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Original Article

Development of a predictive model for recurrence in postoperative glottic laryngeal squamous cell carcinoma patients following adjuvant chemotherapy based on PNI, NLR, and PLR

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Abstract: Objective: To identify key factors influencing postoperative recurrence in patients with glottic laryngeal squamous cell carcinoma (LSCC) and to develop a predictive model incorporating traditional clinicopathological features and novel inflammatory and immune indicators. This model aims to provide a theoretical foundation for individualized prediction of postoperative recurrence risk and support clinical decision-making. Methods: Clinical and laboratory data were collected from 614 patients with glottic laryngeal cancer who underwent surgery between April 2010 and December 2021. The study included inflammatory and immune-related indicators (such as NLR, PLR, PNI, IL-6, IL-8), alongside traditional clinical features like age, T stage, lymph node metastasis, and degree of differentiation. Univariate and multivariate logistic regression, as well as Cox regression analyses, were performed to identify factors associated with recurrence. A Nomogram model was constructed based on Cox regression results. The model's predictive performance was evaluated using ROC curves, the concordance index (C-index), and calibration curves, with validation conducted in both training and validation cohorts. Results: Multivariate analysis identified age, T stage, lymph node metastasis, degree of differentiation, IL-6, IL-8, PNI, and PLR as independent factors influencing postoperative recurrence in patients with glottic laryngeal cancer. The Nomogram model demonstrated excellent predictive performance in both the training and validation cohorts, with AUCs for 12-, 24-, and 36-month recurrence-free survival predictions of 0.887, 0.906, and 0.915 (training cohort) and 0.895, 0.906, and 0.907 (validation cohort), respectively. The model's concordance indices were 0.860 and 0.857 in the training and validation groups, respectively. Calibration curves revealed a high degree of agreement between predicted and actual outcomes. Conclusion: The Nomogram model developed in this study integrates multiple clinical and inflammatory-immune indicators, enabling accurate prediction of 12-, 24-, and 36-month recurrence-free survival rates in post-surgical patients with glottic laryngeal cancer. The model holds significant clinical value, with IL-6, IL-8, and PNI identified as crucial indicators for predicting recurrence risk, providing valuable insights for postoperative follow-up and individualized treatment strategies.

Keywords: Glottic laryngeal cancer, postoperative recurrence, prognostic nutritional index (PNI), inflammatory markers, nomogram model

Introduction

Laryngeal cancer is one of the most prevalent malignant tumors in the head and neck region, with laryngeal squamous cell carcinoma (LSCC) accounting for over 90% of all laryngeal cancer cases [1]. Glottic laryngeal cancer, the most common subtype, represents approximately 60% of all laryngeal cancer cases [2, 3]. According to the 2020 Global Cancer Statistics Report, there are about 180,000 new cases of laryngeal cancer and approximately 100,000 deaths annually [4]. The survival rate for laryngeal cancer is closely associated with its stage, with a 5-year survival rate of 80%-90% for early-stage T1 and T2 patients, while it significantly drops to around 40% for stage IV patients [5]. Despite substantial advances in the

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diagnosis and treatment of laryngeal cancer, surgery remains the primary treatment for patients with glottic laryngeal cancer. However, postoperative recurrence continues to present a major challenge to long-term survival. Literature suggests that patients with recurrent laryngeal cancer after surgery often experience poorer prognoses, higher recurrence rates, and increased mortality, which negatively impacts their quality of life and complicates clinical management [6].

The pathogenesis of laryngeal cancer is complex, with key risk factors including smoking, alcohol consumption, unhealthy lifestyle habits, and environmental pollution [7]. Additionally, human papillomavirus (HPV) infection is considered a contributing factor to laryngeal cancer development, though its exact mechanisms remain controversial [8, 9]. Laryngeal cancer is highly destructive in advanced stages, as tumors can disrupt the anatomical and physiological functions of the upper respiratory and digestive tracts, severely impairing voice, swallowing, and breathing functions, which further diminishes quality of life [10]. Therefore, early prediction of recurrence risk after surgery is crucial for improving patient outcomes and optimizing treatment strategies.

Recent studies have shown that the prognosis of laryngeal cancer patients is closely linked not only to tumor characteristics (such as TNM staging and pathological differentiation) but also to factors like systemic inflammatory status, nutritional health, and immune function [11]. Inflammation plays a critical role in tumor initiation, progression, and recurrence, with systemic inflammatory markers such as neutrophils, lymphocytes, and platelets becoming important indicators in cancer prognosis research. Elevated neutrophil levels are associated with the activation of inflammatory responses, which can promote tumor development by enhancing tumor cell proliferation, angiogenesis, and invasion [12]. Conversely, lymphocytes play a vital role in anti-tumor immunity, and reduced lymphocyte counts often suggest impaired immune function [13]. Platelets, in addition to their role in hemostasis, contribute to tumor cell proliferation, metastasis, and angiogenesis in the tumor microenvironment [14].

Building on studies examining individual blood markers, composite hematological indices such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and prognostic nutritional index (PNI) have emerged as powerful tools [15, 16]. These composite markers not only reflect the patient's systemic inflammatory and immune status but also have high predictive value for the occurrence, progression, and recurrence of malignant tumors. Moreover, inflammatory cytokines such as interleukin-6 (IL-6) and IL-8 are increasingly recognized for their roles in the tumor microenvironment [17]. IL-6 promotes tumor cell proliferation and invasion by activating the JAK-STAT pathway, while IL-8 is involved in angiogenesis and inflammation, both of which are significant risk factors for tumor recurrence [18].

However, the traditional TNM staging system, widely used for tumor prognosis assessment, primarily categorizes tumors based on the extent of invasion, regional lymph node metastasis, and distant metastasis [19]. While TNM staging reflects certain aspects of tumor biology, it does not fully account for the patient's overall condition or the influence of biomarkers, limiting its utility in individualized recurrence risk assessments. To address this limitation, Nomogram models, which integrate multiple clinicopathological features and biomarkers, have been proposed in recent years. A Nomogram is a precise statistical tool that calculates the probability of specific outcomes (such as recurrence or survival) based on weighted scores from multiple variables. Compared to traditional TNM staging, Nomogram models have shown greater flexibility, comprehensiveness, and predictive accuracy in assessing prognosis for various malignant tumors [20].

For patients with glottic laryngeal cancer, postoperative recurrence significantly impacts long-term survival, increases treatment difficulty, and contributes to the economic burden. Therefore, accurately predicting the risk of postoperative recurrence is critical for optimizing treatment plans and improving patient outcomes. The significance of this study lies in combining traditional clinicopathological features (such as T stage, lymph node metastasis, and degree of pathological differentiation) with novel inflammatory and immune-related indica-

