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ORIGINAL RESEARCH

A Survival Prediction Nomogram for Esophageal Squamous Cell Carcinoma Treated with Neoadjuvant Chemoradiotherapy Followed by Surgery

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Background: Neoadjuvant chemoradiotherapy (NCRT) followed by surgery is a component of the standard treatment for resectable locally advanced esophageal squamous cell carcinoma (ESCC), and the parameters for survival prediction are not clear yet. Our study aimed to construct a survival prediction nomogram for ESCC with NCRT followed by surgery.

Methods: We analyzed hematological parameters and related-derivative indexes from 122 ESCC patients treated with NCRT followed by surgery. Univariate and multivariate Cox survival analyses were performed to identify independent prognostic factors to establish a nomogram and predict overall survival (OS). The predictive value of the nomogram for OS was evaluated by the concordance index (C-index), decision curve analysis (DCA), the clinical impact curve (CIC), net reclassification improvement (NRI), and integrated discrimination improvement (IDI).

Results: The pretreatment nutritional candidate, prognostic nutrition index, inflammation-related absolute monocyte count and TNM staging were entered into the nomogram for ESCC with NCRT followed by surgery. The C-index of the nomogram for OS was 0.790 (95% CI = 0.688–0.893), which was higher than that of TNM staging (0.681; 95% CI = 0.565–0.798, P = 0.026). The DCA, CIC, NRI, and IDI of the nomogram showed moderate improvement in predicting survival. Based on the cut point calculated according to the constructed nomogram, the high-risk group had poorer OS than that of the low-risk group ($P < 0.05$).

Conclusion: A novel nomogram based on nutrition- and inflammation-related indicators might help predict the survival of ESCC treated with NCRT followed by surgery.

Keywords: esophageal squamous cell carcinoma, neoadjuvant chemoradiotherapy, surgery, nomogram, survival, prognosis

Introduction

Esophageal cancer (EC) is one of the most common malignant tumors in the world. The prognosis of EC remains poor with the overall 5-year survival rates ranging from 15% to 25%.[1,2] Esophageal squamous cell carcinoma (ESCC) is the most frequent histological subtype, with the highest incidence in some parts of Asia. China alone accounts for more than half of global cases.[3]

Currently, the optimal treatment for ESCC is a debatable point. Surgery is still recommended as the preferred curative treatment. For locally advanced ESCC, neoadjuvant chemoradiotherapy (NCRT) followed by surgery has been proven to achieve more favorable long-term survival than surgery alone.[4–6] Strong evidence suggests that NCRT is expected to kill the micro-metastasis and demote staging to make the operation easier and improve the radical resection rate.[7,8] Furthermore, NCRT offers a potential opportunity for evaluation of tumor sensitivity to chemotherapy drugs in vivo. However, there

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are still some risks in NCRT. This approach is associated with toxicity, which can contribute to subsequent post-operative morbidity and mortality.[9–12] It will also miss the critical opportunity of surgical resection for ESCC patients who are ineffective in NCRT. The Union for International Cancer Control tumor/node/metastasis (TNM) staging system is a widely used tool for predicting the outcome of ESCC.[13] However, the TNM staging is sometimes not accurate because it may happen that some patients with similar TNM stages exhibit inconsistent clinical survival outcomes.[14–18] Therefore, it is necessary to establish a prediction model with additional prognostic factors for these patients treated with NCRT followed by surgery for further study.

In recent years, host immune and inflammatory responses have been considered as a marker of cancer progression and prognosis,[19–22] which can be evaluated by hematological parameters, such as monocyte-to-lymphocyte ratio (MLR) and the absolute monocyte count (AMC). Monocytes play an important role in the inflammatory response produced by tumors. Tumor-associated macrophages (TAMs) derived from circulating monocytes are recruited to the tumor sites by chemotactic factors. TAMs could release many effective angiogenic and lymphangiogenic growth factors, cytokines to enhance angiogenesis and lymphangenesis and promote the invasion and metastasis of cancer cells.[23] Epidemiological study revealed that elevated circulating TAMs are associated with poor prognosis in ESCC.[24]

