobin (HB), Albumin (ALB),Globulin(GLB) ,and C-reactive Protein (CRP). Based on these values, inflammatory indices were calculated, including the Neutrophil-to-lymphocyte ratio (NLR), Platelet-to-lymphocyte ratio (PLR), Lymphocyte-to-monocyte ratio (LMR),

Systemic immune-inflammation index (SII), Systemic inflammatory response index (SIRI), and Pan-immune-inflammation value (PIV).Tumor differentiation was determined according to preoperative biopsy findings. Following the World Health Organization classification and routine clinical practice, tumors were categorized into two groups for analysis: a moderately to well differentiated group (including well differentiated, moderately to well differentiated, and moderately differentiated tumors) and a poorly differentiated group (including moderately to poorly differentiated and poorly differentiated tumors).Tumor staging was performed according to the American Joint Committee on Cancer (AJCC) staging system, 8th edition (2017). All hematological samples were collected within three days prior to surgery.

Research Methods

After applying the predefined inclusion and exclusion criteria, a total of 239 patients were enrolled in this study. Among them, 124 patients were assigned to the training cohort and 115 to the validation cohort. Based on postoperative pathological findings, patients in the training cohort were further classified into cervical lymph node metastasis (CLNM)–positive and CLNM–negative groups.Preoperative variables that were readily available in routine clinical practice were collected from the electronic medical record system, guided by previous literature and clinical experience. Differences between the two groups were then systematically compared. To identify the most informative predictors, least absolute shrinkage and selection operator (LASSO) regression was applied, followed by multivariable logistic regression to determine independent risk factors for CLNM. A nomogram was subsequently developed based on the identified predictors. Its performance was internally validated in the training cohort and externally validated using the independent validation cohort. The predictive accuracy and clinical utility of the nomogram were assessed using the concordance index (C-index), calibration curves, and Decision Curve analysis (DCA).

Statistical methods

The data collected in this study are largely complete, with the proportion of missing data for each variable being less than 5%. Considering the low proportion of missing data and its random nature, this study adopts the method of deleting missing cases for processing. Data analysis was completed using SPSS27.0 (IBM Corporation, Armonk, NY, USA) and R4.5.2 (R Foundation for Statistical Computing, Vienna, Austria) statistical software. Count data were expressed as frequencies (%), and comparisons between groups were conducted using the χ^2 test (including continuity correction method and Fisher's exact probability method); normality tests for measurement data were performed using the K-S test. All data were normally distributed, and comparisons between groups were conducted using independent sample t-tests. The "glmnet" package in R software was used to perform Lasso regression model selection for the optimal subset of omics features. Multivariate logistic regression analysis confirmed independent risk factors. A nomogram was constructed using the "rms" package in R software, and internal validation was conducted through 1000 bootstrap resampling. External validation was completed using a validation set. The "pROC" package was used to draw the receiver operating

characteristic (ROC) curve to evaluate the predictive efficacy of the model, the "rms" package was used to draw the calibration curve, and the "rms" and "readr" packages were used to perform Hosmer-Lemeshow goodness-of-fit test and C-index calculation to evaluate model consistency; the "rms" and "rmda" packages were used for decision curve analysis to evaluate the clinical practicality of the model. A difference was considered` statistically significant at $P < 0.05$.

Result

clinical features

According to the predefined inclusion and exclusion criteria, a total of 239 patients were enrolled in this study. Among them, 124 patients were assigned to the training cohort, including 41 cases (33.06%) with CLNM-positive and 83 cases (66.94%) as CLNM-negative. The validation cohort consisted of 115 patients, of whom 30 cases (26.09%) were classified as CLNM-positive and 85 cases (73.91%) as CLNM-negative.

Differential analysis of OSCC patients

The general data, hematological indicators and clinical characteristics of the CLNM-positive group and the CLNM-negative group in the training set were compared. The results showed that there were statistically significant differences in gender, tumor differentiation degree, history of alcohol consumption, clinical T stage(cT), NEUT/($\times 10^9$/L), NEUT/%, LYMPH/($\times 10^9$/L), LYMPH/%, CRP, NLR, PLR, SII, SIRI, and PIV between the two groups ($P < 0.05$), as shown in Table 1.

Table 1 Comparison of differences between the positive and negative groups in the training set of CLNM

Category	CLNM		χ^2/t	*P*
	negative(*n*=83)	positive(*n*=41)		
Gender/Example(%)			4.554	0.033
Male	52(61.44)	33(80.48)		
Female	32(38.56)	8(19.52)		
Age(year)	57.33±13.51	58.34±15.13	-0.379	0.706
Tumor differentiation degree/Example(%)			14.767	<0.001
Moderately to well differentiated	80(96.38)	30(73.17)		
Poorly differentiated	3(3.62)	11(26.83)		
History of hypertension/Example(%)			0.002	0.964
No	55(66.26)	27(65.85)		
Yes	28(33.74)	14(34.15)		
History of smoking/Example(%)			2.958	0.085
No	50(60.24)	18(43.91)		
Yes	33(39.75)	23(56.09)		
History of alcohol consumption/Example(%)			3.887	0.049
No	48(57.83)	16(39.02)		
Yes	35(42.16)	25(60.98)		
cT/Example(%)			25.951	<0.001
T1	31(37.34)	3(7.32)		
T2	40(48.19)	17(41.46)		
T3	11(13.25)	14(34.15)		
T4	1(1.22)	7(17.07)		
LYMPH/($\times10^9$/L)	1.88±0.89	1.37±0.33	3.579	<0.001
LYMPH/%	30.21±10.18	23.06±6.43	4.104	<0.001
NEUT/($\times10^9$/L)	3.57±1.38	4.15±1.19	-2.321	0.022
NEUT/%	59.56±10.45	65.73±6.81	-3.438	<0.001
MONO/($\times10^9$/L)	0.45±0.17	0.47±0.19	-0.622	0.535