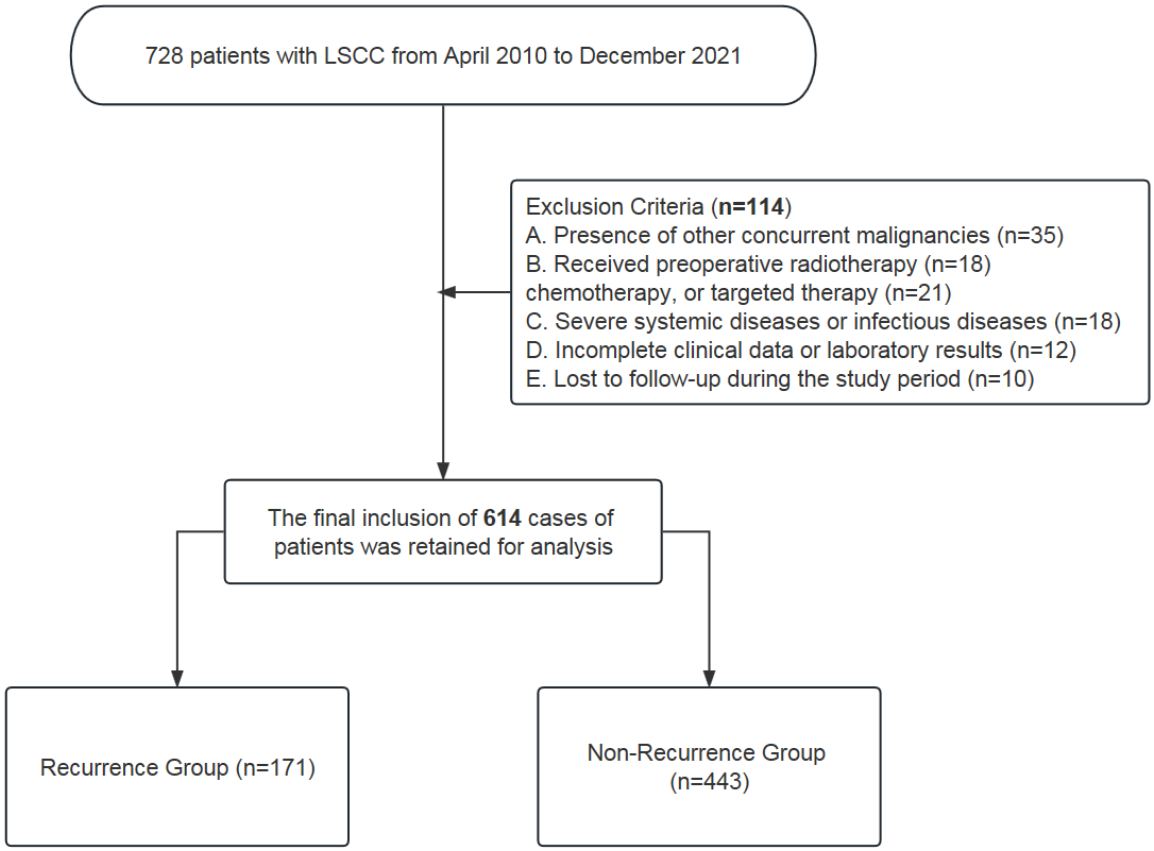

Figure 1. Flow chart of the study sample screening. LSCC, laryngeal squamous cell carcinoma.

tors (such as NLR, PLR, PNI, IL-6, and IL-8) to comprehensively assess their predictive value for postoperative recurrence. Through multivariate analysis, independent factors associated with recurrence were identified, and a Nomogram model was developed to facilitate individualized prediction of postoperative recurrence risk.

This study aims to explore the key factors influencing postoperative recurrence in glottic laryngeal cancer and construct a Nomogram model based on multivariate Cox regression analysis to predict 12-, 24-, and 36-month recurrence-free survival rates. The accuracy and stability of the model were validated, further assessing its clinical applicability and providing a valuable tool for individualized treatment strategies.

Methods and materials

Sample source

This retrospective cohort study that collected clinical data from 614 patients with glottic LSCC who underwent treatment at Sun Yat-Sen Memorial Hospital and The Eighth Affiliated Hospital, Sun Yat-Sen University, between April 2010 and December 2021. The study was approved by the Ethics Committees of Sun Yat-Sen Memorial Hospital and The Eighth Affiliated Hospital, Sun Yat-Sen University (**Figure 1**).

Inclusion and exclusion criteria

Inclusion criteria: Pathologically diagnosed with LSCC [21]; received radical surgical treatment followed by adjuvant chemotherapy; aged ≥ 18 years; and a follow-up period of at least 6 months.

Exclusion criteria: Patients with concurrent malignancies; patients who received preoperative radiotherapy, chemotherapy, or targeted therapy; patients with severe systemic or infectious diseases; and patients with incomplete data or lost to follow-up.

Collection of clinical data

All clinical data were obtained from the hospital's electronic medical record system and were

reviewed for accuracy and completeness. The collected clinical data included: age (≥ 60, < 60 years), gender (male, female), smoking history (yes, no), alcohol consumption history (yes, no), body mass index (BMI: ≥ 25, < 25), tumor T stage (T1, T2, T3), lymph node metastasis (yes, no), degree of pathological differentiation (poorly differentiated, moderately + well differentiated), and postoperative chemotherapy (yes, no). Laboratory indicators included albumin (Alb), neutrophils (Neu), lymphocytes (Lym), platelets (PLT), NLR, PLR, PNI, IL-6, and IL-8 (Note: The data for IL-6 and IL-8 were available for only a subset of patients).

Laboratory testing and formula calculations

Laboratory tests included complete blood count, Neu, Lym, PLT, biochemical indicator Alb, and inflammatory factors IL-6 and IL-8. Complete blood counts were performed using the Sysmex XN-1000 automatic blood analyzer (Sysmex Corporation, Japan). Albumin levels were measured with the Roche Cobas c501 automatic biochemical analyzer (Roche Corporation, Switzerland). IL-6 (ml058097) and IL-8 (ml103387) concentrations were detected using enzyme-linked immunosorbent assay (ELISA) with the Thermo Scientific Multiskan FC microplate reader (Thermo Fisher Scientific Company, USA) and reagent kits provided by Shanghai Enzyme-linked Biotechnology Co., Ltd. Based on these laboratory data, several key ratio indicators were calculated as follows:

NLR: Calculated by dividing the Neu by the Lym.

PLR: Calculated by dividing the PLT by the Lym.

PNI: Calculated using the formula: 10 × Alb (g/L) + 5 × Lym count (10^9/L).

Follow-up

Patient follow-up was conducted through outpatient visits, telephone interviews, and the hospital's electronic medical record system. The follow-up period began post-treatment and continued until recurrence, with the cutoff date for follow-up being December 1, 2024. Follow-up visits were scheduled every 3 months, and recurrence status was recorded. Recurrence was defined as local or distant recurrence, confirmed through imaging or pathological examinations.

Outcome measures

Primary outcome: Recurrence-Free Survival (RFS) was defined as the time from the date of surgery to the first recurrence (considered an event if recurrence was diagnosed during the follow-up period) or the end of follow-up without recurrence.

Recurrence Status: Local recurrence, regional lymph node recurrence, or distant metastasis was confirmed through imaging and pathological examinations during follow-up.

Secondary outcomes: Laboratory Indicator Analysis: The correlation between inflammatory factors (e.g., IL-6, IL-8), blood ratios (e.g., NLR, PLR), and the PNI with postoperative recurrence was assessed.

Model Predictive Ability: A recurrence risk prediction model was developed based on laboratory indicators and clinical features, and the Nomogram model's predictive ability for RFS was validated using metrics such as the concordance index (C-index), receiver operating characteristic (ROC) curves, and calibration curves.

Statistical analysis

All data analyses were performed using SPSS 26.00 (IBM, USA) and R software (version 4.3.2, R Foundation, Austria). Continuous variables were expressed as mean ± standard deviation (for normally distributed data) or median (interquartile range, for non-normally distributed data). Between-group comparisons for continuous variables were conducted using independent samples t-tests or Mann-Whitney U tests. Categorical variables were presented as frequencies and percentages, with group comparisons performed using chi-square tests or Fisher's exact tests. Spearman correlation tests were used to evaluate the relationships between laboratory indicators. Survival analysis was conducted using the Kaplan-Meier (K-M) method to calculate RFS, and differences between groups were compared using the Log-rank test. Logistic regression analysis was employed to identify risk factors for postoperative recurrence, while the Cox proportional hazards model was used to evaluate independent prognostic factors. Based on the Cox regression results, a Nomogram model was con-

structed, and its predictive ability and accuracy were assessed using the concordance index (C-index), receiver operating characteristic (ROC) curves, and calibration curves. For missing data, we used regression interpolation to handle it. All tests were two-sided, and a *P*-value of <0.05 was considered statistically significant.

Results

Comparison of baseline characteristics between recurrence and non-recurrence groups

Significant differences in baseline characteristics were observed between the recurrence and non-recurrence groups. The proportion of patients aged ≥ 60 years was significantly higher in the recurrence group compared to the non-recurrence group (P = 0.021). Additionally, a higher proportion of patients with a history of smoking was observed in the recurrence group compared to the non-recurrence group (P = 0.048). Furthermore, significant differences were found between the two groups in terms of T stage (P < 0.001), lymph node metastasis (P < 0.001), degree of differentiation (P < 0.001), and postoperative chemotherapy (P = 0.026). However, no significant differences were observed in body mass index (BMI) (P = 0.654), gender (P = 0.058), and history of alcohol consumption (P = 0.429) between the groups (P > 0.05), as shown in **Figure 2** and Table S1.

Comparison of laboratory indicators between recurrence and non-recurrence patients

Significant differences in several laboratory indicators were observed between the recurrence and non-recurrence groups. The Alb levels were significantly lower in the recurrence group compared to the non-recurrence group (P < 0.001), and Lym counts were also significantly reduced in the recurrence group (P < 0.001). In contrast, neutrophil (Neu) counts and platelet (PLT) counts were significantly higher in the recurrence group (P < 0.001). Additionally, the PNI was significantly lower in the recurrence group (P < 0.001), while the NLR and PLR were significantly elevated in the recurrence group (P < 0.001). The levels of inflammatory cytokines IL-6 and IL-8 were also significantly higher in the recurrence group compared to the non-recurrence group (both P < 0.001), as shown in **Table 1**.

