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Original Article

Prediction model for occult lymph node metastasis of head and neck squamous cell carcinoma based on multi-dimensional indicators

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Abstract: Objective: To develop and validate a nomogram based on multi-dimensional indicators for predicting occult lymph node metastasis (OLNM) in patients with head and neck squamous cell carcinoma (HNSCC), providing a quantitative tool for individualized clinical decision-making. Methods: Clinical data of 256 cN0 HNSCC patients treated in four centers from January 2021 to June 2025 were retrospectively analyzed. Patients were randomly assigned to a training set (n=179) and an internal validation set (n=77). An independent external set (n=134) was used for external validation. Multivariate logistic regression was performed to identify independent predictors, and a nomogram was constructed. Model performance was evaluated by area under the ROC curve (AUC) with 95% confidence interval (95% CI), calibration curves, and decision curve analysis (DCA). Results: The incidence of OLNM in the training set was 40.78%. Five independent predictors were identified: age <60.5 years (OR=0.037, 95% CI: 0.012-0.110), tumor size ≥3.05 cm (OR=4.200, 95% CI: 1.782-9.902), depth of invasion ≥7.15 mm (OR=12.812, 95% CI: 5.312-30.905), poor pathologic differentiation (OR=2.772, 95% CI: 1.276-6.020), and lymphovascular invasion (OR=1.693, 95% CI: 0.998-2.871). The nomogram showed good discrimination with AUC of 0.848 (95% CI: 0.791-0.906) in the training set, 0.708 (95% CI: 0.636-0.820) in the internal validation set, and 0.827 (95% CI: 0.755-0.899) in the external validation set. Calibration curves showed that the model's predictions followed the general trend of the observed risks. Conclusions: Age, tumor size, depth of invasion, pathologic differentiation, and lymphovascular invasion were key predictors of OLNM in HNSCC. The proposed nomogram provides an intuitive and reliable tool for preoperative OLNM risk assessment and may assist in identifying high-risk patients who could benefit from proactive management.

Keywords: Head and neck squamous cell carcinoma, occult lymph node metastasis, multi-dimensional indicators, prediction model, nomogram

Introduction

Head and neck squamous cell carcinoma (HNSCC) ranks among the most common malignancies worldwide, with approximately 890,000 new cases reported annually, and continues to impose a substantial disease burden [1]. Cervical lymph node metastasis is a major determinant of prognosis and treatment planning, and its accurate assessment is essential for optimizing therapeutic strategies [2]. However, a notable proportion of patients clinically staged as cN0 still harbor occult lymph node metastasis (OLNM), which can only be confirmed by postoperative pathology. Failure to identify OLNM preoperatively may lead to inadequate neck management and increased regional recurrence [3].

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Although ultrasound, CT, and MRI remain the cornerstones of preoperative evaluation, their sensitivity for detecting micrometastasis or early nodal involvement is limited, contributing to both under- and overtreatment in clinical practice [4]. These limitations highlight the need for more reliable tools to refine risk stratification in cN0 patients. Recent studies have explored OLNM from molecular, pathologic and imaging perspectives, suggesting that occult metastasis reflects distinct tumor biology rather than random dissemination [3]. Radiomic-based approaches have shown promise in capturing intratumoral heterogeneity and improving predictive performance, yet their reliance on high-dimensional imaging features and specialized workflows restricts routine clinical application [2, 4]. Existing clinical prediction models have provided useful insight, but most focus on overall lymph node metastasis or specific anatomic subsites, and evidence specifically addressing OLNM in cN0 HNSCC remains limited [5, 6].

Given these gaps, developing a practical and clinically accessible prediction model for OLNM is of considerable value. Integrating demographic characteristics, clinicopathologic features and blood-related biomarkers may offer a more comprehensive assessment of tumor aggressiveness and host status. Therefore, this study aimed to construct and validate a nomogram for predicting OLNM in clinically node-negative HNSCC patients. The innovation of this work lies in its targeted focus on OLNM and its use of routinely obtainable preoperative variables, with the goal of providing a feasible tool to support individualized decision-making and improve clinical management [6].

Patients and methods

Patients

From January 2021 to June 2025, a total of 256 patients with pathologically confirmed head and neck squamous cell carcinoma (HNSCC) and clinically negative cervical lymph nodes (cN0) were retrospectively collected from multiple centers. Inclusion criteria were: (1) age ≥18 years; (2) HNSCC confirmed by postoperative pathologic examination with a clearly defined histological type; (3) preoperative cervical ultrasound, contrast-enhanced CT, or MRI showing no definite evidence of cervical lymph node metastasis; (4) no prior antitumor treatment, including radiotherapy, chemotherapy, targeted therapy, or immunotherapy; and (5) absence of distant metastasis before surgery. Exclusion criteria were: (1) coexistence of other malignant tumors; (2) severe dysfunction of major organs (heart, liver, kidney) precluding surgery; (3) severe infection, autoimmune disease, or hematologic disorders that could affect blood test results; and (4) incomplete clinical data. To further evaluate the generalizability of the model, an independent external set from another center that did not participate in model construction, meeting the same inclusion and exclusion criteria, was additionally collected for external validation.