Moreover, prognostic nutrition index (PNI) is a nutritional assessment and risk prediction established by Japanese scholar Onodera.[25] At present, it is mainly used to evaluate the malignant degree and prognosis of digestive tract tumors such as esophageal cancer,[26,27] gastric cancer[28] and pancreatic cancer.[29,30] Previous studies have showed that malnutrition is associated with an immunosuppressed condition, which provides a good microenvironment for tumor recurrence.[31,32] Nakatani et al reported that PNI is associated with tumor progression and survival in patients with esophageal cancer.[33] However, to our knowledge, there is no study of PNI on the evaluation of ESCC with NCRT followed by surgery.[34] Systemic immune-inflammation index (SII), a new blood-derived inflammatory index, is also considered to be associated with poor outcome in ESCC.[35]

In view of the prospect of hematological immune-inflammation and nutrition biomarkers in predicting survival, we established a novel nomogram for ESCC treated with NCRT followed by surgery and assessed its incremental value to the traditional staging system and clinical treatment for OS.

Methods and Materials

Study Population

We retrospectively analyzed a total of 122 patients with ESCC treated with NCRT followed by surgery, who were recruited from the Cancer Hospital of Shantou University Medical College from 2007 to 2021. We reviewed the detailed medical records of these patients who were diagnosed based on spiral computed-tomography (CT) and endoscopic examination followed by histopathology. According to the results of the medical examinations, patients were tumor-node-metastasis (TNM) staged based on the 8th International Union Against Cancer (UICC) criteria for esophageal carcinoma.[36]

Patients included in the analysis met the following criteria: (1) they were diagnosed as ESCC with histopathological examination; (2) they did not suffer from previous or concomitant malignancies before ESCC diagnosis or receive any anti-cancer treatment; (3) they underwent chest CT examination, and the lung metastatic lesions could be ruled out; (4) they had received NCRT before esophageal cancer surgery; (5) they had complete baseline clinical information, laboratory, and follow-up data. We excluded those patients who died of surgical complications. The OS was defined as the interval between the initial diagnosis and either death of cancer or the last follow-up. In this study, all blood test results were obtained before treatment. This study was approved by the Hospital Ethics Committee in Shantou University Cancer Center. The requirement for informed consent from patients was waived because of its retrospective design. All work was complied with the principles of the Helsinki Declaration.

Neoadjuvant Chemoradiotherapy and Surgery

Neoadjuvant therapy comprised weekly carboplatin (AUC 2 mg/mL per min) and paclitaxel (50 mg/m^2) for 5 weeks combined with daily radiotherapy consisting of 23 fractions of 1.8 Gy (total 41.4 Gy). All patients having treatment with curative intent received neoadjuvant chemoradiotherapy unless considered unfit for multimodal treatment.[5] For patients with tumors mainly involving the gastroesophageal junction, transabdominal resection is beneficial.[37] For intrathoracic esophageal tumors and connective tumors with positive cervical lymph nodes or above, transthoracic lymph node dissection is usually performed. All operations were performed or strictly supervised by experienced upper gastrointestinal surgeons.

Parameters for the Establishment of Nomogram

The following relevant clinicopathological and hematological data were collected for each enrolled patient at the time of diagnosis and before any treatment: gender, age, body mass index (BMI), tumor location, TNM stage, prognostic nutrition index (PNI), systemic immune-inflammation index (SII), white blood cell (WBC), red blood cell (RBC), platelet count (PLT), Hemoglobin (HB), absolute monocyte count (AMC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet lymphocyte ratio (PLR), neutrophil lymphocyte ratio (NLR) and lymphocyte monocyte ratio (LMR). The clinical stage of the disease was determined according to 8th edition of the AJCC TNM stage manual.[38] PNI was calculated by the formula Alb (g/L) + 5 × lymphocyte count ($\times 10^9$/L). SII was calculated by the formula PLT ($\times 10^9$/L) × Neutrophil Count ($\times 10^9$/L) ÷ lymphocyte count ($\times 10^9$/L). In this study, continuous variables were transformed into categorical variables. We used a graphical method, the X-tile plot that shows the robustness of the relationship between a biomarker and outcome by construction of a two-dimensional projection of every possible subpopulation. The best cut-off values for all variables were determined by X-tile.[39]