MONO/%	7.54±2.87	7.67±2.25	-0.249	0.804
PLT/(×10^9/L)	219.02±66.52	204.02±56.32	1.240	0.217
WBC/(×10^9/L)	6.34±2.97	6.49±2.97	-0.266	0.791
RET/(×10^9/L)	0.05±0.03	0.04±0.02	0.131	0.896
RBC/(×10^9/L)	4.32±0.66	4.17±0.65	1.170	0.244
HB/(g/L)	131.20±20.82	129.59±22.38	0.397	0.692
ALB/(g/L)	40.77±3.84	39.44±5.08	1.619	0.108
GLB/(g/L)	25.47±5.20	24.96±5.72	0.501	0.617
AGR	1.68±0.42	1.98±2.29	-1.171	0.244
CRP/(mg/L)	3.22±4.45	8.98±10.98	-4.153	<0.001
SOD(U/mL)	169.10±35.30	161.02±33.69	1.216	0.226
NLR	2.11±0.89	3.17±0.95	-6.079	<0.001
LMR	6.80±19.00	3.53±2.45	1.094	0.276
PLR	132.07±52.77	158.83±58.35	-2.564	0.012
SII	457.51±231.75	644.95±254.86	-4.099	<0.001
SIRI	0.97±0.62	1.51±0.85	-4.001	<0.001
PIV	208.55±145.23	308.71±184.27	-3.298	0.001

This table should follow after"**Differential analysis of OSCC patients**"

Selection of predictive factors

Based on relevant literature and clinical experience, the preliminary examination indicators of the training set were included in the Lasso regression analysis. The optimal λ value was determined using the 10-fold cross-validation method. The best log(λ) value determined by the minimum quadratic deviation was -3.43. A variable selection path diagram was drawn, as shown in Figure 1. At the optimal log(λ) value, a total of 7 non-zero coefficient features were selected, namely: gender, LYMPH/(×10^9/L),PLT/(×10^9/L), GLB, CRP, cT, and NLR were the most predictive parameters. Multivariate logistic regression finally determined 3 independent predictors, namely cT, CRP, and NLR were independent risk factors for CLNM in OSCC patients, as shown in Table 2.

Table 2 Multivariate Logistic Regression

Variable	*β*	*SE*	*Wald* χ^2	*OR*(95%*CI*)	*P*
Gender					
Male				1.000(Reference value)	
Female	-0.532	0.603	0.780	0.587(0.180~1.914)	0.377
LYMPH/(×10^9/L)	-0.757	0.689	1.208	0.469(0.121~1.810)	0.272
PLT/(×10^9/L)	-0.003	0.005	0.283	0.997(0.987~1.007)	0.595
GLB	-0.085	0.053	2.596	0.919(0.829~1.018)	0.107
CRP/(mg/L)	0.111	0.056	3.896	1.117(1.001~1.247)	0.048
cT					
T1				1.000(Reference value)	
T2	2.208	0.807	7.480	9.099(1.870~44.282)	0.006
T3	2.796	0.895	9.747	16.373(2.831~94.702)	0.002
T4	4.146	1.419	8.541	63.185(3.918~1019.043)	0.003
NLR	0.797	0.355	5.035	2.218(1.106~4.449)	0.025

Construction of the nomogram prediction model

Based on the above independent risk factors, a nomogram prediction model was constructed (Figure 2). Each variable in the model corresponds to a score, and the sum of all scores becomes the total score. The total score ranges from 0 to 240, corresponding to a risk of metastasis ranging from 0.01 to 0.99. By adding up the scores of each factor, the total score perpendicular to the CLNM risk axis is obtained, which represents the final risk of CLNM for an individual. The higher the score, the higher the risk of CLNM occurrence.

Internal verification and external verification

Internal validation was conducted by repeating 1000 times using the Bootstrap method, and external validation was performed using the validation set. The ROC curve was plotted based on the nomogram. The C-index of the model was 0.864 (95% CI 0.802 - 0.927) in the training set and 0.832 (95% CI 0.746 - 0.919) in the validation set (Figure 3), indicating that the nomogram has good predictive performance. The calibration curves of the training set and validation set were relatively close to the reference diagonal, indicating that the calibration of the prediction model was good. The H-L goodness-of-fit test of the training set showed that $\chi^2 = 4.356$, $P = 0.824$ ($P > 0.05$), and the H-L goodness-of-fit test of the validation set showed that $\chi^2 = 8.473$, $P = 0.389$ ($P > 0.05$), indicating that there is a good consistency between the prediction results of the nomogram and the actual CLNM status (Figure 4). The DCA of the

training set nomogram showed that this model predicted the net benefit of CLNM within the range of threshold probabilities of 0.03 to 0.91 higher than the two reference lines, and the DCA of the validation set showed that this model predicted the net benefit of CLNM within the range of threshold probabilities of 0.06 to 0.80 higher than the two reference lines (Figure 5). This indicates that the nomogram model established in this study has good clinical applicability and clinical benefits.

Discussion

Oral squamous cell carcinoma (OSCC) is one of the most prevalent malignancies in the head and neck region and is characterized by aggressive biological behavior and a strong tendency toward cervical lymph node metastasis (CLNM). Previous studies have demonstrated that the occurrence of CLNM leads to a marked decline in prognosis, with the 5-year survival rate decreasing by approximately 40%–50%, along with substantially increased risks of local recurrence and distant metastasis [1, 21]. Therefore, accurate preoperative assessment of CLNM risk is of great clinical importance, particularly when determining whether prophylactic neck dissection is necessary and defining its appropriate extent.

