Development and validation of nomogram to predict risk of survival in patients with laryngeal squamous cell carcinoma

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Research

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Abstract

Background: Due to a wide variation of tumor behavior, prediction of survival in laryngeal squamous cell carcinoma (LSCC) patients received curative-intend surgery is an important but formidable challenge. We attempted to establish a nomogram to precisely predict survival probability in LSCC patients.

Methods: A total of 369 consecutive LSCC patients underwent curative resection between 2008 and 2012 at Hunan Province Cancer Hospital were included in this study. Subsequently, 369 LSCC patients were assigned to a training set (N=261) and a validation set (N=108) at random. On the basis of multivariable Cox regression analysis results, we developed a nomogram. The predictive accuracy and discriminative ability of the nomogram were confirmed by calibration curve and a concordance index (C-index), and compared with TNM stage system by C-index, receiver operating characteristic (ROC) analysis. Decision curve analysis (DCA) was conducted to estimate clinical usefulness of our nomogram.

Results: Six independent parameters to predict prognosis were age, pack years, N-stage, lymph node ratio (LNR), anemia and albumin, which were all assembled into the nomogram. The calibration curve verified excellent models' concordance. The C-index of the nomogram was 0.73 (0.68-0.78), and the area under curve (AUC) of nomogram in predicting overall survival (OS) were 0.766, which were significantly higher than traditional TNM stage. Decision curve analysis further demonstrated that our nomogram had larger net benefit than TNM stage.

Conclusion: A risk prediction nomogram for patients with LSCC, incorporating easily assessable clinicopathologic factors, generates more precise estimations of the survival probability when compared TNM stage alone, but still need additional data before being used in clinical application.

Introduction

Laryngeal squamous cell carcinoma(LSCC) is among the most frequently diagnosed head and neck squamous cell cancers (HNSCC), with almost 26,300 new cases and about 14,500 deaths in China in 2015[1]. According to reports, the five-year overall survival rate varies between approximately 50% and 60%, depending on treatment model, tumor-related factors, and patient-related factors [2]. A variety of treatments are applied to cure LSCC patients, including surgery, radiotherapy and chemotherapy [3]. Despite advances in therapies, the five-year survival rate was still on the decline according to the review of American Cancer Society [4, 5]. On account of a broad spectrum of tumor histological subtypes and diverse clinical behaviors, the prediction of survival risk in patients with LSCC is a difficult task for clinicians. Therefore, it is of great importance to identify reliable and convenient predictive parameters/models to predict survival and optimize therapeutic strategies in LSCC patients.

A mass of predictive variables have been found in LSCC patients [6–7]. Unfortunately, due to the small number of patients, heterogeneous histological subtype and treatment modalities, the impact of clinical factors on survival risk was inconsistent and varies widely. Currently, the tumor-node-metastasis (TNM) stage [8], based on anatomical information, is a common tool to evaluate the prognosis of patients.

Though the TNM stage works well on the population level, it less effectively prognosticates at an individual level. Several nomograms, are visual description of predictive statistical models for personalized patients, have been built to predict the survival probability in patients with laryngocarcinoma [9–13]. But these studies enrolled different patient cohorts (eg, laryngeal cancer, advanced laryngeal cancer, and distant metastatic laryngeal carcinoma), and treatment modalities (ie, radiotherapy vs surgery). Moreover, all these prediction models were created based on the population of western countries [9–13]. Due to difference in environmental exposures, ethnical diversity [14], adjuvant treatment after operation and treatment modalities, the clinical features of LSCC in eastern countries are also different from western countries. Such discrepancies may lead to inaccurate prediction of clinical outcome if using the same model for the eastern population. For example, the infection rate of human papillomavirus (HPV) is observably different between westerner and easterner in laryngeal carcinoma [15], and HPV positive patients were sensitive to radiotherapy and chemotherapy and showed superior survival [16–17]. Furthermore, the difference of demographic and socio-economic status (SES) may also affect survival outcome of LSCC patients [18].

In the present study, we attempted to develop and internally validate a nomogram to aid decision making in Asian patients with LSCC after surgical resection. Additionally, we compared prediction performance and clinical usability between the nomogram and TNM stage. Notably, the nomogram will allow for tailoring of the therapy to personalized patients in the long term (e.g., for the choice adjuvant treatment).

Methods

Patients

Patients with LSCC who after radical surgery were consecutively recorded between October 2008 and November 2012 at Hunan Province Cancer Hospital, with follow up until March 2018. The inclusion criteria were as follows: (a) patients were older than 18 years old; (b) patients with LSCC diagnosed by multidisciplinary teams, including clinicians, radiologist and pathologist; (c) without neoadjuvant chemotherapy or radiotherapy before underwent laryngectomy. The exclusion criteria were as follows: (a) patients with metastasis at diagnosis; (b) patients with other synchronous cancers; (c) indeterminate or incomplete clinicopathologic information; Consequently, a total of 369 patients with LSCC, were enrolled in this study, diagnosed from October 2008 to November 2012. Subsequently, 369 LSCC patients were assigned to a training set (N = 261) and a validation set (N = 108) by R software at random. This retrospective study was endorsed by the ethics committee of Hunan Province Cancer Hospital, which waived the need for informed consent. The trial was registered with ClinicalTrials.gov (NCT03747783).