Statistical Analyses

Statistical analyses were performed using SPSS software, version 19.0 (IBM Corp., Chicago, IL, USA) and R (version 4.0.3, http://www.R-project.org) for Windows. The Kaplan–Meier curves were used to calculate the survival rate, and the Log rank test was used to compare them. Univariate analysis was to select the most useful prognostic variables. Variables with a significant level of $P \leq 0.1$ in univariate analysis were analyzed using multivariate Cox regression. A dynamic predictive nomogram model is built using all variables with a P-value of less than 0.05 in a multivariate model. The discriminative ability, accuracy and incremental predictive value of the prognostic nomogram to the traditional TNM staging system for individualized survival was evaluated by the Harrell's concordance index (C-index), decision curve analysis (DCA),[40] net reclassification improvement (NRI),[41] and integrated discrimination improvement (IDI).[42] Throughout the study, statistical significance was set at $P < 0.05$ (two-tailed).

Results

Patient Characteristics

In our study, a total of 122 eligible patients were analyzed. The median follow-up was 22.0 months (interquartile range (IQR): 12.0–42.0). The median age for these patients was 59 years (IQR: 55–64 years), of which 98 (80.3%) were males

Table 1 Patient Demographics and Clinical Characteristics

Characteristics	No	%	Characteristics	No	%
Gender			PLT (10^9/L)		
Male	98	80.3	≤338	95	77.9
Female	24	19.7	>338	27	22.1
Age (years)			AMC (10^9/L)		
≤62	85	69.7	≤0.6	70	57.4
>62	37	30.3	>0.6	52	42.6
BMI			ANC (10^9/L)		
≤21.2	67	54.9	≤5.0	68	55.7
>21.2	55	45.1	>5.0	54	44.3
Location			ALC (10^9/L)		
Up	27	22.1	≤1.7	51	41.8
Middle	81	66.4	>1.7	71	58.2
Low	14	11.5	PLR		
TNM stage			≤153.3	58	47.5
II	10	8.2	>153.3	64	52.5
III	57	46.7	NLR		
IVa	49	40.2	≤2.3	47	38.5
IVb	6	4.9	>2.3	75	61.5
PNI			LMR		
≤50.5	106	86.9	≤3.4	59	48.4
>50.5	16	13.1	>3.4	63	51.6
SII					
≤852.9	69	56.6			
>852.9	53	43.4			
WBC (10^9/L)					
≤7.6	64	52.5			
>7.6	58	47.5			
RBC (10^{12}/L)					
≤4.5	42	34.4			
>4.5	80	65.6			
HB (g/L)					
≤132.7	52	42.6			
>132.7	70	57.4			

Abbreviations: BMI, body mass index; PNI, prognostic nutrition index; SII, systemic immune-inflammation index; WBC, white blood cell; RBC, red blood cell; HB, hemoglobin; PLT, platelet count; AMC, absolute monocyte count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; PLR, platelet lymphocyte ratio; NLR, neutrophil lymphocyte ratio; LMR, lymphocyte monocyte ratio.

and 24 (19.7%) were females. There were 27, 81 and 14 patients with esophageal neoplasm located in upper, middle and lower chest, respectively. Patient demographic and clinical characteristics are summarized in Table 1. The best cut-off values for all variables were as follows: age (62 years), BMI (21.2), PNI (50.5), SII (852.9), WBC (7.6×10^9/L), RBC (4.5×10^{12}/L), PLT (338×10^9/L), HB (132.7g/L), AMC (0.6×10^9/L), ANC (5.0×10^9/L), ALC (1.7×10^9/L), PLR (153.3), NLR (2.3) and LMR (3.4).