The study was approved by the Ethics Committee of Liuzhou People's Hospital, the Ethics Committee of Wuming Hospital Affiliated to Guangxi Medical University, the Ethics Committee of Liuzhou Workers' Hospital, and the Ethics Committee of Jingmen Central Hospital, and informed consent was waived due to the retrospective design.

Data collection

A unified data collection form was used across all centers. Patient information was extracted from electronic medical records. To reduce variability in imaging assessments across centers, we used standardized imaging protocols for preoperative evaluations (ultrasound, contrast-enhanced CT, or MRI) at each institution. During data screening, imaging results from different centers were carefully reviewed and discussed together to ensure consistent and reliable interpretation.

Demographic characteristics collection: Collected variables included: age, sex, BMI, smoking history, alcohol consumption, hypertension, diabetes, and family history.

Clinical characteristics collection: The clinical and pathologic data of the patients were collected and jointly reviewed and confirmed by 2 senior pathologists and 1 clinical physician. The details included: ① Tumor-related information: primary site (oral cavity, pharynx, larynx, nasal cavity and paranasal sinuses); ② Tumor size (continuous variable, unit: cm, measured by the maximum diameter of the tumor from the postoperative pathology specimen);

③ Depth of invasion (DOI: continuous variable, unit: mm, measured by 2 senior pathologists under a microscope from the distance from the basal membrane to the deepest infiltration point of the tumor, taking the average value); ④ Pathologic features: pathological differentiation degree (high differentiation, moderate differentiation, low differentiation), lymphovascular invasion (LVI) (Yes/No, indicating whether tumor cells invade blood vessels or lymphatic vessels), nerve invasion (Yes/No, indicating whether tumor cells invade nerve sheaths or nerve fibers).

All laboratory tests were obtained from routine preoperative blood samples collected within one week before surgery. Blood-related indicators collection: Including: ① Tumor markers: Squamous Cell Carcinoma Antigen (SCC-Ag), Carcinoembryonic Antigen (CEA), Alpha-Fetoprotein (AFP); ② Inflammatory indicators: Neutrophil count (NEU), Platelet count (PLT), Lymphocyte count (LYM), Neutrophil/Lymphocyte ratio (NLR), Platelet/Lymphocyte ratio (PLR); ③ Nutritional indicators: Albumin (ALB), Prealbumin (PA). All blood tests were performed in the respective central laboratories and followed the uniform testing standards and quality control procedures.

Grouping and outcome evaluation

We considered that Liuzhou People's Hospital, Wuming Hospital Affiliated to Guangxi Medical University, and Liuzhou Workers' Hospital were all located in the same region. Therefore, the data from these three hospitals were merged and then divided into the training cohort and the internal validation cohort. In contrast, Jingmen Central Hospital is located in a different region, and thus its relevant data were incorporated as the external validation cohort. According to postoperative pathology results, patients were classified into the OLNM group (presence of metastatic cancer cells in cervical lymph nodes) and the non-OLNM group (no metastatic involvement). The 256 patients were randomly divided into a training set (n=179) and an internal validation set (n=77) at a 7:3 ratio. Jingmen Central Hospital as an external validation set (n=134) to further assess model performance.

Statistical methods

Continuous variables were described as mean ± standard deviation or median (interquartile range) and compared using the t-test, Mann-Whitney U test, or Kruskal-Wallis test as appropriate. Categorical variables were expressed as counts and percentages and compared using the chi-square test or Fisher's exact test.

Baseline characteristics were compared among the OLNM group, the non-OLNM group, and the external validation set. Univariate analysis was conducted to screen potential predictors of OLNM, and variables with P<0.05 were entered into multivariate logistic regression to identify independent risk factors.

A nomogram was constructed based on the final logstic regression model. Model discrimination and calibration were evaluated in the training set, internal validation set, and external validation set using ROC curves, AUC values, and calibration plots. Decision curve analysis (DCA) was performed to assess clinical utility. Sensitivity analyses were conducted to examine the robustness of the model. A two-sided P<0.05 was considered significant.