Data extraction and follow-up

Clinicopathologic baseline characteristics, including demographics, laboratory tests and pathologic reports were retrospectively extracted for each patient from the HIS medical system of our hospital. According to American Joint Committee on Cancer (AJCC) tumor-node -metastasis (TNM) stage system eighth edition, the TNM stage of LSCC was affirmed by primarily pathological results and secondly

imaging reports [8]. Laboratory analysis of hemoglobin and albumin was done via routine blood detections within 1 week before surgery. Anemia was defined as hemoglobin level below 13.7 g/dL for men and below 12.1 g/dL for woman, which corresponds to 8.5 mmol/L and 7.5 mmol/L respectively. The threshold value for albumin level was < 3.5 g/dL and ≥ 3.5 g/dL, according to the normal range used at our institution. After classifying the patients with survival status, we computed the optimal cutoff pointes of lymph node ratio (LNR) by receiver operating curve (ROC) analysis according to maximum Youden index (sensitivity + specificity − 1).

The standard operation for LSCC was a total or subtotal laryngectomy or transoral laser microsurgery determined according to the characteristics of the case (mainly the stage) by the Head and Neck Cancer Committee, with preserving the function of the larynx as much as possible. Curative resection was defined as no tumor remaining after removal, both macroscopically and microscopically. The clinical end point was overall survival (OS), defined as the time from surgery to death. In addition, patients who were alive were counted as censored observations at the time of last follow-up. After completion of surgical therapy, patients received regular follow-up from their surgeon and/or the surveillance team every 3 months for the first year, every 3–6 months for the second and third years, and every 6 months thereafter. All living patients who did not show up for a scheduled check up or who were lost to follow up were reminded by telephone.

Statistical analysis

Nonnormally distributed data were described as median interquartile range and normally distributed data were presented as mean (standard deviation), which were tested by Wilcoxon rank sum tests or t tests following the distribution of the parameters. Categorical variables were reported as number (percentage), which were compared using Chi-square or Fisher's exact tests.

Given the potential prognostic value of the clinicopathologic variables, univariate Cox regression analysis were applied to preliminarily identify clinical risk parameters related to OS in the training set. Linearity assumption for continuous variables were evaluated by restricted cubic splines [19]. According to clinical reasoning, categorical variables were grouped, which were made before modeling. Variables were subjected to multivariable Cox regression analysis when its P value below 0.05 or less in the univariate analyses. Additionally, to investigate the degree of multicollinearity among variables, the variance inflation factor (VIF) was calculated in the multivariable Cox regression analysis. If VIF was > 10, then multicollinearity was high [20].

According to the results of multivariable Cox regression analysis, a nomogram was constructed, which select the significantly relevant OS factors by a backward step-down process with the Akaike information criterion [21]. The performance of the nomogram was evaluated in training and validation sets in terms of discrimination and calibration. The discrimination performance for predicting recurrence was numerically assessed by calculating Harrell's concordance index (C-index).In additional, according to the height of the linear predictor which is summed up all regression coefficients from an individual patient, we investigated discrimination ability by dividing the dataset into four groups. Discrimination was visualized by plotting a

Kaplan–Meier curve with Log-rank test for all four groups. The calibration curve was plotted to evaluate the degree of fitting of the nomogram.

Furthermore, receiver operating characteristic (ROC) curves analysis was carried out to estimate and compare the discrimination ability of the nomogram to TNM stage for predicting 3-year and 5-year RFS with area under curve (AUC) value. To evaluate the clinical usability of the nomogram, decision curve analysis (DCA), as a comprehensive method for estimating and comparing between nomogram and TNM stage, was conducted by computing the net benefits for a range of threshold probabilities[22].

The VIFs were done by "car" package. The ROC curves were plotted by "surivivalROC" package. Nomogram establishment and calibration plots were conducted using the "rms" package. DCA was performed using the "stdca.R". SPSS statistics 22.0 and R software (R version 3.5.2) were used to perform the statistical analysis. A two-sided P value of .05 or less was considered significant.

Results

Basic clinicopathologic characteristics

Table 1 displayed the characteristics of 261 LSCC patients in the training cohort and 108 patients in the validation cohort. The median follow-up time was 46 months (range = 2 to 67 months) and 45 months (range = 2 to 67 months) for training set and validation set, respectively. Of all the 369 LSCC patients, 249 patients (67.5%) survived during follow-up. The estimated 3-year and 5-year OS rates were 74% (70-78.1%) and 63.5% (58.8-68.2%) in the training set, respectively. Similarly, the estimated 3-year and 5-year OS rates were 73.9% (67.4-80.4%) and 67.7% (60.8-74.6%) in the validation set, respectively. **TableS1** summarized a detailed analysis of both sets**.**

Identification of OS relevant factors

Based on univariate analysis in the training set, we appraised eight parameters, including age, pack years, N-stage, number of positive of lymph node (PLNs), lymph node ratio (LNR), TNM stage, anemia and albumin, were associated with OS probability (**Table 2**). Multivariable analyses continued to confirm that age, pack years, N-stage, lymph node ratio (LNR), anemia and albumin, were independent risk factors for OS. In terms of the collinearity diagnosis, the VIFs of the six predictors varied between 1.02 and 2.58, confirming that there were no collinearity.