Clinical T stage is a key parameter reflecting the local extent and invasive depth of the primary tumor and has long been recognized as an important predictor of CLNM in OSCC. As T stage increases, tumor volume and infiltration depth also increase, facilitating tumor cell penetration of the basement membrane and subsequent spread through the lymphatic system, thereby significantly elevating the risk of lymph node metastasis [22, 23]. Patients with advanced tumors (T3–T4) exhibit a markedly higher incidence of CLNM compared with those in early stages (T1–T2). A multicenter retrospective study by Silva J et al. confirmed that T stage is an independent risk factor for CLNM in OSCC, with higher T stages associated with a significantly increased metastatic risk [24]. Moreover, the 8th edition of the AJCC staging system further underscores the prognostic relevance of local invasion characteristics [25]. Consistent with these findings, the present study confirms that clinical T stage remains an indispensable indicator in the preoperative evaluation of CLNM risk in OSCC.

In addition to tumor-related anatomical factors, increasing evidence highlights the role of systemic inflammatory responses in tumor progression and metastasis. The neutrophil to lymphocyte ratio (NLR) is a simple and reproducible marker reflecting systemic inflammation and immune status and has been widely applied in prognostic and metastatic risk assessment across various solid tumors. Elevated preoperative NLR has been shown to correlate with poor prognosis, increased recurrence, and higher risk of lymph node metastasis in OSCC [26, 27]. A systematic review and meta-analysis by Wang Y et al. further demonstrated a significant association between high NLR and CLNM, supporting its potential as a predictive biomarker [28]. Mechanistically, neutrophils can promote tumor invasion and metastasis by releasing pro-inflammatory cytokines, enhancing angiogenesis, and inducing epithelial–mesenchymal transition, whereas lymphocytes are essential for antitumor immune surveillance; a reduced lymphocyte count reflects compromised immune defense [14]. Accordingly, an elevated NLR indicates an imbalance

between enhanced pro-tumor inflammation and weakened antitumor immunity. The results of the present study identify preoperative NLR as an independent predictor of CLNM, in agreement with prior reports and further supporting its clinical value in preoperative risk stratification.

C-reactive protein (CRP) is another widely used marker reflecting systemic inflammatory status. In recent years, its prognostic and predictive value in malignant tumors has attracted increasing attention. Elevated preoperative CRP levels have been associated with advanced stage, lymph node metastasis, and poor outcomes in head and neck squamous cell carcinoma [29, 30]. In OSCC, tumor cells and the surrounding microenvironment can secrete inflammatory mediators such as interleukin-6, which stimulate hepatic CRP production and contribute to tumor proliferation, invasion, and lymphangiogenesis, thereby promoting metastatic progression [31]. A retrospective study by Acharya S et al. demonstrated that high CRP levels significantly increased the risk of CLNM in OSCC patients [32]. Consistently, our findings indicate that elevated preoperative CRP is an independent risk factor for CLNM, suggesting that CRP provides complementary information on tumor-associated inflammation and enhances preoperative risk assessment.

Although clinical T stage, NLR, and CRP individually contribute to CLNM prediction, the predictive performance of single indicators is often limited and susceptible to non-tumor-related influences. Previous studies have reported that the area under the curve (AUC) for individual inflammatory markers in predicting CLNM typically ranges between 0.6 and 0.7, which is insufficient for precise clinical decision-making [33]. To address this limitation, the present study integrated clinical T stage with NLR and CRP to construct a combined prediction model, resulting in a significant improvement in predictive accuracy. The nomogram demonstrated favorable discrimination, calibration, and stability, highlighting the advantage of integrating multidimensional clinical and laboratory information. Given its simplicity, low cost, and ease of implementation, this model is particularly suitable for routine clinical practice and resource-limited settings, providing practical support for individualized treatment planning in OSCC.

Several limitations of this study should be acknowledged. First, its retrospective design inevitably introduces selection bias. Second, variations in surgical techniques and temporal differences in pathological assessment standards may affect result consistency. Third, the study population was derived from a single institution, which may limit generalizability. In addition, imaging features were not included due to a high rate of missing data, which would have compromised sample validity. Lifestyle factors such as smoking and alcohol consumption were initially considered but lacked quantitative measures, reducing their modeling value. Future studies should involve multicenter cohorts, expand sample diversity, and integrate multimodal data, including radiomic features, to develop more robust and comprehensive predictive models.

In conclusion, clinical T stage, CRP, and NLR are independent risk factors for cervical lymph node metastasis in OSCC. The nomogram developed based on these variables enables more accurate preoperative assessment of CLNM risk, supports individualized treatment decision-making, and has meaningful potential for clinical application.

Conclusion

This study analyzed clinical data from patients with oral squamous cell carcinoma and identified key predictors of cervical lymph node metastasis using statistical modeling. C-reactive protein, neutrophil-to-lymphocyte ratio, and clinical T stage were confirmed as three independent risk factors and were incorporated into a nomogram for individualized risk prediction. The model demonstrated good predictive performance across internal evaluation, internal validation, and external validation. By enabling more accurate preoperative assessment of cervical lymph node metastasis risk, this nomogram may support clinical decision-making and has considerable potential for practical application.