ROC curve analysis and dichotomization of laboratory indicators

ROC curve analysis was conducted to determine the optimal cutoff values for each laboratory indicator, allowing for the transformation of continuous variables into binary variables for subsequent logistic regression analysis. IL-6 had the highest predictive ability with an AUC of 0.764 and a critical value of 12.550. In contrast, Neu had the lowest AUC of 0.652 and an optimal critical value of 5.250. The remaining laboratory indicators showed the following AUC values: Alb (0.749), PNI (0.750), PLT (0.663), IL-6 (0.764), IL-8 (0.677), NLR (0.722), and PLR (0.753). These results are summarized in **Figure 3**.

Spearman correlation analysis and variable elimination

Spearman correlation tests revealed a strong correlation between Alb and PNI (R = 0.990, P < 0.001). Significant correlations were also found between Neu and NLR (R = 0.475, P < 0.001), Lym and PLR (R = -0.745, P < 0.001), and PLT and PLR (R = 0.341, P < 0.001). Due to these strong correlations, which could lead to multicollinearity, Alb, Neu, Lym, and PLT were excluded from subsequent regression analyses to maintain the accuracy of the results (**Figure 4**).

Logistic regression analysis of risk factors for postoperative recurrence in glottic LSCC patients

Univariate logistic regression analysis identified age, gender, smoking history, T stage, lymph node metastasis, degree of differentiation, postoperative chemotherapy, IL-6, IL-8, PNI, NLR, and PLR as significant factors associated with postoperative recurrence in glottic LSCC patients (P < 0.05). Specifically, PNI (OR = 5.621, P < 0.001) acted as a strong risk factor for recurrence, while IL-6 (OR = 0.045, P < 0.001) and PLR (OR = 0.185, P < 0.001) were strong protective factors, negatively associated with recurrence. T stage (OR = 1.568, P < 0.001) and postoperative chemotherapy (OR = 1.607, P = 0.021) were also identified as risk factors for recurrence, indicating an increased

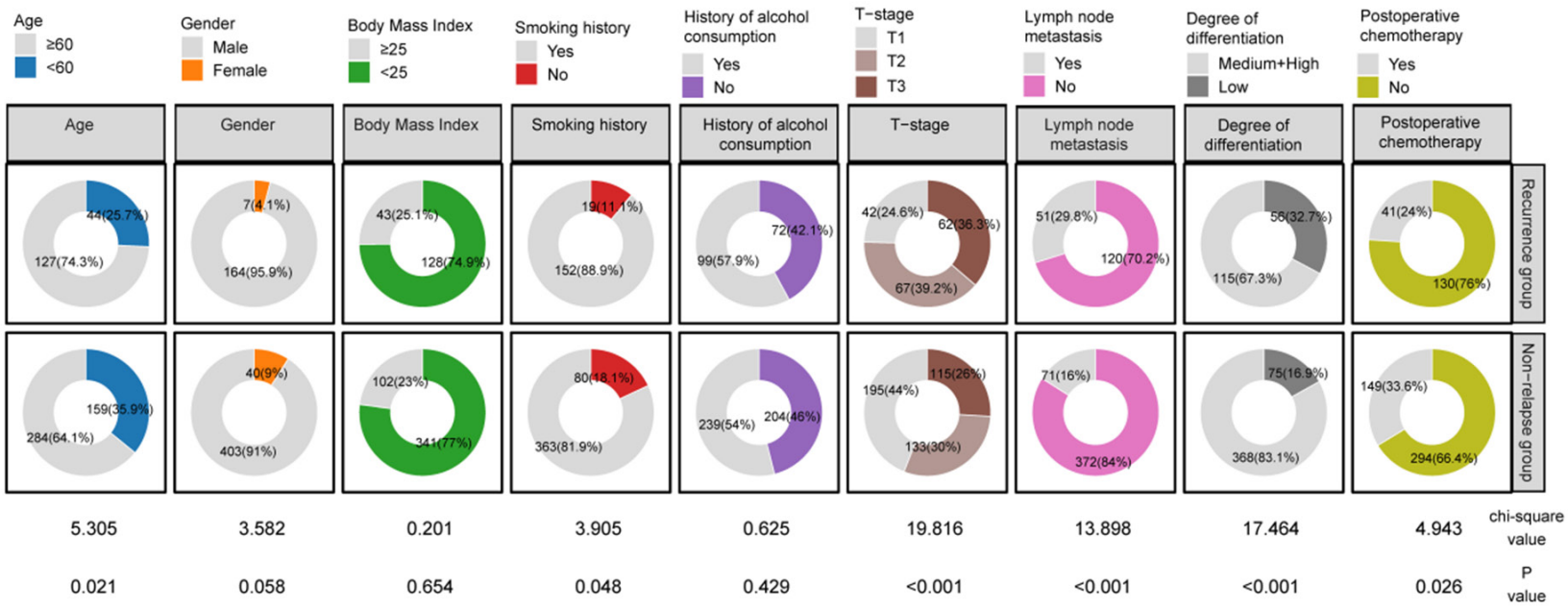

Figure 2. Comparison of baseline characteristics of patients between the recurrence and non-recurrence groups. Note: BMI, Body mass index; T stage, pathological T stage; LNM, lymph node metastasis.

Table 1. Comparison of laboratory indicators between recurrence and non-recurrence patients

Variable	Method	Total	Recurrence Group (n = 171)	Non-Recurrence Group (n = 443)	Statistic	*P*-value
Alb (g/L)	t-test	45.019 ± 5.151	41.960 ± 3.991	46.199 ± 5.065	9.828	< 0.001
Lym (10^9/L)	Mann-Whitney U (Z value)	2.10 [1.60, 2.50]	1.60 [1.10, 2.20]	2.20 [1.70, 2.60]	7.857	< 0.001
Neu (10^9/L)	Mann-Whitney U (Z value)	4.30 [3.10, 5.70]	5.40 [3.65, 7.10]	4.00 [3.00, 5.20]	5.841	< 0.001
PLT (10^9/L)	t-test	237.544 ± 46.370	256.421 ± 46.651	230.257 ± 44.203	6.473	< 0.001
PNI	t-test	450.196 ± 51.509	419.611 ± 39.908	462.002 ± 50.650	9.828	< 0.001
NLR	Mann-Whitney U (Z value)	2.10 [1.42, 3.11]	3.17 [2.04, 4.80]	1.89 [1.32, 2.57]	8.532	< 0.001
PLR	Mann-Whitney U (Z value)	114.85 [88.98, 158.35]	160.53 [116.38, 224.33]	103.33 [84.63, 134.38]	9.716	< 0.001
IL-6 (ng/L)	t-test	10.392 ± 3.395	12.987 ± 4.418	9.391 ± 2.208	13.357	< 0.001
IL-8 (ng/L)	t-test	90.332 ± 7.449	93.881 ± 8.018	88.963 ± 6.744	7.672	< 0.001

Note: Alb, Albumin; Lym, lymphocyte count; Neu, neutrophil count; PLT, platelet count; PNI, prognostic nutritional index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; IL-6, interleukin-6; IL-8, interleukin-8.