Results

Analysis of demographic characteristics of HNSCC patients

A total of 256 patients with cN0 HNSCC were included in the study. After integrating data from the four participating centers, 179 patients were assigned to the training set and 77 to the internal validation set in a 7:3 ratio. An additional set of 134 patients from an independent center was used for external validation. The baseline characteristics of the three sets are summarized in **Table 1**. Differences were observed in gender distribution and family history of malignancy (P<0.05), while all other variables were comparable across the sets.

Comparison of demographic characteristics between OLNM and non-OLNM groups

By comparing the demographic characteristics of the two groups, the results showed a significant difference in age between the two groups (P<0.05) (**Table 2**).

Analysis of clinical characteristics of HNSCC patients

Comparing the clinical characteristics of the two groups, the results showed that there were

Table 1. Baseline characteristics of patients in the training, internal validation, and external validation set

Indicator	Training set (n=179)	Internal validation set (n=77)	External validation set (n=134)	Statistic	*P*
Age (years)	58.11±9.88	59.10±8.84	58.24±9.47	F=0.308	0.735
BMI (kg/m^2)	24.30±2.45	24.69±2.51	24.52±2.46	F=0.741	0.477
Tumor size (cm)	2.80 (2.5, 3.1)	2.70 (2.5, 3.0)	2.80 (2.4, 3.1)	H=1.439	0.487
Depth of invasion (mm)	7.20 (6.2, 8.1)	6.80 (6.2, 7.5)	7.10 (6.2, 7.9)	H=2.218	0.330
Neutrophils (×10^9/L)	5.70±1.61	5.78±1.46	5.69±1.66	F=0.081	0.922
Platelets (×10^9/L)	249.75±43.84	248.56±54.07	238.80±43.53	F=2.358	0.095
Lymphocytes (×10^9/L)	1.76±0.40	1.75±0.39	1.79±0.40	F=0.436	0.646
NLR	3.22 (2.6, 4.0)	3.32 (2.8, 3.9)	3.15 (2.5, 3.8)	H=2.293	0.317
PLR	141.33 (119.6, 173.3)	146.95 (114.0, 176.3)	132.60 (110.0, 162.9)	H=4.172	0.124
Prealbumin (mg/L)	310.93±39.74	311.68±40.47	312.47±41.30	F=0.056	0.945
Albumin (g/L)	42.28±4.78	41.70±4.66	42.24±5.11	F=0.419	0.657
SCC-Ag (ng/mL)	2.02±0.49	2.02±0.52	2.03±0.50	F=0.002	0.997
CEA (μg/L)	3.54±0.79	3.59±0.79	3.60±0.86	F=0.257	0.773
AFP (μg/L)	5.02±1.06	5.12±0.86	5.09±0.99	F=0.370	0.690
Gender [n (%)]	123/179 (68.7%)	38/77 (49.4%)	75/134 (56.0%)	χ^2=10.212	0.006
Smoking history [n (%)]	87/179 (48.6%)	36/77 (46.8%)	65/134 (48.5%)	χ^2=0.081	0.960
Drinking history [n (%)]	73/179 (40.8%)	24/77 (31.2%)	58/134 (43.3%)	χ^2=3.146	0.207
Hypertension history [n (%)]	60/179 (33.5%)	31/77 (40.3%)	57/134 (42.5%)	χ^2=2.864	0.238
Diabetes history [n (%)]	39/179 (21.8%)	20/77 (26.0%)	31/134 (23.1%)	χ^2=0.532	0.766
Family history [n (%)]	18/179 (10.1%)	16/77 (20.8%)	14/134 (10.4%)	χ^2=6.391	0.041
Primary tumor site [n (%)]	44/179 (24.6%)	18/77 (23.4%)	32/134 (23.9%)	χ^2=0.812	0.991
Pathological differentiation degree [n (%)]	79/179 (44.1%)	32/77 (41.6%)	54/134 (40.3%)	χ^2=0.637	0.958
Lymphovascular invasion [n (%)]	54/179 (30.2%)	21/77 (27.3%)	45/134 (33.6%)	χ^2=0.970	0.615
Nerve invasion [n (%)]	42/179 (23.5%)	17/77 (22.1%)	35/134 (26.1%)	χ^2=0.510	0.774
OLNM [n (%)]	73/179 (40.78%)	23/77 (40.78%)	57/134 (40.78%)	χ^2=3.625	0.163

Note: BMI: Body Mass Index; NLR: Neutrophil-to-Lymphocyte Ratio; PLR: Platelet-to-Lymphocyte Ratio; SCC: Squamous Cell Carcinoma Antigen; CEA: Carcinoembryonic Antigen; AFP: Alpha-Fetoprotein; OLNM: Occult Lymph Node Metastasis.

significant differences in tumor size, DOI, degree of tumor differentiation, and LVI between the two groups (P<0.05) (**Table 3**).