Abbreviations

OSCC	Oral Squamous Cell Carcinoma
CLNM	Cervical Lymph Node Metastasis
CRP	C-reactive Protein
NLR	Neutrophil-to-Lymphocyte Ratio
PLR	Platelet-to-Lymphocyte Ratio
SII	Systemic Immune Inflammation Index
SIRI	Systemic Inflammatory Response Index
PIV	Pan-immune Inflammation Index
DCA	Decision Curve Analysis
MRI	Magnetic Resonance Imaging
WBC	White Blood Cell
NEUT	Neutrophil
MONO	Monocyte
PLT	Platelet
LYMPH	Lymphocyte
RET	Reticulocyte Count
GLB	Globulin
AGR	Albumin-to-Globulin Ratio
RBC	Red Blood Cell
HB	Hemoglobin
ALB	Albumin
ROC	Receiver Operating Characteristic
cT	clinical T stage
LASSO	Least Absolute Shrinkage and Selection Operator

Declarations

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Not applicable.

Authors' contributions

Yixuan Liao and Yangxiao Zhang contributed equally to this work and should be considered co-first authors. Conception and design: L.J.; Data acquisition: Y.L. and Y.Z.; Statistical analysis and interpretation of data: R.Q. and M.Z.; Drafting the manuscript: J.L. and Z.S.; Figures and tables: L.S. and Z.M. All authors reviewed the manuscript.

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Data availability

The clinical data and model code during the current study are available upon reasonable request from the corresponding author.

Ethics approval and consent to participate

This in vitro study was conducted in 2020 at Bengbu Medical University after obtaining ethical permission from the Research Council (Ethics Code: No.2020LK075). As the study was based on anonymized, retrospective data, the requirement for informed consent was waived by the ethics committee.

Human ethics and consent to participate declarations

The study followed the ethical guidelines of the Declaration of Helsinki. We are committed to protecting the privacy and personal information of the participants throughout the study and to ensuring that all procedures performed in the study follow applicable ethical standards.

Consent for publication

All authors are satisfied with the publication of this article.

Competing interests

The authors declare no competing interests.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May-Jun;74(3):229-263.

2. Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE, Grandis JR. Head and neck squamous cell carcinoma. Nat Rev Dis Primers. 2020;6(1):92.
3. Rivera C. Essentials of oral cancer. Int J Clin Exp Pathol. 2015;8(9):11884–11894.
4. Lydiatt WM, Patel SG, O'Sullivan B, Brandwein MS, Ridge JA, Migliacci JC, et al. Head and neck cancers—major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer J Clin. 2017;67(2):122–137.
5. Woolgar JA. Histopathological prognosticators in oral and oropharyngeal squamous cell carcinoma. Oral Oncol.2006 Mar;42(3):229-39.
6. Huang SH, O'Sullivan B. Overview of the 8th edition TNM classification for head and neck cancer. Curr Opin Otolaryngol Head Neck Surg. 2017 Jul;18(7):40.
7. Mirhashemi M, Sadeghi M, Ghazi N, Saghravanian N, Dehghani M, Aminian A. Prognostic value of CD44 expression in oral squamous cell carcinoma: A meta-analysis. Ann Diagn Pathol. 2023 Dec;67:152213. doi: 10.1016
8. Cheol Park G, Roh JL, Cho KJ, Seung Kim J, Hyeon Jin M, Choi SH, Yuhl Nam S, Yoon Kim S.18F-FDG PET/CT vs. human papillomavirus, p16 and Epstein-Barr virus detection in cervical metastatic lymph nodes for identifying primary tumors. Int J Cancer. 2017 Mar 15;140(6):1405-1412.
9. Mihailovic J, Killeen RP, Duignan JA. PET/CT Variants and Pitfalls in Head and Neck Cancers Including Thyroid Cancer. Semin Nucl Med. 2021 Sep;51(5):419-440.
10. Xiao L, Zhou J, Tan W, Liu Y, Zheng H, Wang G, Zheng W, Pei X, Yang A, Liu L. Contrast-enhanced US with Perfluorobutane to Diagnose Small Lateral Cervical Lymph Node Metastases of Papillary Thyroid Carcinoma. Radiology. 2023 May;307(4):e221465.
11. Struckmeier AK, Yekta E, Agaimy A, Kopp M, Buchbender M, Moest T, Lutz R, Kesting M. Diagnostic accuracy of contrast-enhanced computed tomography in assessing cervical lymph node status in patients with oral squamous cell carcinoma. J Cancer Res Clin Oncol. 2023 Dec;149(19):17437-17450.
12. Takamura M, Nikkuni Y, Hayashi T, Katsura K, Nishiyama H, Yamazaki M, Maruyama S, Tanuma J-i. Comparing the Diagnostic Accuracy of Ultrasonography, CT, MRI, and PET/CT in Cervical Lymph Node Metastasis of Oral Squamous Cell Carcinoma.Biomedicines. 2023; 11(12):3119.
13. Xia C, Zhou Q, Zhang Q, Hu S, Meacci E, Matsuura Y, Durand M, Hu Q, Cai H, Wang Y. Comparative study on the diagnostic value of intravenous/peritumoral injection of indocyanine green for metastatic lymph node location in patients with head and neck squamous cell carcinoma (HNSCC). Ann Transl Med. 2021 Mar;9(6):507.
14. Hanahan D. Hallmarks of cancer: new dimensions. Cancer Discov. 2022;12(1):31–46.
15. Perisanidis C, Kornek G, Pöschl PW, Holzinger D, Pirklbauer K, Schopper C, Ewers R. High neutrophil-to-lymphocyte ratio is an independent marker of poor disease-specific survival in patients with oral cancer. Med Oncol. 2013 Mar;30(1):334.
16. Cho U, Sung Y-E, Kim M-S, Lee Y-S. Prognostic Role of Systemic Inflammatory Markers in Patients Undergoing Surgical Resection for Oral Squamous Cell Carcinoma. Biomedicines. 2022; 10(6):1268.