Cox Proportional Hazards Regression Analysis of the Overall Survival

As shown in Table 2, the univariate analysis indicates that TNM stage (P = 0.012), PNI (P = 0.010), SII (P = 0.088), WBC (P = 0.044), PLT (P = 0.028), AMC (P = 0.019), ANC (P = 0.040) and HB (P = 0.083) were associated with OS of patients. Then they were included in the multivariate Cox proportional risk regression analysis of OS. The results show that the following variables remained independently prognostic: PNI (P = 0.006, HR = 3.986; 95% CI: 1.488–10.677), AMC (P = 0.047, HR = 2.569; 95% CI: 1.013–6.516) and TNM stage (P = 0.008, HR =2.618; 95% CI: 1.280–5.313). According to Cox proportional hazards regression analysis, the forest plot shows the hazard ratios and 95% confidence intervals for OS (Figure 1).

Construction of the Multi-Parametric Prognostic Nomogram

Using these selected markers, the nomogram was constructed for OS prediction (Figure 2). From the nomogram,

Table 2 Univariate and Multivariate Cox Proportional Hazards Regression Analysis for OS

Characteristics	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Gender				
Male	0.512 (0.148–1.775)	0.291		
Female	Reference			
Age (years)				
≤62	0.698 (0.252–1.930)	0.487		
>62	Reference			
BMI				
≤21.2	0.496 (0.187–1.317)	0.159		
>21.2	Reference			
Location				
Up	1.584 (0.319–7.874)	0.574		
Middle	1.154 (0.257–5.184)	0.853		
Low	Reference			
TNM stage			2.608 (1.280–5.313)	0.008
II	0.067 (0.007–0.663)	0.021		
III	0.089 (0.021–0.382)	0.001		
IVa	0.173 (0.046–0.654)	0.010		
IVb	Reference			
PNI			3.986 (1.488–10.677)	0.006
≤50.5	3.804 (1.443–10.02)	0.010		
>50.5	Reference			
SII				
≤852.9	2.190 (0.890–5.389)	0.088		
>852.9	Reference			
WBC (10^9/L)				
≤7.6	2.753 (1.028–7.375)	0.044		
>7.6	Reference			

(*Continued*)

Table 2 (Continued).

Characteristics	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
RBC (10^{12}/L) ≤4.5 >4.5	1.514 (0.563–4.071) Reference	0.411		
HB (g/L) ≤132.7 >132.7	0.443 (0.176–1.112) Reference	0.083		
PLT (10^9/L) ≤338 >338	2.793 (1.121–6.961) Reference	0.028		
AMC (10^9/L) ≤0.6 >0.6	3.026 (1.202–7.618) Reference	0.019	2.569 (1.013–6.516)	0.047
ANC (10^9/L) ≤5.0 >5.0	2.807 (1.048–7.514) Reference	0.040		
ALC (10^9/L) ≤1.7 >1.7	2.07 (0.785–5.454) Reference	0.141		
PLR ≤153.3 >153.3	1.375 (0.562–3.367) Reference	0.485		
NLR ≤2.3 >2.3	1.63 (0.624–4.261) Reference	0.319		
LMR ≤3.4 >3.4	0.532 (0.211–1.342) Reference	0.181		

Abbreviations: OS, overall survival; BMI, body mass index; PNI, prognostic nutrition index; SII, systemic immune-inflammation index; WBC, white blood cell; RBC, red blood cell; HB, hemoglobin; PLT, platelet count; AMC, absolute monocyte count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; PLR, platelet lymphocyte ratio; NLR, neutrophil lymphocyte ratio; LMR, lymphocyte monocyte ratio.

TNM stage had the greatest impact on OS, followed by PNI and AMC. A larger total point score indicates a shorter OS. The nomogram was used by summing the points identified on the points scale for each variable. The total points projected on the bottom scales indicate the probability of 1-, 3-, and 5-year survival. For example, a patient, regardless of age or sex, with PNI > 56.4, AMC > 0.6×10^9/L, and TNM stage II had a total of 75 points indicating an estimated 1-, 3-, and 5-year OS of 87%, 70%, and 66%, respectively. The calibration plots for the probability of survival at 1-, 3-, and 5-year showed the prediction of the nomogram was well matched with the actual observation (Figure S1A–C).