Analysis of blood-related indicators in HNSCC patients

In comparing the information of blood related indicators between the two groups, there was no significant difference in all indicators between the two groups (P>0.05) (**Table 4**).

Logistic regression analysis of OLNM in HNSCC patients

ROC analysis determined optimal cut-off values: age 60.5 years, tumor size 3.05 cm, and DOI 7.15 mm. The occurrence of OLNM (0 = no, 1 = yes) served as the dependent variable, while age, tumor size, DOI, pathologic differentiation, and LVI were entered as independent predictors. The coding scheme used for the regression analysis is summarized in **Table 5**.

Multivariate logistic regression identified four independent predictors of OLNM in HNSCC patients (**Table 6**). Age <60.5 years was associated with a significantly lower risk of OLNM (*OR*=0.037, 95% *CI*: 0.012-0.110, *P*<0.001). Tumor size ≥3.05 cm (*OR*=4.200, 95% *CI*: 1.782-9.902, *P*=0.001), DOI ≥7.15 mm (*OR*=12.812, 95% *CI*: 5.312-30.905, *P*<0.001), and poor pathological differentiation (*OR*=2.772, 95% *CI*: 1.276-6.020, *P*=0.010) were all significantly associated with increased OLNM risk. LVI showed borderline significance (*OR*=1.693, 95% *CI*: 0.998-2.871, *P*=0.051) and was retained in the model due to its established clinical relevance.

Performance of the nomogram

Using the five variables included in the final model (age, tumor size, DOI, pathologic differentiation, and lymphovascular invasion), a nomogram was constructed to estimate the probability of OLNM in HNSCC patients (**Figure**

Table 2. Demographic characteristics of patients in the training set

Indicator	OLNM group (n=73)	non-OLNM group (n=106)	t/χ^2	P
Age (years)	55.21±8.34	60.10±10.38	-3.353	0.001
BMI(kg/m^2)	24.25±2.40	24.33±2.50	-0.226	0.821
Gender [n (%)]			1.076	0.300
Female	26 (35.62)	30 (28.30)		
male	47 (64.38)	76 (71.70)		
Smoking history [n (%)]			0.203	0.652
No	39 (53.42)	53 (50.00)		
Yes	34 (46.58)	53 (50.00)		
Drinking history [n (%)]			0.300	0.584
No	45 (61.64)	61 (57.55)		
Yes	28 (38.36)	45 (42.45)		
Hypertension history [n (%)]			2.074	0.150
No	53 (72.60)	66 (62.26)		
Yes	20 (27.40)	40 (37.74)		
Diabetes history [n (%)]			0.111	0.739
No	58 (79.45)	82 (77.36)		
Yes	15 (20.55)	24 (22.64)		
Family history [n (%)]			0.460	0.498
No	67 (91.78)	94 (88.68)		
Yes	6 (8.22)	12 (11.32)		

Note: BMI: Body Mass Index; OLNM: Occult Lymph Node Metastasis.

1). The model demonstrated good discrimination in the training set, with an AUC of 0.848 (95% CI: 0.791-0.906). The calibration curve in the training set showed that the predicted probabilities were generally close to the observed outcomes, with only mild deviation at higher predicted risk levels. Decision curve analysis indicated that the model provided a net clinical benefit across a broad range of threshold probabilities compared to the "treat-all" and "treat-none" strategies.

Internal and external validation

In the internal validation set, the nomogram achieved an AUC of 0.708 (95% CI: 0.636-0.820). The calibration plot showed moderate agreement between predicted and observed risks, with some fluctuation at the extremes of the prediction range. The decision curve suggested that the model offered modest clinical utility within intermediate threshold ranges. In the external validation set, the model maintained good discriminatory ability, with an AUC of 0.827 (95% CI: 0.755-0.899). The calibration curve demonstrated acceptable alignment between predicted and observed probabilities, and the decision curve showed a consistent net benefit across most clinically relevant thresholds (**Figure 2**).