17. Zhang Y, Su X, Qiao Y, Huang S, Kou Y. Occult lymph node metastasis in the contralateral neck of oropharyngeal squamous cell carcinoma: a meta-analysis and literature review. Eur Arch Otorhinolaryngol. 2022 Apr;279(4):2157-2166.
18. Sai CY, Wen YW, Lee SR, Ng SH, Kang CJ, Lee LY, Hsueh C, Lin CY, Fan KH, Wang HM, Hsieh CH, Yeh CH, Lin CH, Tsao CK, Fang TJ, Huang SF, Lee LA, Fang KH, Wang YC, Lin WN, Hsin LJ, Yen TC, Cheng NM, Liao CT. Early relapse is an adverse prognostic factor for survival outcomes in patients with oral cavity squamous cell carcinoma: results from a nationwide registry study. BMC Cancer. 2023 Feb 7;23(1):126.
19. Alqutub S, Alqutub A, Bakhshwin A, Mofti Z, Alqutub S, Alkhamesi AA, Nujoom MA, Rammal A, Merdad M, Marzouki HZ. Histopathological predictors of lymph node metastasis in oral cavity squamous cell carcinoma: a systematic review and meta-analysis. Front Oncol. 2024 May 14;14:1401211.
20. Tsai YT, Fang KH, Hsu CM, Lai CH, Chang SW, Huang EI, Tsai MS, Chang GH, Luan CW. Prognostic Role of High-Sensitivity Modified Glasgow Prognostic Score for Patients With Operated Oral Cavity Cancer: A Retrospective Study. Front Oncol. 2022 Feb 15;12:825967.
21. Shen H, Zhang T, Wang S. A Prediction Model for Lymph Node Metastasis of Oral Squamous Cell Carcinoma Based on Multiple Risk Factors. Clin Exp Dent Res. 2024 Dec;10(6):e70046.
22. Almangush A, Bello IO, Keski-Säntti H, Mäkinen LK, Kauppila JH, Pukkila M, Hagström J, Laranne J, Tommola S, Nieminen O, Soini Y, Kosma VM, Koivunen P, Grénman R, Leivo I, Salo T. Depth of invasion, tumor budding, and worst pattern of invasion: prognostic indicators in early-stage oral tongue cancer. Head Neck. 2014 Jun;36(6):811-8.
23. Huang SH, O'Sullivan B. Overview of the 8th Edition TNM Classification for Head and Neck Cancer. Curr Treat Options Oncol. 2017 Jul;18(7):40.
24. Silva J, Souza M, Lima R. Nodal metastasis in oral squamous cell carcinoma: an analysis of risk factors and influence on overall survival. Rev Bras Cancerol. 2024;70(3):123–134.
25. Amin MB, Edge SB, Greene FL, et al. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017.
26. Yang L, Huang Y, Zhou L, Dai Y, Hu G. High pretreatment neutrophil-to-lymphocyte ratio as a predictor of poor survival prognosis in head and neck squamous cell carcinoma: Systematic review and meta-analysis. Head Neck. 2019 May;41(5):1525-1535.
27. Hasegawa T, Iga T, Takeda D, Amano R, Saito I, Kakei Y, Kusumoto J, Kimoto A, Sakakibara A, Akashi M. Neutrophil-lymphocyte ratio associated with poor prognosis in oral cancer: a retrospective study. BMC Cancer. 2020 Jun 17;20(1):568.
28. Wang Y, Wang P, Andrukhov O, Wang T, Song S, Yan C, Zhang F. Meta-analysis of the prognostic value of the neutrophil-to-lymphocyte ratio in oral squamous cell carcinoma. J Oral Pathol Med. 2018 Apr;47(4):353-358.
29. Ruiz-Ranz M, Lequerica-Fernández P, Rodríguez-Santamarta T, Suárez-Sánchez FJ, López-Pintor RM, García-Pedrero JM, de Vicente JC. Prognostic implications of preoperative systemic inflammatory

markers in oral squamous cell carcinoma, and correlations with the local immune tumor microenvironment. Front Immunol. 2022 Jul 26;13:941351.

30. Chen HH, Chen IH, Liao CT, Wei FC, Lee LY, Huang SF. Preoperative circulating C-reactive protein levels predict pathological aggressiveness in oral squamous cell carcinoma: a retrospective clinical study. Clin Otolaryngol. 2011 Apr;36(2):147-53.
31. Roxburgh CS, McMillan DC. Cancer and systemic inflammation: treat the tumour and treat the host. Br J Cancer. 2014 Mar 18;110(6):1409-12.
32. Acharya S, Kale J, Hallikeri K, Anehosur V, Arnold D. Clinical significance of preoperative serum C-reactive protein in oral squamous cell carcinoma. Int J Oral Maxillofac Surg. 2018 Jan;47(1):16-23.
33. Li X, Ou C, He A. Construction of artificial neural network (ANN) based on predictive value of prognostic nutritional index (PNI) and neutrophil-to-lymphocyte ratio (NLR) in patients with cervical squamous cell carcinoma. Medicine (Baltimore). 2024 Apr 5;103(14):e37680.