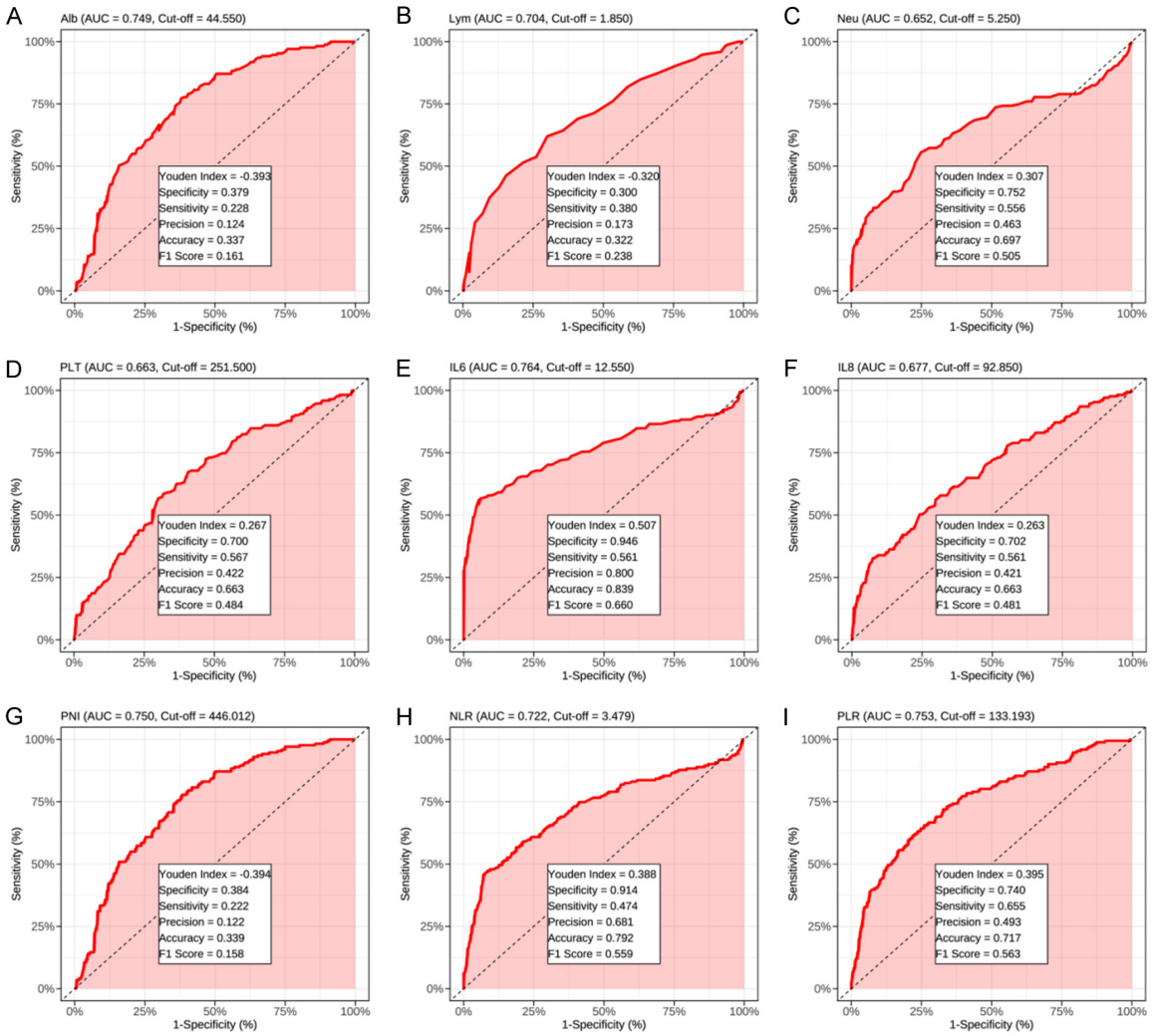

Figure 3. Receiver Operating Characteristic (ROC) curve analysis and cut-off values for laboratory indicators predicting postoperative recurrence in glottic laryngeal carcinoma. A. ROC curve for Alb in predicting postoperative recurrence. B. ROC curve for Lym in predicting postoperative recurrence. C. ROC curve for Neu in predicting postoperative recurrence. D. ROC curve for PLT in predicting postoperative recurrence. E. ROC curve for IL-6 in predicting postoperative recurrence. F. ROC curve for IL-8 in predicting postoperative recurrence. G. ROC curve for PNI in predicting postoperative recurrence. H. ROC curve for NLR in predicting postoperative recurrence. I. ROC curve for PLR in predicting postoperative recurrence. Note: Alb, Albumin; Lym, lymphocyte count; Neu, neutrophil count; PLT, platelet count; PNI, prognostic nutritional index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; IL-6, interleukin-6; IL-8, interleukin-8.

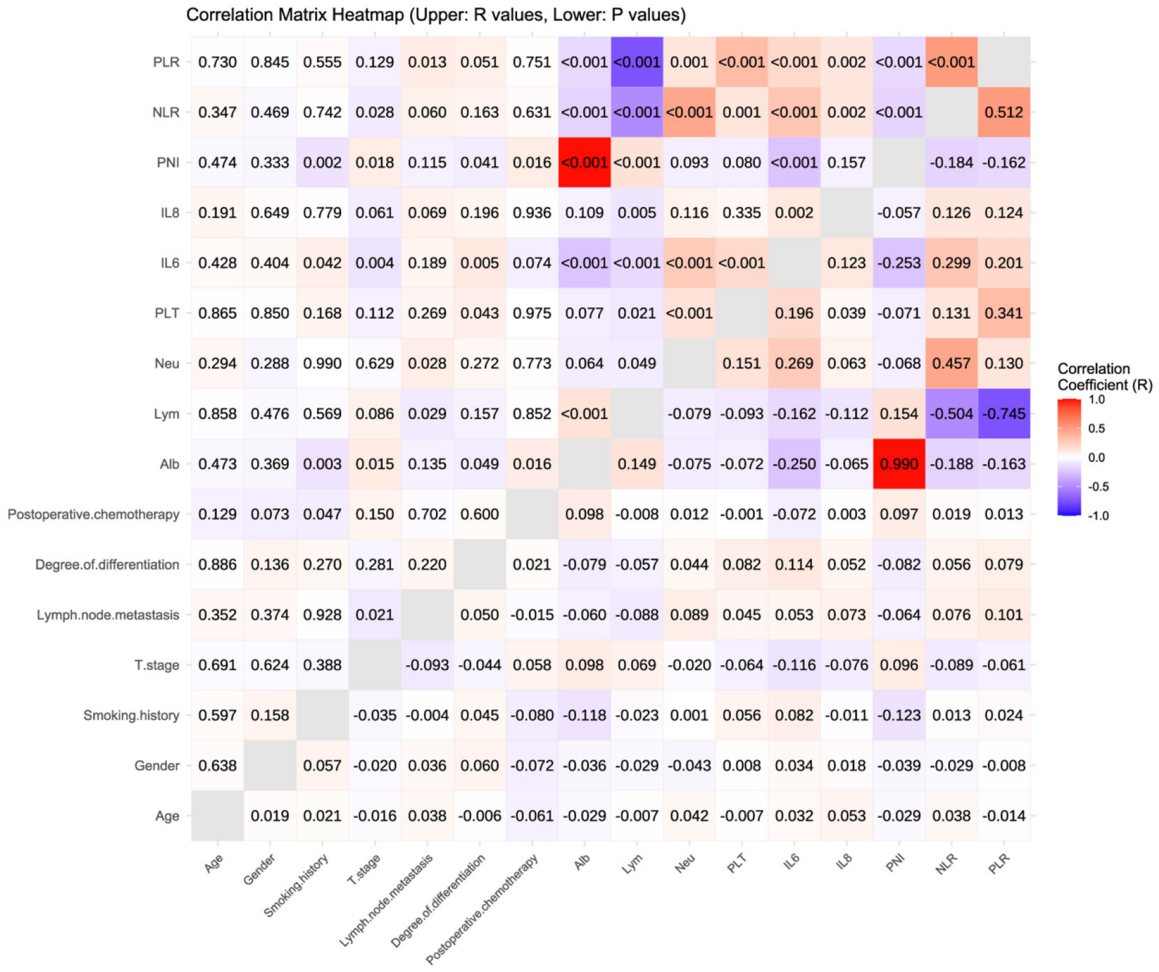

Figure 4. Spearman correlation matrix heatmap of variables after assignment. Note: Alb, Albumin; Lym, lymphocyte count; Neu, neutrophil count; PLT, platelet count; PNI, prognostic nutritional index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; IL-6, interleukin-6; IL-8, interleukin-8; Recurrence, recurrence.

likelihood of recurrence. These results are shown in **Tables 2** and **3**.

Multivariate logistic regression analysis further identified age (OR = 0.563, P = 0.047), lymph node metastasis (OR = 0.464, P = 0.014), degree of differentiation (OR = 0.497, P = 0.022), IL-6 (OR = 0.052, P < 0.001), IL-8 (OR = 0.356, P < 0.001), PNI (OR = 3.895, P < 0.001), NLR (OR = 0.253, P < 0.001), and PLR (OR = 0.331, P < 0.001) as independent factors influencing postoperative recurrence. PNI continued to show a strong protective effect (OR = 3.895, P < 0.001), while IL-6 exhibited the most significant negative impact (OR = 0.052, P < 0.001). Gender, smoking history, T stage, and postoperative chemotherapy did not show statistical significance in the multivariate analysis (P > 0.05), as presented in **Table 4**.