Development and Validation of the Nomogram

According to the results of multivariable Cox regression analysis, we built nomogram to predict 1-year, 3-year and 5-year OS in the training set (**Figure 1**). The C-index of the nomogram for OS prediction was 0.73

(0.68-0.78) (**Table 3**), and in **Figure 2A and S1A**, the calibration plot represent that predicted survival is corresponding with actual survival. Likewise, consistent findings were also presented in the validation set. The C-index of the nomogram for OS prediction was 0.84(0.78-0.89) (**Table 3**) and also presented good consistency between the predicted OS and the actual OS **(Figure 2B, S1B)**.Additionally, based on the linear predictor, we divided the data into four groups. The Kaplan-Meier analysis (Log-rank P<0.0001) of the four risk subgroups indicated the great discrimination of the nomogram in training set (**Figure 3A**) and in validation set (**Figure 3B**).

Comparison of predictive accuracy and clinical usefulness between nomogram and TNM stage

To further evaluate the predictive ability of nomogram, we compared nomogram with TNM stage model in both set. As was shown at **Table 3**, the C-index of nomogram was better than that of TNM stage, 0.59(0.54-0.65) in the training set and 0.57(0.49-0.66) in the validation set. Likelihood ratio test, linear trend $\chi 2$ test and akaike information criterion all demonstrated that the nomogram had better prediction efficiency than the TNM stage alone. ROC analysis also indicated that the nomogram was better than TNM stage alone (3-year AUC 0.762 vs 0.619 for the training set, 3-year AUC 0.902 vs 0.582 for the validation set & 5-year AUC 0.766 vs 0.597 for the training set, 5-year AUC 0.924 vs 0.568 for the validation set) in predicting 3-year OS (**Figure S2A, Figure S2B**) and 5-year OS (**Figure 4A, Figure 4B**). Finally, DCA was applied to compare the clinical useful of the nomogram to that of traditional TNM stage. DCA graphically showed that the nomogram was better than traditional TNM stage in both set in predicting 3 years OS **(Figure S3A, Figure S3B)** and 5 years OS **(Figure 5A, Figure 5B)**.

Discussion

Using a multivariate Cox regression analysis for a number of readily available clinicopathologic variables in a large group of unselected patients with LSCC, we developed a visual, ready-to-use nomogram for LSCC patients to predict survival outcome following curative resection. The nomogram accurately predicted survival probability, with a bootstrapped corrected C-index of 0.73, and 0.84 with an internal validation cohort. Additionally, the nomogram shown better predictive ability and clinical usability than TNM stage for predicting the survival of LSCC patients.

A number of risk-prediction nomograms have been published in recent years.

Egelmeer et al. [9] conducted the initial nomogram using a study cohort of 994 patients with laryngeal cancer receiving radiotherapy alone from 1977 to 2008 in the Netherlands. Consistent with our findings, they revealed that older age, hemoglobin level and higher N status to be poor prognosis for OS. The model might produce pessimistic survival estimates on account of continual refinement and evolution of treatment over the past four decades. In 2017, Multidisciplinary Larynx Cancer Working Group [10], using data from University of Texas MD Anderson Cancer Center database, constructed a dynamic risk model and clinical nomogram in locally advanced laryngeal patients by conditional survival analysis. They

uncovered age and nodal burden to be significant for 3-year or 6-year OS in the multivariate analysis, in compliance with our results. As the authors point out, the model might not be generalizable due to absence of external validation. Another risk prediction model based on 2752 LSCC patients underwent neck dissection in the Surveillance, Epidemiology, and End Results (SEER) database between 1988 and 2008 has been developed by Shi et al. [11]. The nomogram was constructed following eight independent prognostic clinical variables. However, only 20 patients were in undifferentiated subset, which likely reduced the accuracy of the prediction. Sequentially, Hoban et al. [12] established a prognostic model for patients with laryngeal cancer. The analysis data set was collected in University of Michigan Health System, which included 246 cases confirmed by biopsy, TNM stage I to IVb, previously untreated with laryngeal squamous cell carcinoma between 2003 and 2014.Missing variables were a source of imperfection in this estimation, which lead to potentially biassed results and a loss of statistical power [23].Recently, Petersen et al. study [13], which mined data covering patients diagnosed with advanced LSCC in the Netherlands (1991–2010), developed and validated a nomogram to predict 5-year OS in advanced SCC of the larynx. The study provides a C-index of 0.65, and 0.59 with an external validation set. The accuracy of this nomogram may have been limited by its neglect of several important clinical and laboratory prognostic indices, such as smoking status, hemoglobin value, and albumin level that are not available in the database.