Figures

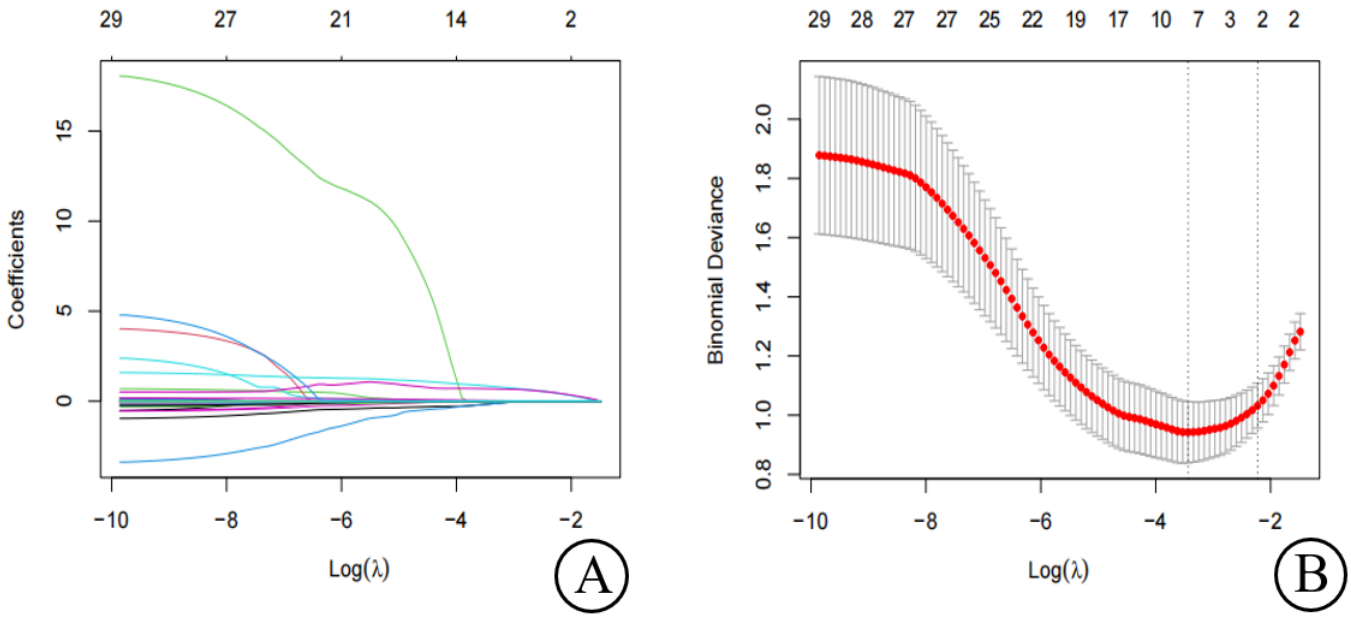


Figure 1

Feature Selection via Lasso Regression

A: Cross-validation curve. The optimal value of log(λ) determined based on the minimum sum of squared deviations is -3.43; B: Regression coefficient path diagram. At the optimal value of log(λ), draw a vertical line, and a total of 7 non-zero coefficient features are selected.