Univariate cox regression analysis and K-M survival analysis of significant indicators

Univariate Cox regression analysis revealed that age, T stage, lymph node metastasis, degree of differentiation, postoperative chemotherapy, IL-6, IL-8, PNI, NLR, and PLR were all significantly associated with recurrence-free survival (RFS) (P < 0.05), as shown in **Table 5**. Notably, PNI and IL-6 had the strongest predictive effects on RFS. Higher PNI levels were significantly associated with longer RFS (HR < 1, P < 0.001), while higher IL-6 levels were associated with shorter RFS (HR > 1, P < 0.001). K-M survival curves were plotted to validate these indicators' effects on survival (**Figure 5**). The results showed that the high PNI group had significantly higher RFS compared to the low PNI group (Log-rank P < 0.001), while the high IL-6,

Table 2. Variable assignment for logistic regression analysis

Variable	Assigned Values
Age	≥ 60 = 1, < 60 = 2
Gender	Male = 1, Female = 2
Smoking History	Yes = 1, No = 2
T Stage	T1 = 1, T2 = 2, T3 = 3
Lymph Node Metastasis	Yes = 1, No = 2
Degree of Differentiation	Poorly Differentiated = 1, Moderately + Well Differentiated = 2
Postoperative Chemotherapy	Yes = 1, No = 2
Alb (g/L)	< 44.55 = 2, ≥ 44.55 = 1
Lym (10^9/L)	< 1.85 = 2, ≥ 1.85 = 1
Neu (10^9/L)	< 5.25 = 2, ≥ 5.25 = 1
PLT (10^9/L)	< 251.5 = 2, ≥ 251.5 = 1
PNI	< 445.51 = 2, ≥ 445.51 = 1
NLR	< 3.479 = 2, ≥ 3.479 = 1
PLR	< 133.193 = 2, ≥ 133.193 = 1
IL-6 (ng/L)	< 12.55 = 2, ≥ 12.55 = 1
IL-8 (ng/L)	< 92.85 = 2, ≥ 92.85 = 1
Recurrence	Yes = 1, No = 2

Note: Alb, Albumin; Lym, lymphocyte count; Neu, neutrophil count; PLT, platelet count; PNI, prognostic nutritional index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; IL-6, interleukin-6; IL-8, interleukin-8; Recurrence, recurrence.

Table 3. Univariate logistic regression analysis of factors associated with postoperative recurrence

Variable	Estimate	Std. Error	*P* Value	OR	Lower	Upper
Age	-0.480	0.201	0.017	0.619	0.414	0.912
Gender	-0.844	0.42	0.045	0.430	0.173	0.922
Smoking History	-0.567	0.273	0.038	0.567	0.324	0.949
T Stage	0.450	0.112	< 0.001	1.568	1.261	1.958
Lymph Node Metastasis	-0.801	0.211	< 0.001	0.449	0.297	0.681
Degree of Differentiation	-0.871	0.206	< 0.001	0.419	0.279	0.628
Postoperative Chemotherapy	0.474	0.205	0.021	1.607	1.082	2.424
IL-6	-3.107	0.26	< 0.001	0.045	0.026	0.073
IL-8	-1.104	0.186	< 0.001	0.332	0.23	0.476
PNI	1.726	0.208	< 0.001	5.621	3.77	8.544
NLR	-2.261	0.229	< 0.001	0.104	0.066	0.162
PLR	-1.689	0.194	< 0.001	0.185	0.126	0.269

Note: OR, Odds Ratio; PNI, Prognostic Nutritional Index; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; IL-6, Interleukin-6; IL-8, Interleukin-8; T Stage, T Stage.

NLR, and PLR groups exhibited significantly lower RFS than their low-level counterparts (Log-rank P < 0.001), as shown in **Figure 5**.

Multivariate cox regression analysis of recurrence-free survival and selection of independent predictive factors

Multivariate Cox regression analysis identified age, T stage, lymph node metastasis, degree of differentiation, postoperative chemotherapy, IL-6, IL-8, PNI, and PLR as independent factors affecting postoperative RFS (P < 0.05). Specifically, patients under 60 years of age had significantly higher RFS compared to those aged ≥ 60 years (HR = 0.612, P = 0.008). T stage showed that patients at T3 had a significantly higher risk of recurrence compared to those at T1 (HR = 2.087, P = 0.001), while T2 was not statistically significant (P = 0.103). Patients

Table 4. Multivariate logistic regression analysis of factors associated with postoperative recurrence

Variable	Estimate	Std. Error	*P* Value	OR	Lower	Upper
Age	-0.574	0.288	0.047	0.563	0.316	0.983
Gender	-0.975	0.581	0.093	0.377	0.112	1.109
Smoking History	-0.330	0.395	0.402	0.719	0.323	1.526
T Stage	0.222	0.162	0.170	1.249	0.908	1.718
Lymph Node Metastasis	-0.768	0.314	0.014	0.464	0.251	0.863
Degree of Differentiation	-0.700	0.306	0.022	0.497	0.273	0.907
Postoperative Chemotherapy	0.316	0.297	0.287	1.372	0.772	2.479
IL-6	-2.948	0.335	< 0.001	0.052	0.026	0.099
IL-8	-1.032	0.267	< 0.001	0.356	0.21	0.599
PNI	1.360	0.277	< 0.001	3.895	2.284	6.797
NLR	-1.375	0.335	< 0.001	0.253	0.13	0.483
PLR	-1.106	0.301	< 0.001	0.331	0.183	0.597

Note: OR, Odds Ratio; PNI, Prognostic Nutritional Index; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; IL-6, Interleukin-6; IL-8, Interleukin-8; T Stage, T Stage.

Table 5. Univariate cox regression analysis of factors associated with recurrence-free survival

Variable	Beta	Std. Error	*P* Value	HR	Lower	Upper
Age						
≥ 60						
< 60	-0.394	0.175	0.024	0.675	0.479	0.951
Gender						
Male						
Female	-0.751	0.386	0.052	0.472	0.221	1.005
Smoking History						
Yes						
No	-0.468	0.243	0.055	0.627	0.389	1.009
T Stage						
T1						
T2	0.736	0.197	< 0.001	2.087	1.419	3.07
T3	0.84	0.2	< 0.001	2.317	1.566	3.428
Lymph Node Metastasis						
Yes						
No	-0.659	0.167	< 0.001	0.518	0.373	0.718
Degree of Differentiation						
Poorly Differentiated						
Moderately + Well Differentiated	-0.727	0.163	< 0.001	0.483	0.351	0.666
Postoperative Chemotherapy						
Yes						
No	0.357	0.179	0.046	1.43	1.006	2.031
IL-6	0.237	0.017	< 0.001	1.268	1.226	1.311
IL-8	0.078	0.01	< 0.001	1.081	1.059	1.104
PNI	-0.015	0.002	< 0.001	0.985	0.982	0.988
NLR	0.275	0.024	< 0.001	1.317	1.255	1.381
PLR	0.005	0	< 0.001	1.005	1.004	1.006

Note: HR, Hazard Ratio; PNI, Prognostic Nutritional Index; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; IL-6, Interleukin-6; IL-8, Interleukin-8; T Stage, T Stage.