To the best of our knowledge, this is the first study established a nomogram to predict survival probability in Asian patients with LSCC. We identified six independent predictors that age, pack years, N-stage, LNR, anemia and albumin, were extraordinarily frequent reported prognostic predictors in patients with LSCC [9–13, 24–27]. In the current study, in terms of risk stratification of the model, ability of discrimination and homogeneity, the performance of the nomogram in predicting survival ability is superior to the TNM staging. The strength of the current nomogram is that it incorporated clinicopathological factors, which are critically of importance for predicting recurrence risk, but cannot be adopted by TNM stage system. Remarkably, DCA results showed that LSCC survival-related treatment decision according to the nomogram led to more net benefit than treatment decision based on TNM stage, or treating either all patients or none. Taken together, the present nomogram would be clinically useful for the clinicians in tailoring survival-associated treatment decision.

Although our nomogram demonstrated impressive performance in LSCC survival prediction, there are specific limitations associated with our trial. First, study is a typical retrospective analysis conducted in a single institution. Because the database derived from a single tertiary cancer center, the model may only represent a kind of patient sample that cannot be extended to the general population. In spite of with perfect internal validation, the presented nomogram was not yet suitable for wide use prior to validation of external cohorts. Thus, external and multicenter prospective cohorts with large sample sizes are still needed to validate the clinical application of our model.

Second, this study is an observational cohort trial, which enrolled LSCC patients who underwent laryngectomy alone at our institution. Given treatment decision was made before inclusion in the trial,

there is a potential selection bias. Moreover, our nomogram was not applied to predict survival in LSCC patients with other radical treatment models, including radiotherapy and chemotherapy.

Third, the factors we choose were limited to those available in our database. Considering the database was confined, we cannot extend our variables. To begin with, comorbidity scores can be of great importance in survival predictions. Nevertheless, comorbidity scores were of absence in our cohort. In 2013, a risk-prediction nomogram for head and neck cancer incorporated the Adult Comorbidity Evaluation-27 (ACE-27) as a prognostic factor [28]. The effect of severe comorbidity seems to be comparable to that of T4 tumors or N3 on overall survival in their models. Another nomogram with exploratory post hoc analysis, adding American Society of Anesthesiologists (ASA) score which served as a replacement measure for comorbidity scores as a prognostic factor, increased C-index from 0.65 to 0.68 in advanced larynx cancer [13].but we were not able to integrated the impact of comorbidity on nomogram which may limit its performance of prediction. Though comorbidity would certainly affect overall survival estimates, our nomogram yielded similar C-index in the validation datasets and was much better than TNM stage. Next, we did not take into consider socio-economic status (SES). A number of studies have proven the value of SES in HNSCC [29–31]. Hence, we recommend that future studies should investigate whether SES might be value prediction to survival outcome in LSCC, and evaluate the additional worth of this factor in a multivariable prediction model. Final, the nomogram did not consider human papillomavirus (HPV). Published researches and meta-analysis indicated HPV positivity in patients with LSCC could be associated with a favorable prognosis, independently of other clinical-pathological factors [32, 33].

Fourth, anemia is considered to be one of the diagnostic standard for tumor cachexia, accompanied by weight loss. As we know, tumor cachexia have a negative effect on OS, so it may be a potential confounding factor. [34]. Hence, the role of anemia and cancer cachexia as independent predictors of survival needs further research.

Fifth, with the advent of modern gene-array and immunohistochemistry technology, molecular variables may help predict survival probability of LSCC. As we know, LSCC is a heterogeneous disease, which means that it needed better tools to assist patients and physicians to make choices in treatment options. The combination of clinical, pathologic and molecular variables maybe finally uncover more robust and powerful measures for stratification of disease risk than any single approach.

Conclusion

We have built visual, easy-to-use nomogram, based on a large system coding database, for the prediction of survival and with several easily available clinicopathologic variables in patients with LSCC. The predictive ability and clinical usefulness of nomogram is significantly better than of the TNM stage alone. Although it is not a substitute for clinical reasoning, it may be helpful to the decision-making process of LSCC patients.

Abbreviations

LSCC
laryngeal squamous cell carcinoma; ROC:receiver operating characteristic; OS:overall survival; AUC:area under curve; DCA:decision curve analysis; LNR:lymph node ratio; HNSCC:head and neck squamous cell cancers; AJCC:American Joint Committee on Cancer; TNM:tumor-node-metastasis; HPV:human papillomavirus; SES:socio-economic status; VIF:variance inflation factor; SEER:Surveillance, Epidemiology, and End Results; HNC:head and neck cancer; ACE-27:Adult Comorbidity Evaluation-27; ASA:American Society of Anesthesiologists.

Declarations

Ethics approval and consent to participate

This retrospective study was endorsed by the ethics committee of Hunan Province Cancer Hospital, which waived the need for informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

The dataset analyzed for the current study are available from the corresponding author on reasonable request.

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Authors' contributions

JC*, GLL, HY, and JC conceived and designed the study. LPW, XJT, WSZ, and ZC drafted the manuscript. GLL, JC* and HY analyzed and interpreted all the data. JC, GLL, and LPW prepared the figures and tables. JC*, GLL, HY, and ZC reviewed and revised the manuscript. All authors have read and approved the manuscript for publication.*: Corresponding author (Jie Chen).