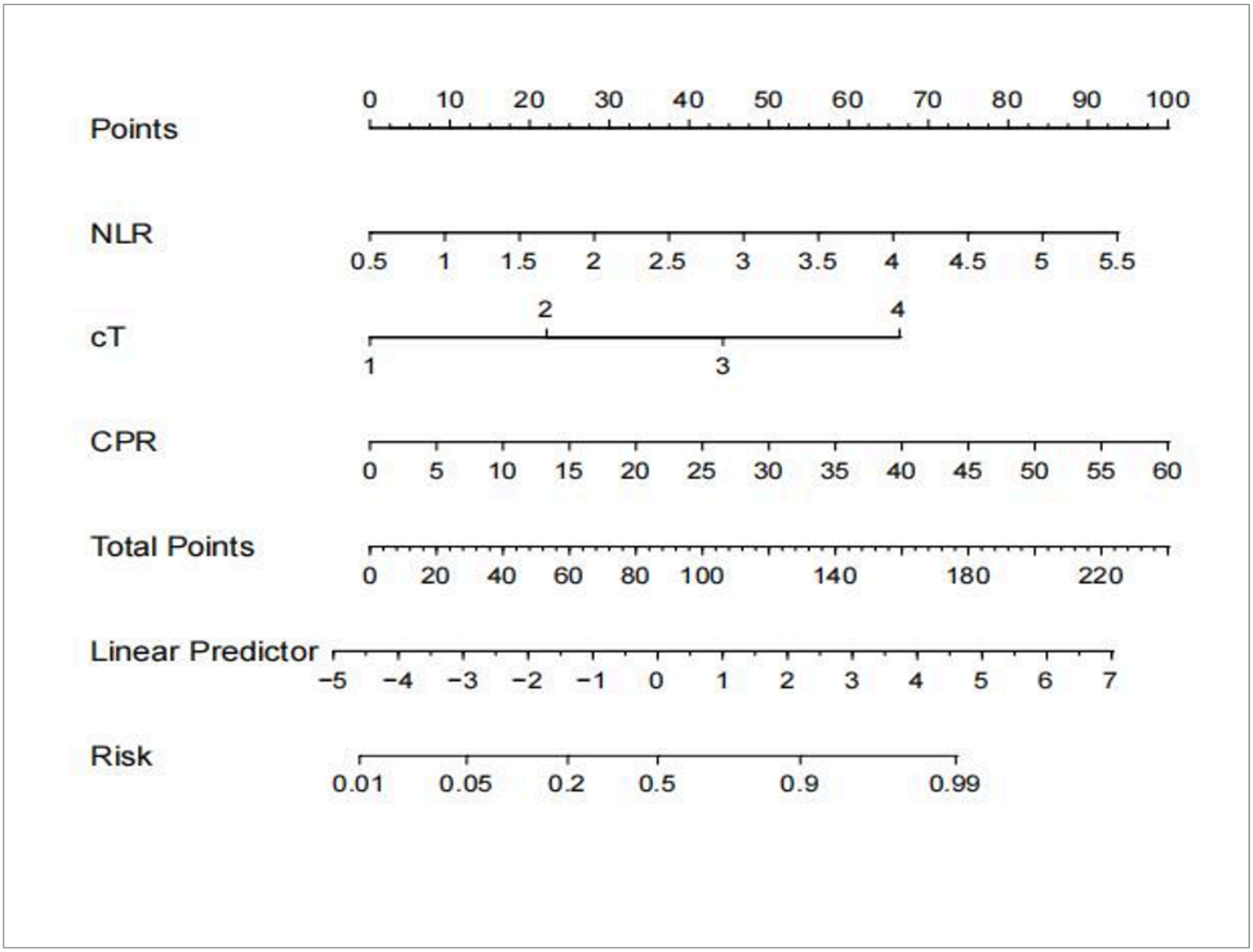


Figure 2

Nomogram for Predicting the Risk of CLNM in Oral Squamous Cell Carcinoma

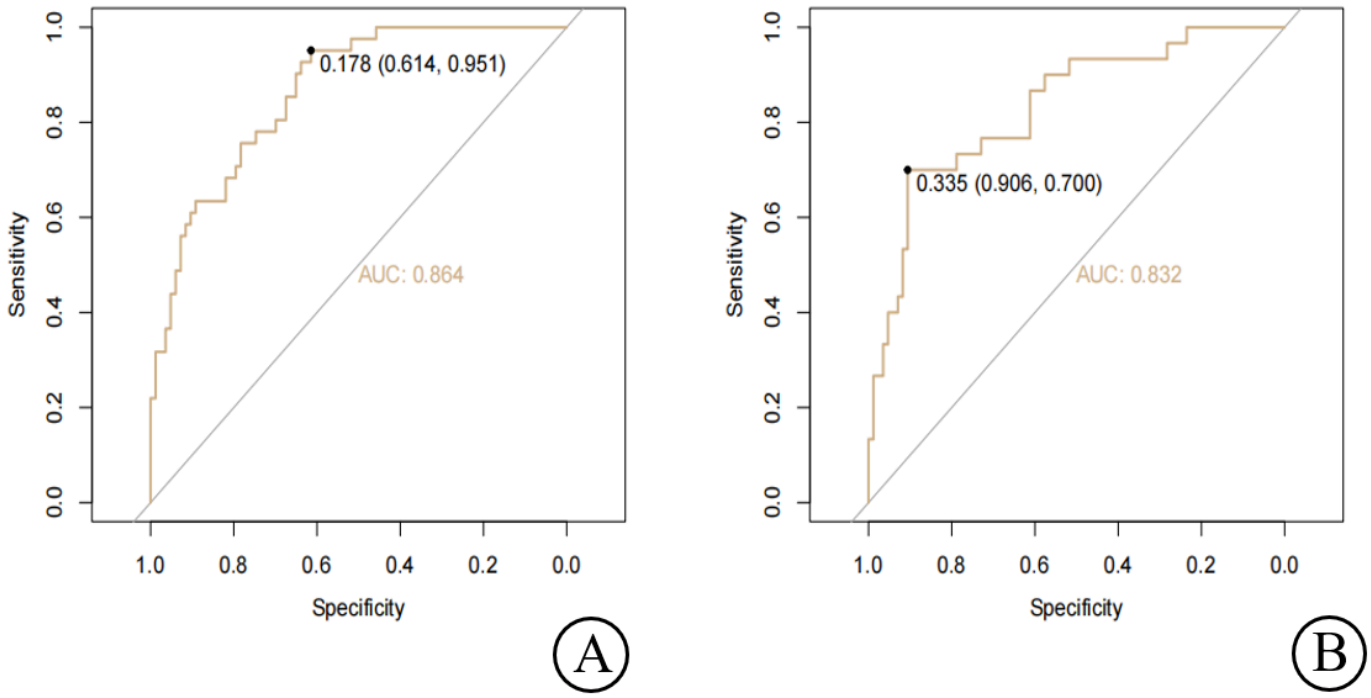


Figure 3

Discrimination assessment (ROC curve) of the prediction model for CLNM in oral squamous cell carcinoma in the training set and validation set

A: Training set; B: Validation set.