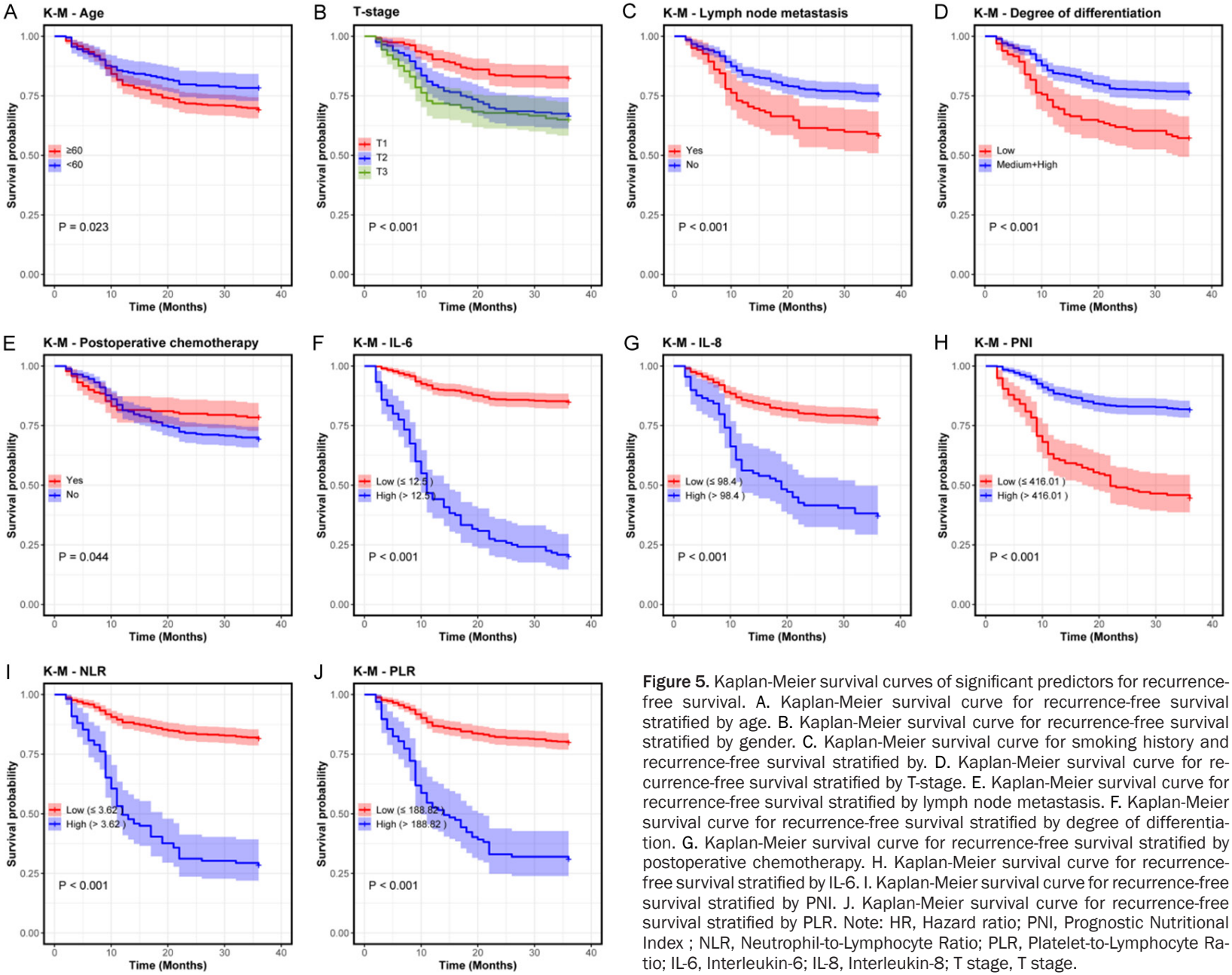

Figure 5. Kaplan-Meier survival curves of significant predictors for recurrence-free survival. A. Kaplan-Meier survival curve for recurrence-free survival stratified by age. B. Kaplan-Meier survival curve for recurrence-free survival stratified by gender. C. Kaplan-Meier survival curve for smoking history and recurrence-free survival stratified by. D. Kaplan-Meier survival curve for recurrence-free survival stratified by T-stage. E. Kaplan-Meier survival curve for recurrence-free survival stratified by lymph node metastasis. F. Kaplan-Meier survival curve for recurrence-free survival stratified by degree of differentiation. G. Kaplan-Meier survival curve for recurrence-free survival stratified by postoperative chemotherapy. H. Kaplan-Meier survival curve for recurrence-free survival stratified by IL-6. I. Kaplan-Meier survival curve for recurrence-free survival stratified by PNI. J. Kaplan-Meier survival curve for recurrence-free survival stratified by PLR. Note: HR, Hazard ratio; PNI, Prognostic Nutritional Index ; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; IL-6, Interleukin-6; IL-8, Interleukin-8; T stage, T stage.

Table 6. Multivariate cox regression analysis of independent factors associated with recurrence-free survival

Variable	Beta	Std. Error	*P* Value	HR	Lower	Upper
Age						
≥ 60						
< 60	-0.491	0.185	0.008	0.612	0.426	0.879
T Stage						
T1						
T2	0.339	0.208	0.103	1.404	0.934	2.111
T3	0.736	0.221	0.001	2.087	1.353	3.221
Lymph Node Metastasis						
Yes						
No	-0.784	0.188	< 0.001	0.457	0.316	0.66
Degree of Differentiation						
Poorly Differentiated						
Moderately + Well Differentiated	-0.553	0.166	0.001	0.575	0.416	0.796
Postoperative Chemotherapy						
Yes						
No	1.105	0.215	< 0.001	3.019	1.981	4.599
IL-6	0.146	0.018	< 0.001	1.158	1.118	1.199
IL-8	0.048	0.01	< 0.001	1.049	1.028	1.07
PNI	-0.012	0.002	< 0.001	0.988	0.984	0.991
NLR	0.035	0.039	0.362	1.036	0.96	1.118
PLR	0.004	0.001	< 0.001	1.004	1.002	1.006

Note: HR, Hazard Ratio; PNI, Prognostic Nutritional Index; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; IL-6, Interleukin-6; IL-8, Interleukin-8; T Stage, T Stage.

without lymph node metastasis had significantly higher RFS than those with lymph node metastasis (HR = 0.457, P < 0.001). Additionally, patients with moderately to well-differentiated tumors had a significantly lower risk of recurrence compared to those with poorly differentiated tumors (HR = 0.575, P = 0.001). Postoperative chemotherapy served as a significant protective factor, with those who did not receive chemotherapy exhibiting a higher recurrence risk (HR = 3.019, P < 0.001). Both IL-6 and IL-8 were important risk factors for recurrence, with elevated levels significantly increasing the risk (IL-6: HR = 1.158, P < 0.001; IL-8: HR = 1.049, P < 0.001). PNI remained a protective factor, with higher levels reducing recurrence risk (HR = 0.988, P < 0.001). PLR was also significantly associated with an increased risk of recurrence (HR = 1.004, P < 0.001). However, NLR showed significance in the univariate analysis but did not provide independent predictive value in the multivariate analysis (P = 0.362), as detailed in **Table 6**.

Construction of the nomogram model and comparison of baseline characteristics

Using the independent factors identified through Cox regression analysis (age, T stage, lymph node metastasis, degree of differentiation, postoperative chemotherapy, IL-6, IL-8, PNI, and PLR), we constructed a Nomogram model to predict postoperative RFS (**Figure 6**). The risk formula is as follows: Logit(P) = -1.288 - 0.468 × Age < 60 + 0.413 × T-stageT2 + 0.777 × T-stageT3 - 0.765 × Lymph node metastasis-No + 0.650 × Degree of Low + 1.106 × Postoperative chemotherapy-No + 0.156 × IL6 + 0.050 × IL8 - 0.012 × PNI + 0.004 × PLR.

Prior to model construction, the data were randomly divided into a training cohort (n = 411) and a validation cohort (n = 203). Baseline characteristics between the two cohorts were compared (Table S2), revealing no significant differences between the groups regarding recurrence status, age, T stage, lymph node

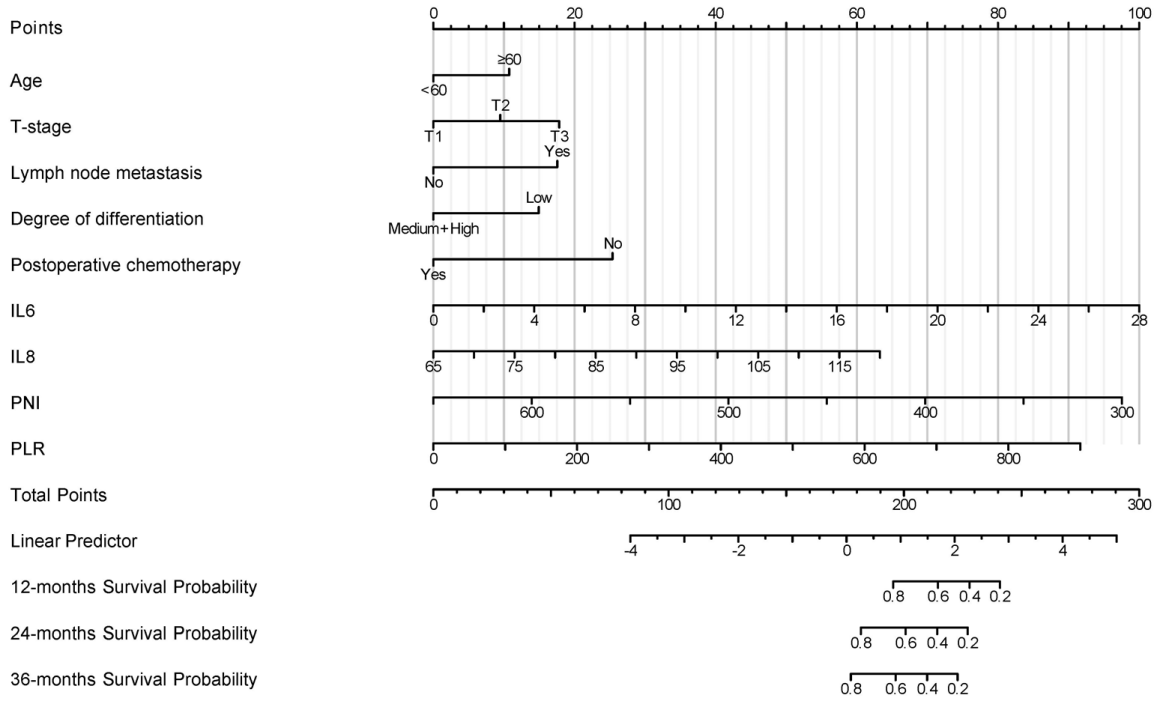

Figure 6. Nomogram model constructed based on independent factors selected from multivariate cox regression analysis.

metastasis, degree of differentiation, postoperative chemotherapy, IL-6, IL-8, PNI, PLR, and risk scores (all P > 0.05).