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Tables

Table1.Characteristics of patient in the training set and validation set

		Training set		Validation set	
Variable	Category	(n=261)	%	(n=108)	%
Age	median(years)	60		59	
	range(years)	36-80		36-77	
Sex	male	250	95.8	99	91.7
Tumor site	supraglottic	94	36	37	34.3
	glottic	161	61.7	67	62
	subglottic	6	2.3	4	3.7
Smoking	yes	159	60.9	71	65.7
Mean pack years	median	20		20	
	range	0-50		0-50	
Alcohol	yes	78	29.9	32	29.6
T-stage	T1	27	10.3	6	5.6
	T2	102	39.1	45	41.7
	T3	105	40.2	49	45.4
	T4a	27	10.3	8	7.4
N-stage	N0	157	60.2	66	61.1
	N1	58	22.2	30	27.8
	N2	46	17.2	12	11.1
	N3	1	0.4	0	0
Number of LN	median	9		12	
	range	0-58		0-58	
Number of positive LN	median	0		0	
	range	0-28		0-14	
LNR	< 0.13 g/dL	205	78.5	78	72.2
	≥ 0.13 g/dL	56	21.5	30	27.8
TNM stage	Stage I	21	8.8	5	4.6
	Stage II	78	29.9	33	30.6
	Stage III	101	38.7	50	46.3
	Stage IVa	61	23.4	20	18.5
Histology grade	Moderate-Well	249	95.4	103	95.4
	Poor	12	4.6	5	4.6
Anemia	yes	69	26.4	27	25
Albumin	< 3.5 g/dL	45	17.2	20	18.5
	≥ 3.5 g/dL	216	82.8	88	81.5

Abbreviations: LN: lymph node; LNR: lymph node ratio; TNM: tumor-node-metastasis.

Table2. Univariable and multivariable Cox regression analysis for the prediction of survival.

Factors	Subgroup	Univariable analysis		Multivariable analysis	
		HR(95%CI)	*P*	HR(95%CI)	*P*
Age		1.04(1.02-1.07)	0.002*	1.03(1.01-1.06)	0.021*
Sex	female	1			
	male	4.49(0.63-32.3)	0.135	NA	NA
Tumor site	glottic	1			
	supraglottic	1.53(0.99-2.37)	0.057	NA	NA
	subglottic	1.68(0.52-5.41)	0.384	NA	NA
Smoking	no	1		1	
	yes	1.54(0.98-2.44)	0.063	1.37(0.49-3.82)	0.549
Pack years		1.02(1.01-1.03)	0.008*	1.02(1.01-1.03)	0.017*
Alcohol	no	1			
	yes	1.01(0.64-1.61)	0.962	NA	NA
T-stage	T1	1			
	T2	1.32 (0.58-3.0)	0.506	NA	NA
	T3	1.73(0.77-3.88)	0.181	NA	NA
	T4a	1.86(0.68-5.14)	0.229	NA	NA
N-stage	N0	1	1		
	N1	2.84(1.72-4.71)	0.000*	1.95(1.08-3.52)	0.028*
	N2-3	3.02(1.77-5.16)	0.000*	1.54(1.01-2.25)	0.048
Number of LN		1.0(0.98-1.03)	0.726	NA	NA
PLN		1.06(1.01-1.12)	0.023*	0.97(0.88-1.07)	0.576
LNR	< 0.14 g/dL	1		1	
	≥ 0.14 g/dL	2.58(1.68-4.07)	0.001*	2.26(1.42-3.60)	0.001*
TNM stage	Stage I	1			
	Stage II	0.96(0.35-2.60)	0.936	NA	NA
	Stage III	2.09(1.03-5.33)	0.042*	1.59(0.82-4.26)	0.122
	Stage IVa	2.50(1.26-6.51)	0.014*	1.80(0.96-5.51)	0.101
Histology grade	Moderate-Well	1			
	Poor	1.59(0.69-3.64)	0.276	NA	NA
Anemia	no	1		1	
	yes	1.82(1.12-2.87)	0.008*	1.81(1.15-2.88)	0.011*
Albumin	≥ 3.5 g/dL	1		1	
	< 3.5 g/dL	1.68(1.02-2.78)	0.042*	1.69(1.01-2.83)	0.046*

Abbreviations: HR=hazard ratio, CI =confidence intervals, LN= lymph node, PLN= Number of positive LN, LNR=Lymph node ratio

NOTE: NA, not available. These variables were eliminated in the multivariate cox regression model, so the HR and *P* values were not available.