Discussion

Occult cervical lymph node metastasis (OLNM) of HNSCC, one of the most common malignant tumors in the world, is a key problem in clinical treatment decision-making that directly affects the prognosis and quality of life of patients [7]. In this study, clinical data from 256 cN0 HNSCC patients were retrospectively analyzed. Five preoperative variables were included in the final model. Among them, age, tumor size, depth of invasion, and pathological differentiation showed independent associations with OLNM in the multivariate analysis. Lymphovascular invasion did not reach statistical significance but was retained in the nomogram because of its recognized clinical relevance in the metastatic process. This decision was supported by established evidence linking LVI to lymphatic metastasis in HNSCC and its role as a key pathologic indicator recommended by current clinical guidelines for neck management decision-making [8, 9]. The research results showed that the incidence of OLNM in the training set in this study was 40.78%, which was slightly higher than 32.05% reported by Gaudioso et al. [10] and lower than 51.10% reported by Lan et al. [11]. The reason for the difference in the incidence of OLNM in different studies may be related to the composition of primary tumor sites, preoperative evaluation methods and pathologic diagnostic criteria. Beyond differences in incidence across studies, our analysis also highlighted several tumor-related factors associated with OLNM. Poor pathologic differentiation showed an independent association with metastatic risk, consistent with the understanding that less differentiated tumors tend to exhibit more aggressive

Table 3. Clinical characteristics of patients in the training set

Indicator	OLNM group (n=73)	non-OLNM group (n=106)	t/χ^2	P
Primary tumor site [n (%)]			2.352	0.503
Oral cavity	36 (49.31)	48 (45.28)		
Pharynx	19 (26.03)	25 (23.59)		
larynx	14 (19.18)	20 (18.87)		
Nasal cavity and paranasal sinuses	4 (5.48)	13 (12.26)		
Tumor size (cm)	3.13±0.48	2.57±0.43	8.102	<0.001
Depth of invasion (mm)	7.50±1.43	6.86±1.35	3.083	0.002
Pathological differentiation degree [n (%)]			7.663	0.022
High differentiation	22 (30.14)	47 (44.34)		
Moderate differentiation	32 (43.83)	47 (44.34)		
Low differentiation	19 (26.03)	12 (11.32)		
LVI [n (%)]			8.850	0.003
No	42 (57.53)	83 (78.30)		
Yes	31 (42.47)	23 (21.70)		
Nerve invasion [n (%)]			1.062	0.303
No	53 (72.60)	84 (79.25)		
Yes	20 (27.40)	22 (20.75)		

Note: LVI: Lymphovascular Invasion; OLNM: Occult Lymph Node Metastasis.

Table 4. Blood-related indicators of patients in the training set

Indicator	OLNM group (n=73)	non-OLNM group (n=106)	t/Z	P
NEU (10^9L)	5.90±1.64	5.57±1.57	1.376	0.171
LYM (10^9L)	1.76±0.41	1.77±0.40	-0.168	0.867
NLR	3.16 (2.41, 4.52)	3.25 (2.63, 3.77)	-0.373	0.709
PLT (10^9L)	256.06±41.14	245.41±45.28	1.605	0.110
PLR	144.47 (122.28, 173.74)	138.77 (116.60, 173.25)	-0.854	0.393
PA (mg/L)	310.94±37.71	310.92±41.25	0.003	0.998
ALB (g/L)	42.18±4.51	42.36±4.98	-0.237	0.813
SCC-Ag (ng/mL)	2.09±0.44	1.98±0.52	1.440	0.152
CEA (μg/L)	3.48±0.68	3.58±0.85	-0.843	0.401
AFP (μg/L)	4.96±1.04	5.05±1.08	-0.555	0.580

Note: NEU: Neutrophil Count; LYM: Lymphocyte Count; NLR: Neutrophil-to-Lymphocyte Ratio; PLT: Platelet Count; PLR: Platelet-to-Lymphocyte Ratio; ALB: Albumin; SCC: Squamous Cell Carcinoma Antigen; CEA: Carcinoembryonic Antigen; AFP: Alpha-Fetoprotein; OLNM: Occult Lymph Node Metastasis.

biological behavior and a greater propensity for regional spread. Logistic regression analysis showed that age was an independent protective factor for OLNM, and the younger the age, the higher the risk of OLNM. This result is consistent with the findings of Liu et al. [12]. Previous studies have pointed out that tumors of young cancer patients may present unique methylation profiles, and these changes may affect the function of genes related to cell invasion and other factors, making tumors more invasive and metastatic potential [13]. Thus, although younger patients are generally in better systemic condition, the biological behavior of their tumors may be more aggressive, leading to an increased risk of OLNM. This emphasizes that the factor of age cannot be ignored when assessing the risk of metastasis in HNSCC patients, especially for young patients, and greater vigilance should be maintained [14].