Performance evaluation and calibration validation of the nomogram model

The performance of the Nomogram model was assessed using both the training and validation cohorts (**Figure 7**). In the training cohort, the K-M survival curve (**Figure 7A**) demonstrated the high-risk score group exhibited markedly lower survival rates than the low-risk score group (Log-rank P < 0.001). ROC curve analysis (**Figure 7B**) revealed AUC values of 0.887, 0.910, and 0.915 for predicting 12-month, 24-month, and 36-month RFS, respectively, indicating high discriminative ability. Calibration curves (**Figure 7C**) confirmed a strong agreement between predicted and actual survival rates. The concordance index (C-index) for the training cohort was 0.860 (95% CI: 0.843-0.877), demonstrating the model's reliability and accuracy.

In the validation cohort, the K-M survival curve (**Figure 7D**) similarly showed that the high-risk score group had significantly lower RFS compared to the low-risk score group (Log-rank P < 0.001). ROC curve analysis (**Figure 7E**) indicated that the Nomogram model maintained strong discriminative ability, with AUC values of 0.895, 0.908, and 0.907 for predicting 12-month, 24-month, and 36-month RFS, respectively. The calibration curves (**Figure 7F**) showed good consistency between the predicted probabilities and actual survival rates. The concordance index (C-index) for the validation cohort was 0.857 (95% CI: 0.835-0.880). Additionally, global statistical tests, including the Likelihood ratio test, Wald test, and Score test, were all significant (P < 0.001) in both the training and validation cohorts, further validating the Nomogram model's reliability and stability in predicting postoperative recurrence-free survival.

Discussion

This retrospective study analyzed data from 614 patients with LSCC to identify key factors influencing postoperative recurrence and to construct a predictive model. The model was based on both traditional clinicopathological features and novel inflammatory and immune indicators. The results showed that age, T

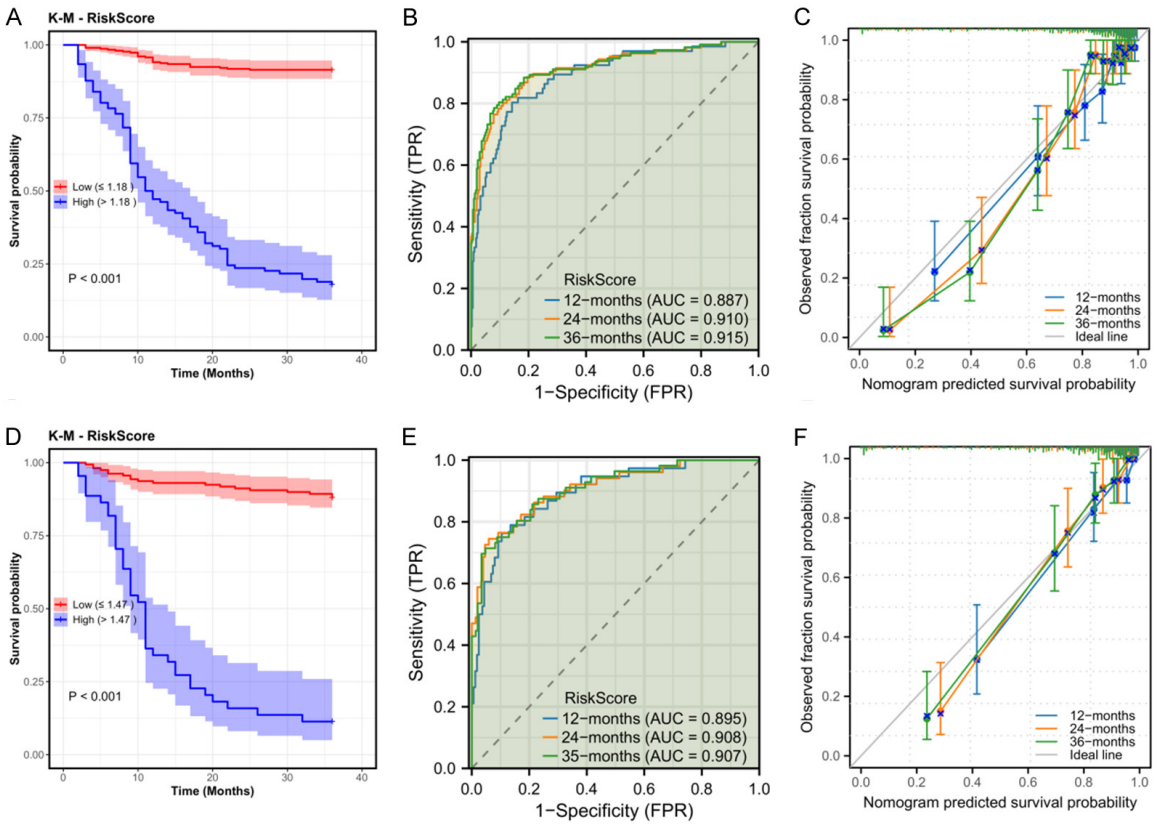

Figure 7. Performance evaluation of the nomogram model in the training and validation cohorts. A. Kaplan-Meier survival curve of RiskScore in the training cohort. B. ROC curve for 12-month, 24-month, and 36-month survival prediction in the training cohort. C. Calibration curve for 12-month, 24-month, and 36-month survival prediction in the training cohort. D. Kaplan-Meier survival curve of RiskScore in the validation cohort. E. ROC curve for 12-month, 24-month, and 36-month survival prediction in the validation cohort. F. Calibration curve for 12-month, 24-month, and 36-month survival prediction in the validation cohort. Note: AUC, Area under the curve; C-index, concordance index; ROC, receiver operating characteristic; K-M, Kaplan-Meier.

stage, lymph node metastasis, degree of differentiation, IL-6, IL-8, PNI, and PLR were independent factors affecting postoperative recurrence. The developed Nomogram model exhibited excellent predictive performance in both the training and validation cohorts. In the training cohort, the AUC values for 12-month, 24-month, and 36-month RFS were 0.887, 0.910, and 0.915, respectively. In the validation cohort, these values were 0.895, 0.908, and 0.907. The C-index values were 0.860 and 0.857, and the calibration curves demonstrated a high degree of agreement between the model's predictions and actual outcomes. These findings indicate that the predictive model, which integrates traditional clinicopathological features with novel inflammatory and immune indicators, has significant advantages in assessing the risk of postoperative recurrence in patients with glottic laryngeal cancer, providing a scientific basis for clinical decision making.

Compared to existing literature, this study not only confirms the importance of the TNM staging system in the prognostic evaluation of laryngeal cancer [22], but also, for the first time, systematically incorporates inflammatory and immune indicators (such as IL-6, IL-8, PNI, and PLR) into the recurrence prediction model, significantly enhancing the accuracy and comprehensiveness of predictions [23]. Previous studies have primarily focused on individual blood indices or traditional clinicopathological features in tumor prognosis, often neglecting the impact of the patient's overall condition and immune function on tumor recurrence [24]. By integrating multiple indicators, this study developed a more comprehensive and accurate Nomogram model, further validating the poten-

tial value of inflammatory and immune indicators in predicting tumor recurrence. Notably, IL-6 and IL-8 play crucial roles in the tumor microenvironment by promoting tumor cell proliferation, angiogenesis, and metastasis, thereby significantly influencing tumor recurrence and progression [25]. Additionally, PNI, as a prognostic nutritional index, reflects the patient's nutritional status and immune function, further validating its protective role in predicting recurrence risk [26].