**P* < 0.05

Table3. Assessing the prognostic performance of the TNM stage and nomogram in training set and validation set

Cohort	Model	Homogeneity monotonicity and discriminatory ability			
		Likelihood ratio(LR) test*	Linear trend χ2 test**	C-index (95% CI) ***	Akaike information criterion(AIC)****
raining set	TNM stage	10.3	9.6	0.59(0.54-0.65)	892.4
	Nomogram	56.4	62.1	0.73 (0.68-0.78)	856.3
Validation set	TNM stage	1.8	1.8	0.57(0.49-0.66)	320.3
	Nomogram	58.3	61	0.84(0.78-0.89)	275.5

*Higher homogeneity likelihood ratio indicates a smaller difference within the staging system, it means better homogeneity

**Higher discriminatory ability linear trend indicates a higher linear trend between staging system, it means better discriminatory ability and gradient monotonicity

***A higher c-index means better discriminatory ability.

****Smaller AIC values indicate better optimistic prognostic stratification

Figures

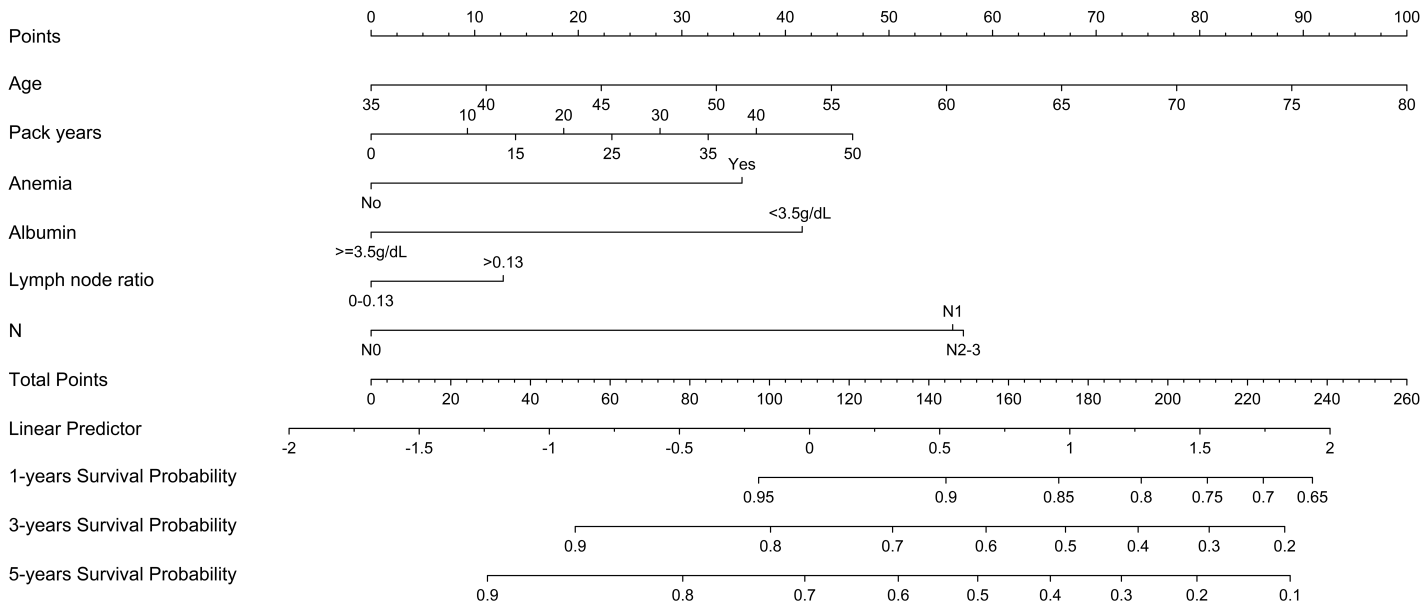

Figure 1

Nomogram for predicting 1-year, 3-year and 5-year survival probability of LSCC after laryngectomy. To estimate risk, calculate points for each variable by drawing a straight line from patient's variable value to the axis labeled "Points." Sum all points and draw a straight line from the total point axis to the 1-year, 3-year and 5-year survival axis.