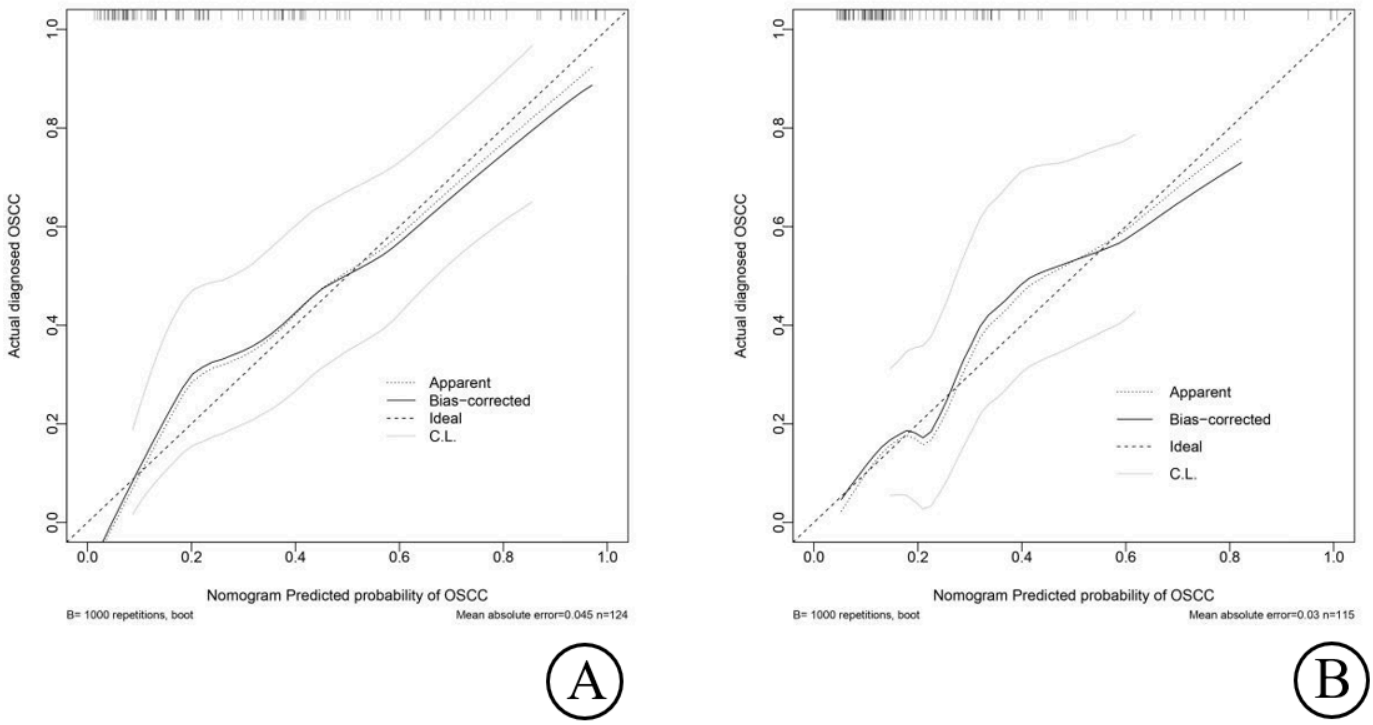


Figure 4

Discrimination assessment (calibration curve) of the prediction model for CLNM in oral squamous cell carcinoma in the training set and validation set

A: Training set; B: Validation set.

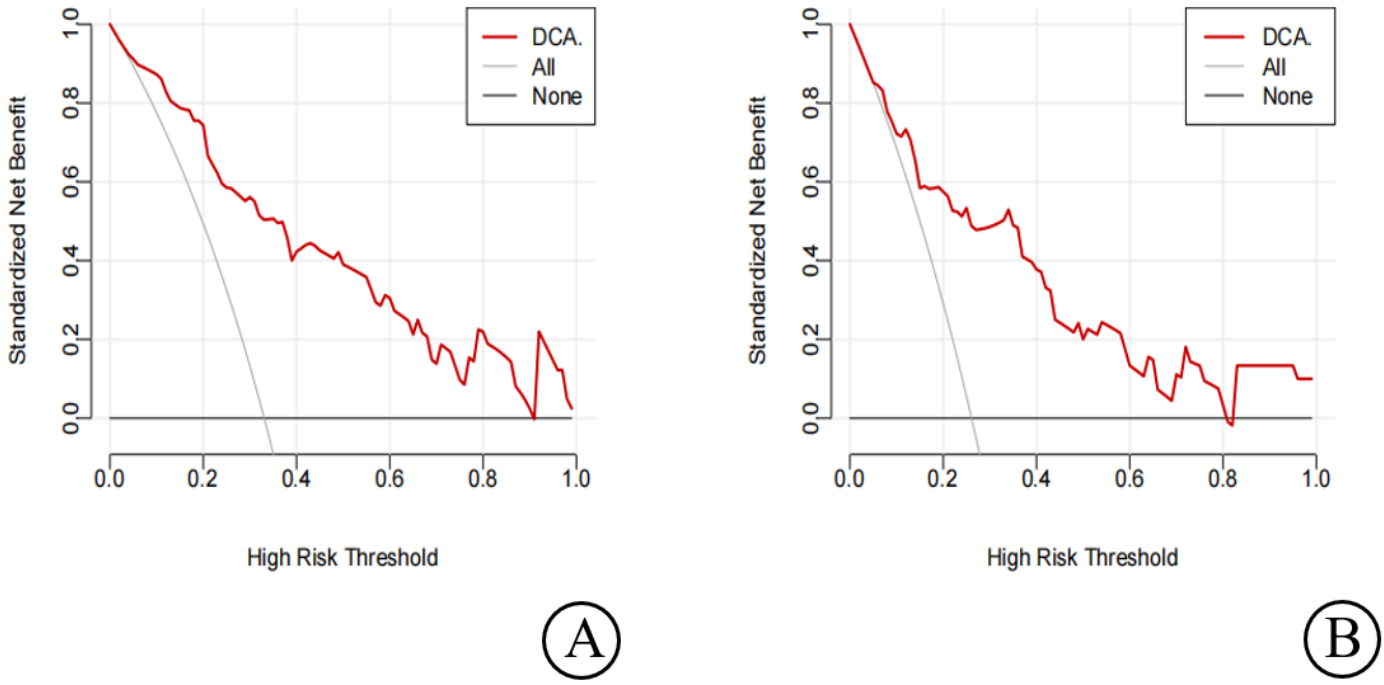


Figure 5

Discrimination assessment (DCA curve) of the prediction model for CLNM in oral squamous cell carcinoma based on the training set and validation set

A: Training set; B: Validation set.