Regarding clinicopathological factors, van de Weerd et al. [27] found that patients aged ≥ 60 years had a significantly higher risk of postoperative recurrence compared to those aged < 60 years. This may be due to a decline in immune function, poorer physical condition, and altered tumor biology in elderly patients. As age increases, the immune system weakens, reducing the body's ability to combat tumor cells and increasing the risk of recurrence [28]. Moreover, elderly patients often suffer from multiple chronic diseases, which may affect postoperative recovery and the efficacy of antitumor treatments, indirectly increasing recurrence risk. High T3 stage and the presence of lymph node metastasis significantly increased the risk of recurrence, indicating strong tumor invasiveness and high metastatic potential [29]. T staging reflects the local invasiveness of the tumor, with T3 tumors typically exhibiting deeper infiltration, which heightens the likelihood of postoperative recurrence. Lymph node metastasis is an important marker of tumor spread, indicating that tumor cells have overcome local defenses and possess strong dissemination capabilities, thus increasing the risk of recurrence and metastasis [30]. In terms of differentiation, poorly differentiated tumor cells exhibit high atypia, rapid proliferation, and a higher propensity for recurrence, which are closely linked to the malignancy and biological behavior of the cells. Poorly differentiated tumors tend to be more invasive and adaptable, enabling them to evade immune surveillance more effectively and thus increasing the risk of recurrence.

Inflammatory and immune indicators demonstrated significant predictive value in this study. Zhang et al. [23] proposed that IL-6 and IL-8, as key inflammatory cytokines, promote tumor growth, angiogenesis, and metastasis within the tumor microenvironment. IL-6 activates the JAK-STAT pathway, enhancing tumor cell proliferation and invasion, which increases the cell survival capacity. IL-8 is involved in angiogenesis and inflammatory responses, enhancing the metastatic potential of tumors [25]. These inflammatory cytokines not only reflect changes in the tumor microenvironment but also directly affect tumor recurrence and progression by regulating the interactions between tumor cells and immune cells. Moreover, PNI, NLR, and PLR, as composite inflammatory and immune indicators, reflect the patient's nutritional status and immune function. A higher PNI indicates better nutritional and immune status, which helps suppress tumor recurrence [31], while elevated NLR and PLR reflect activated inflammatory states and immune suppression, thereby increasing the risk of recurrence [32]. Specifically, PNI serves as a comprehensive reflection of nutritional and immune status, demonstrating a significant protective effect against tumor recurrence. Meanwhile, NLR and PLR, as sensitive indicators of systemic inflammation, effectively reflect the level of inflammation and immune function, playing important roles in assessing recurrence risk [33, 34].

Furthermore, other studies have confirmed the prognostic value of NLR and PLR across different cancer types, further supporting their application in this study. For instance, Liu et al. [35] evaluated peripheral blood markers in 157 patients with advanced non-small cell lung cancer (NSCLC) undergoing immunotherapy and found that NLR and red blood cell distribution width (RDW) were independent predictors of PFS and OS. High NLR and RDW were associated with poorer PFS and OS, indicating that these blood markers can predict the efficacy of immunotherapy. Similarly, Pu et al. [36] conducted a retrospective study assessing the relationship between inflammatory-nutritional indicators (such as NLR, PLR, and ALB) and survival in advanced NSCLC patients receiving PD-1 inhibitor therapy. The results showed that high NLR and PLR, as well as low Alb, were associated with poorer OS, while high absolute eosinophil count (AEC) and high absolute monocyte count (AMC) were associated with reduced survival risk. These findings further support the importance of NLR and PLR as predictors of recurrence risk and demonstrate that

integrating multiple blood markers can enhance the accuracy of prognostic assessments.

The construction of the Nomogram model and its excellent predictive performance have significant clinical implications. Firstly, the model's ability to assess individual risk enables clinicians to develop personalized follow-up plans and treatment strategies based on each patient's specific condition. High-risk patients can receive more frequent monitoring and more aggressive adjuvant therapies, thereby reducing the risk of recurrence and improving survival rates [23]. Additionally, similar predictive models in other cancer types have demonstrated their clinical utility, further validating the effectiveness of combining multiple indicators for risk assessment. For example, Faria et al. [37] developed a prognostic model for early-stage breast cancer by integrating NLR with clinicopathological features, which effectively stratified patients into different recurrence-risk groups. Tada et al. [38] proposed a new index based on inflammatory markers to predict the efficacy of Nivolumab treatment in patients with recurrent/metastatic head and neck cancer, suggesting that combining multiple indicators for risk assessment is highly effective. Furthermore, the model can be used to evaluate the necessity of adjuvant chemotherapy, optimize resource allocation, enhance treatment efficacy, and improve patient prognosis.

The strengths of this study lie in its large sample size (614 patients) and the comprehensive integration of multiple indicators, combining traditional clinicopathological features with novel inflammatory and immune markers. This approach significantly enhanced the comprehensiveness and accuracy of the predictive model. The constructed Nomogram model demonstrated excellent predictive performance in both the training and validation cohorts, exhibiting good stability and generalizability, which provides a valuable reference for clinical application. However, the study also has limitations. Firstly, the retrospective study design may introduce selection bias and information bias, affecting the generalizability of the results. Secondly, external validation was not performed, and some potential factors, such as HPV infection status and lifestyle, were not included, which may affect the comprehensiveness of recurrence-risk assessment. Future studies should conduct multicenter prospective research, integrate more biomarkers (such as miRNA and gene mutations), optimize model performance, enhance predictive accuracy, and improve clinical applicability to provide more precise tools for assessing tumor recurrence risk.

Conclusion

This study successfully constructed an efficient Nomogram model for predicting postoperative recurrence by integrating traditional clinicopathological features with novel inflammatory and immune indicators. The model demonstrated excellent predictive performance in both the training and validation cohorts, indicating its substantial clinical applicability. Key indicators such as IL-6, IL-8, and PNI played significant roles in predicting recurrence risk, providing a scientific basis for follow-up management and individualized treatment of postoperative patients.

Disclosure of conflict of interest

None.

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Table S1. Baseline data sheet

Factor	Total	Recurrence Group (n= 171)	Non-Recurrence Group (n = 443)	Statistic	*P*-value
Age					
≥ 60	411	127	284	5.755	0.016
< 60	203	44	159		
Gender					
Male	567	164	403	4.252	0.039
Female	47	7	40		
BMI (kg/m^2)					
≥ 25	145	43	102	0.308	0.579
< 25	469	128	341		
Smoking History					
Yes	515	152	363	4.403	0.036
No	99	19	80		
Alcohol Consumption History					
Yes	338	99	239	0.776	0.378
No	276	72	204		
T Stage					
T1	237	42	195	19.816	<0.001
T2	200	67	133		
T3	177	62	115		
Lymph Node Metastasis					
Yes	122	51	71	14.752	<0.001
No	492	120	372		
Degree of Differentiation					
Poorly Differentiated	131	56	75	18.394	<0.001
Moderately + Well Differentiated	483	115	368		
Postoperative Chemotherapy					
Yes	190	41	149	5.385	0.020
No	424	130	294		

Note: Age, Gender, Body Mass Index (BMI), Smoking History, Alcohol Consumption History, T Stage, Lymph Node Metastasis, Degree of Differentiation, and Postoperative Chemotherapy are baseline characteristics of the patients.

Table S2. Comparison of baseline characteristics between training and validation cohorts

Factor	Total	Training Cohort (n = 411)	Validation Cohort (n = 203)	Statistic	*P*-value
Recurrence					
Yes	171	113	58	0.079	0.779
No	443	298	145		
Age					
≥ 60	411	276	135	0.026	0.872
< 60	203	135	68		
T Stage				0.122	0.941
T1	237	160	77		
T2	200	132	68		
T3	177	119	58		
Lymph Node Metastasis				0.328	0.567
Yes	122	79	43		
No	492	332	160		
Degree of Differentiation				0.125	0.724
Poorly Differentiated	131	86	45		
Moderately + Well Differentiated	483	325	158		
Postoperative Chemotherapy				0.001	0.973
Yes	190	127	63		
No	424	284	140		
IL-6 (ng/L)	10.00 [8.22, 11.90]	10.00 [8.20, 11.90]	10.00 [8.45, 11.85]	0.111	0.912
IL-8 (ng/L)	90.332 ± 7.449	90.327 ± 7.488	90.344 ± 7.387	-0.028	0.978
PNI	450.196 ± 51.509	450.886 ± 51.025	448.798 ± 52.574	0.472	0.637
PLR	114.85 [88.98, 158.35]	114.62 [88.23, 155.94]	115.00 [90.31, 162.66]	0.156	0.876
RiskScore	0.28 [-0.49, 1.30]	0.27 [-0.49, 1.25]	0.28 [-0.49, 1.34]	0.121	0.903

Note: Recurrence, Age, T Stage, Lymph Node Metastasis, Degree of Differentiation, Postoperative Chemotherapy, IL-6, IL-8, PNI, PLR, and RiskScore are baseline characteristics compared between the training and validation cohorts.