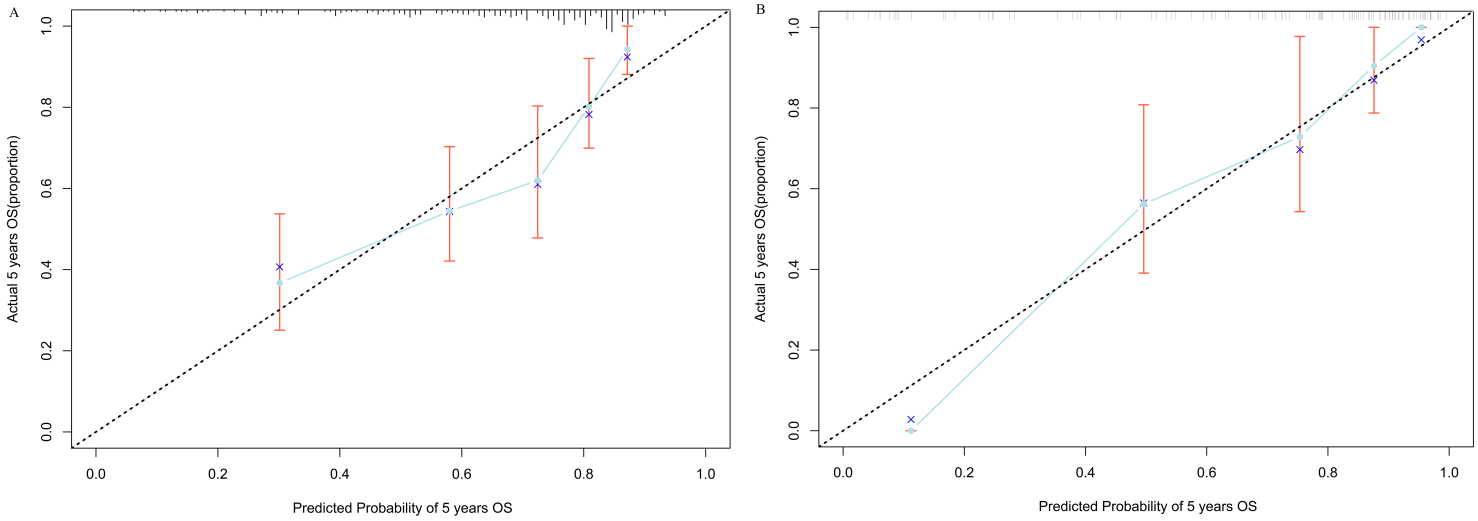

Figure 2

Calibration curves for (A) 5-year nomogram in the training set, and (B) 5-year nomogram in the validation set. Patients were grouped by octiles of predicted risk. x-axis is nomogram-predicted probability of survival(LSCC). y-axis is observed probability of LSCC (Kaplan-Meier estimates). Broken line = ideal nomogram; circles = apparent predictive accuracy, calculated by plotting the mean Kaplan-Meier estimate

for each octile versus the mean nomogram-predicted probabilities for patients in each octile; X's = bootstrap-corrected estimates; vertical bars = 95% CIs.

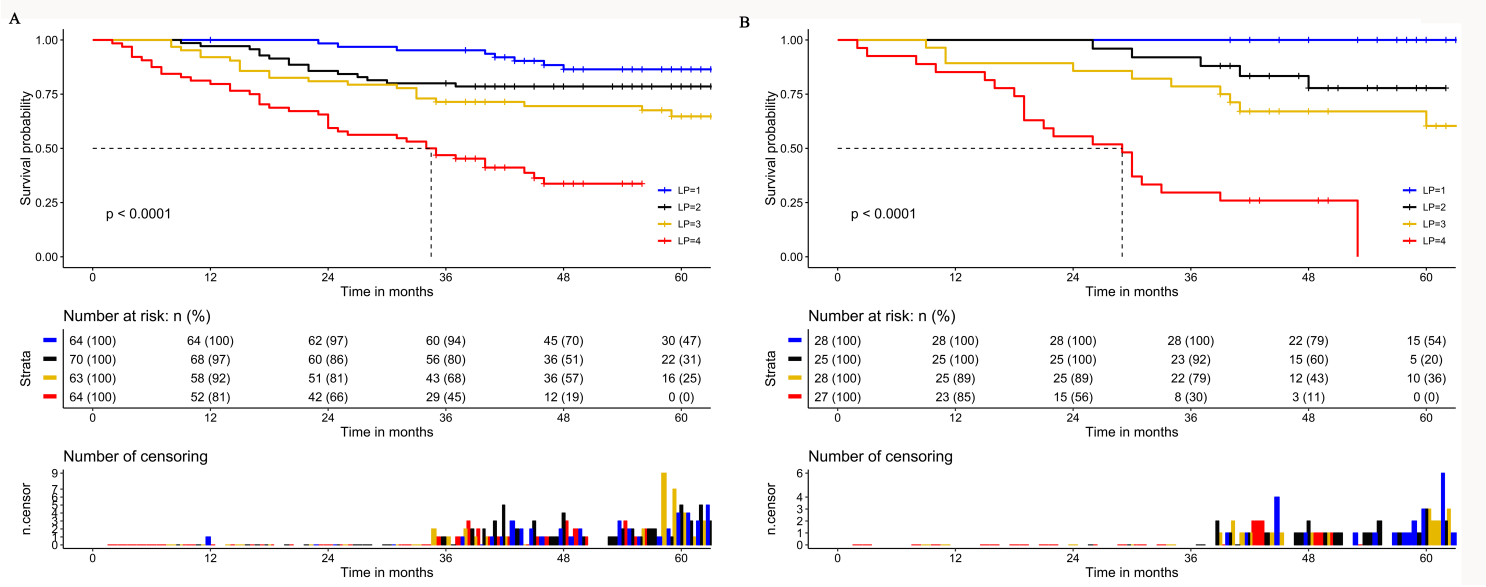

Figure 3

Kaplan–Meier curves of four groups based on the linear predictor (A) in the training set, and (B) in the validation set.