As important indicators reflecting the degree of local invasion, tumor size, and DOI are both key

Table 5. Assignment and description

Variable	Cut-off value	Sensitivity	Specificity	Youden index	Assignment of value
Age (years)	60.5	74.0%	50.0%	0.240	Values ≥ the cut-off were classified as high-risk.
Tumor size (cm)	3.05	57.5%	88.7%	0.462	
Depth of invasion (mm)	7.15	64.4%	59.4%	0.238	
Pathological differentiation degree	-				High differentiation = 0, moderate differentiation = 1, low differentiation = 2
lymphovascular invasion	-				No = 0, Yes = 1

Table 6. Logistic regression analysis of OLNM occurrence in HNSCC patients

Variablek	*β*	*S.E.*	*Wald*	*P*	*OR*	95% CI
Age (<60.5 years)	-3.299	0.556	-5.932	<0.001	0.037	0.012-0.110
Tumor size (≥3.05 cm)	1.435	0.438	3.280	0.001	4.200	1.782-9.902
Depth of invasion (≥7.15 mm)	2.550	0.449	5.677	<0.001	12.812	5.312-30.905
Pathological differentiation degree	1.020	0.396	2.577	0.010	2.772	1.276-6.020
lymphovascular invasion	0.527	0.270	1.954	0.051	1.693	0.998-2.871

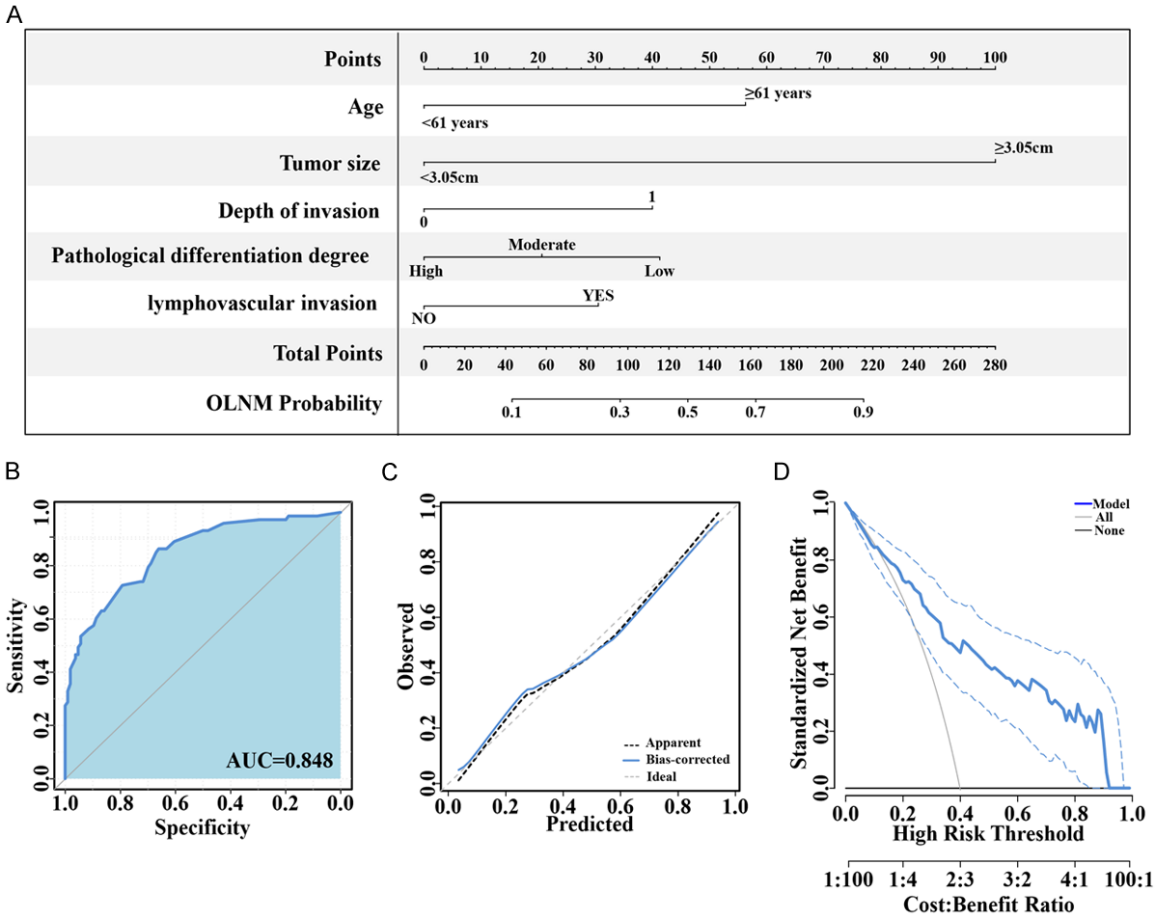

Figure 1. Development and validation of the predictive model for OLNM. Note: (A) Nomogram for OLNM prediction. (B) ROC curve showing model discrimination (AUC=0.848, 95% CI: 0.791-0.906). (C) Calibration curve comparing predicted and observed probabilities. (D) Decision curve analysis evaluating the clinical net benefit of the model. OLNM: Occult Lymph Node Metastasis; AUC: Area Under The Receiver Operating Characteristic Curve.