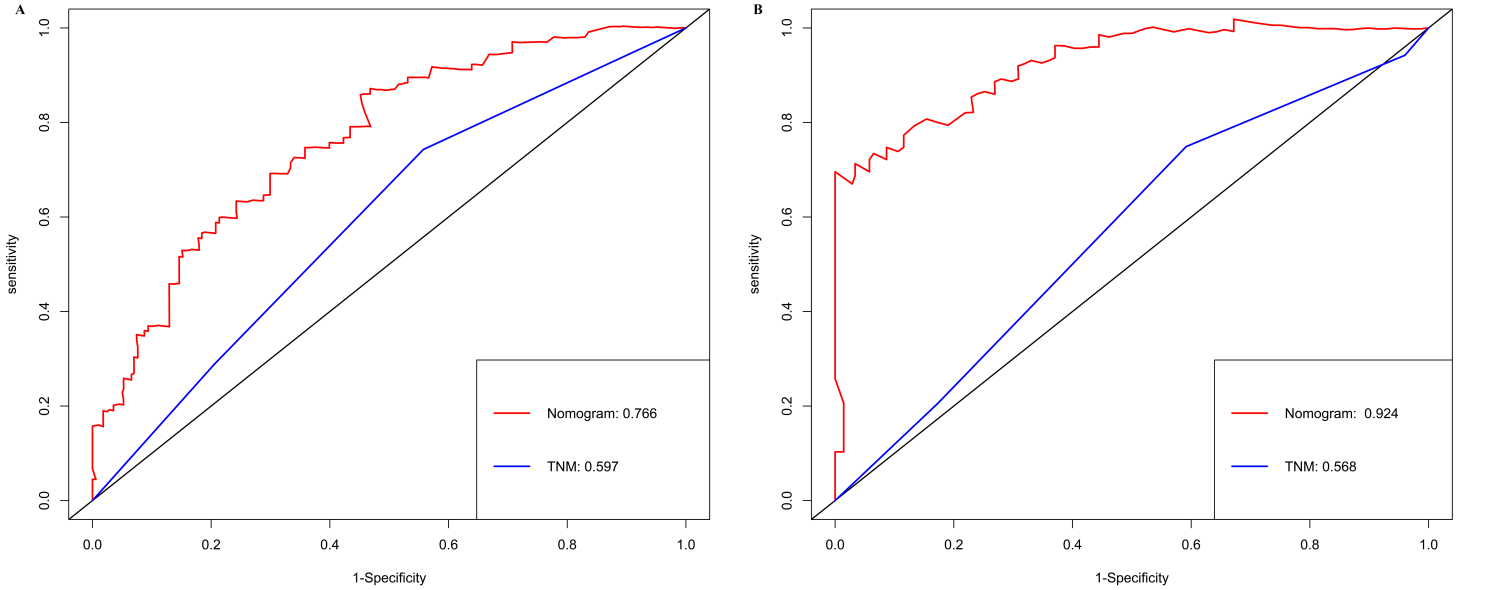

Figure 4

ROC curves compare the prediction accuracy of the nomogram with TNM stage in predicting 5-year OS (A) in the training set, and (B) in the validation set.

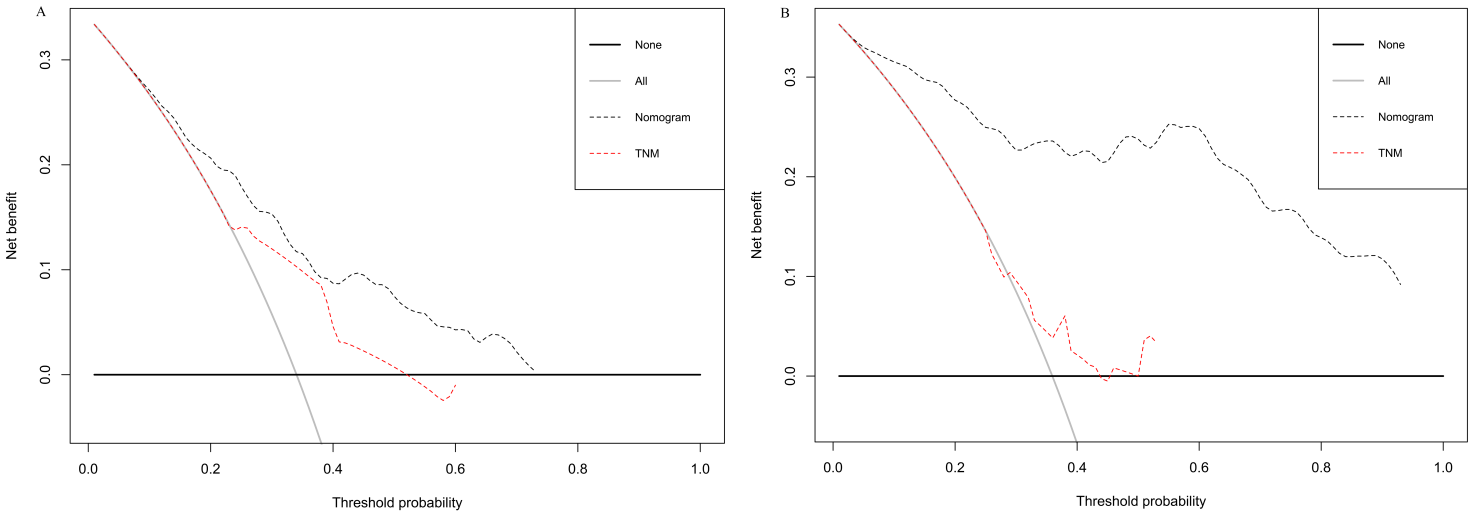

Figure 5

Decision curve analysis for the nomogram and TNM stage in prediction of prognosis of patients at 5-year point (A) in the training set, and (B) in the validation set.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TableS1.doc
- FigureS1.tif
- FigureS3.tif
- FigureS2.tif