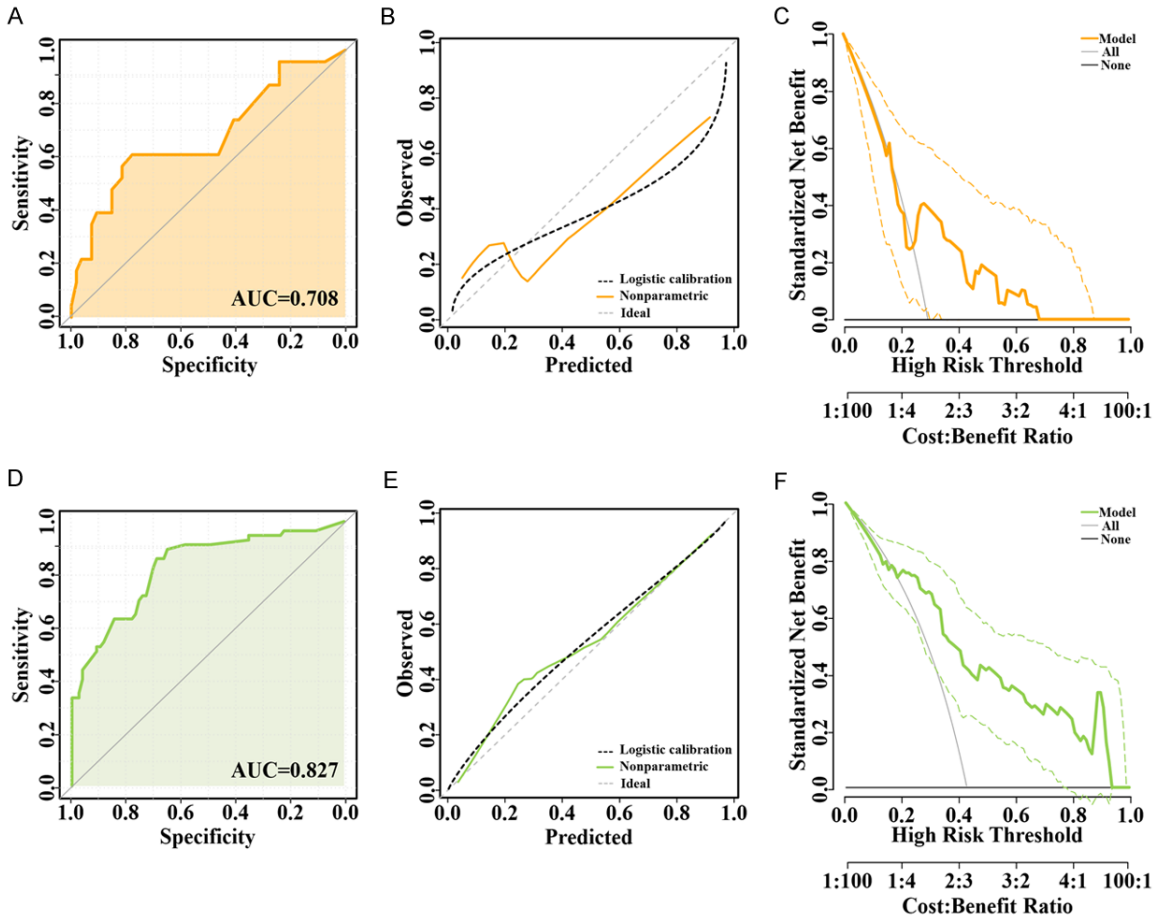

Figure 2. Model performance in the internal and external validation sets. Note: (A-C) Internal validation set. (A) shows the model's discrimination (AUC=0.708, 95% CI: 636-0.820); (B) presents calibration performance using logistic and nonparametric smoothing against the ideal reference; (C) displays the clinical utility assessed by decision curve analysis. (D-F) External validation set. (D) demonstrates discrimination in the independent dataset (AUC=0.827, 95% CI: 0.755-0.899); (E) illustrates calibration; (F) shows the net clinical benefit across threshold probabilities. OLNM: Occult Lymph Node Metastasis; AUC: Area Under The Receiver Operating Characteristic Curve.

factors affecting OLNM in HNSCC patients in this study, which is consistent with the results of previous studies [15-17]. As a core indicator of tumor burden, the mechanism of association between tumor size and OLNM has been widely confirmed. The study of Haque et al. [18] showed that when the tumor size of squamous cell carcinoma increased by 1 cm, the risk of OLNM increased by 10-14%. Hoda et al. [19] found that patients with tumors >4 cm were more likely to have lymph node metastasis. The DOI reflects the ability of tumor cells to invade deep tissue and is a key pathologic indicator to evaluate the degree of tumor malignancy [20]. From the anatomic point of view, the submucosa and muscle layer of the head and neck are rich in lymphatic vascular network. The deeper the tumor invasion depth, the higher the probability of contacting lymphatic vessels, and the chance of tumor cells invading lymphatic vessels also increases [21]. Hoda et al. [22] found in a study of 319 patients with oral squamous cell carcinoma that the incidence of OLNM reached 25.39% when the depth of tumor invasion was more than 4 mm, while it was only 4.70% when the depth of tumor invasion was less than 4 mm, which was similar to the results of this study. The above results suggest that in the clinicopathologic evaluation, the tumor size and DOI should be taken as an important basis for judging the prognosis of patients and making treatment plans, for patients with large tumors or deep invasion, more extensive lymph node dissection should be considered to reduce the risk of postoperative recurrence and metastasis [23, 24].

LVI was confirmed to be an independent predictor of OLNM in this study, which is consistent with the conclusions of many studies [25, 26]. The key role of LVI in the process of lymphatic metastasis in HNSCC has been fully confirmed. LVI refers to the invasion of tumor cells into blood vessels or lymphatic lumen, which is a necessary step for tumor cells to spread from the primary tumor to distant lymph nodes, and its presence directly indicates that the tumor has metastatic potential [27]. The results of Alqutub et al. [28] showed that the presence of LVI significantly increased the risk of OLNM in HNSCC patients. Therefore, for HNSCC patients with LVI, even if the preoperative imaging evaluation is cN0, one should be vigilant for the presence of occult metastasis, and more aggressive subsequent treatment or closer follow-up should be considered [9]. In addition, the nomogram model based on the identified predictors showed good discrimination in both the training and validation sets and acceptable calibration across the observed risk range [29]. Rather than replacing clinical judgment, this tool is intended to complement existing decision-making processes. In practical terms, the nomogram may help clinicians estimate the individual probability of OLNM before surgery and stratify patients into lower- and higher-risk groups [30]. For patients with a relatively low predicted risk, a more conservative neck management strategy may be considered, whereas those with higher predicted probabilities may be more suitable candidates for elective neck dissection or closer postoperative surveillance. In this way, the model may contribute to balancing the risks of overtreatment and undertreatment in cN0 HNSCC.

In our set, hematological and inflammation-related indicators did not show a clear association with OLNM. This outcome may relate to several characteristics of the study population and the nature of these markers. All enrolled patients were clinically node-negative, and systemic inflammatory activity in such individuals is often subtle, making it difficult for routine laboratory parameters to reflect early metastatic behavior. These indicators are also easily influenced by short-term physiological fluctuations or minor subclinical conditions, which may weaken their ability to distinguish patients with occult nodal disease. Some studies in specific head and neck cancer subgroups have reported modest associations between inflammatory ratios such as NLR or PLR and occult nodal involvement, but their predictive performance has generally been limited [31, 32]. The variability observed across different sets is consistent with our findings and may help explain why hematological indicators did not enter the final model in this study.

This study had some limitations [33]: The interpretation of our findings should take several constraints into account. The moderate decrease in AUC from the training set (0.848) to the internal validation set (0.708) may partly reflect overfitting given the relatively small sample size of the validation cohort and the inclusion of five predictors. However, the external validation AUC of 0.827 approached the training performance, suggesting reasonable generalizability. Because this study was retrospective, the possibility of selection bias cannot be completely excluded, even with consistent inclusion criteria across centers. Subtle differences in imaging evaluation, pathologic assessment, and laboratory procedures may still have existed among institutions, and such variations could have influenced the observed associations. The validation set was relatively small, and its internal nature limits the strength of conclusions regarding generalizability. Although an external dataset was included, larger prospective cohorts would provide a more reliable assessment of the model's performance in broader clinical settings. The model was developed using routinely available clinicopathologic variables. Indicators derived from radiomics or molecular pathology, which may capture tumor heterogeneity more comprehensively, were not included. Incorporating these dimensions in future work may help refine risk stratification and improve predictive performance.

In conclusion, this study developed and validated a nomogram for predicting occult lymph node metastasis in patients with head and neck squamous cell carcinoma. The analysis identified age, tumor size, DOI, pathologic differentiation, and lymphovascular invasion as key predictors of OLNM. The model demonstrated good discrimination and calibration across cohorts and offers a practical tool for estimating individual preoperative risk. Its use may help clinicians identify patients who are

more likely to benefit from proactive neck management and may support more informed treatment planning.

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Disclosure of conflict of interest

None.

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