Assessment of Performance of Prognostic Nomogram

Nomogram discrimination was evaluated using the C-index, which enumerated the level of concordance between the predicted and observed OS. From Table 3, the C-index based on the nomogram (0.790; 95% CI, 0.688–0.893) for OS in the cohort was much higher than that of the TNM stage (0.681; 95% CI, 0.565–0.798; P = 0.026). The nomogram showed better discrimination than a single component to predict OS (Figure 3).

Due to the small sample size in this study, we applied DCA to evaluate the net benefit of the nomogram and NRI and IDI to assess predictive accuracy. The DCA curve suggested that

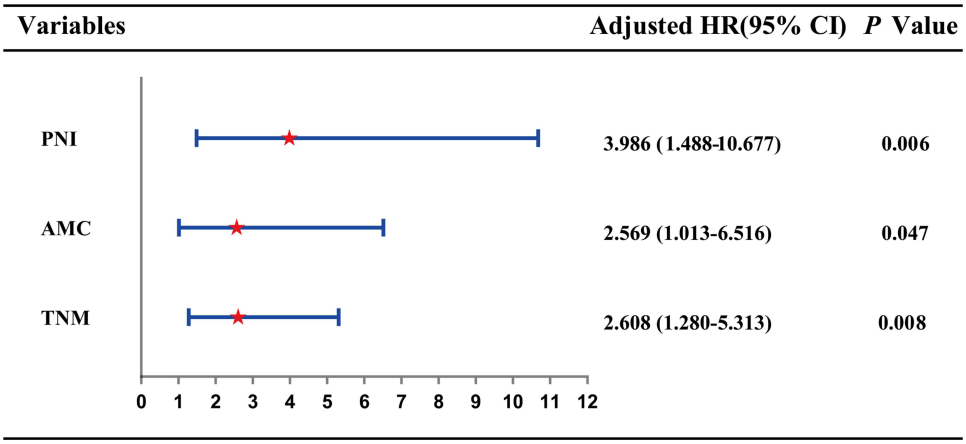

Figure 1 Forest plot showed the hazard ratio for overall survival according to the Cox proportional hazards regression analysis in ESCC patients.
Abbreviation: ESCC, esophageal squamous cell carcinoma.

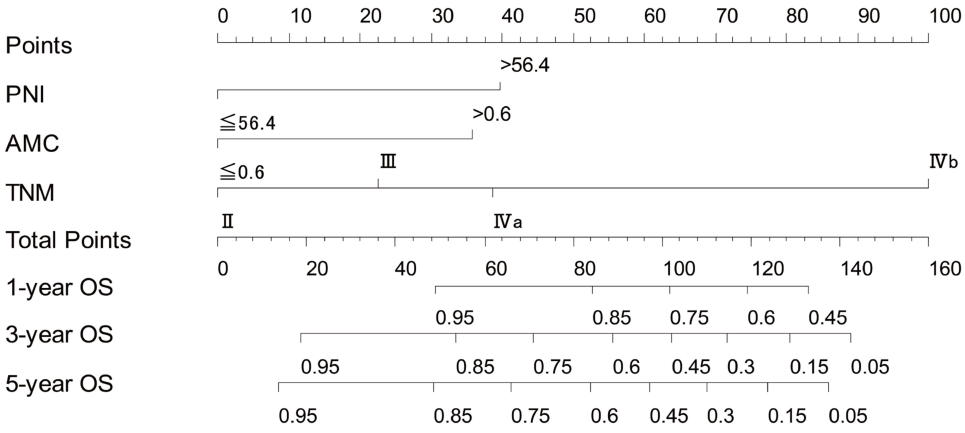

Figure 2 Nomogram model based on PNI, AMC and TNM stage in the prediction of 1-, 3- and 5-year overall survival in ESSC patients.
Abbreviations: PNI, prognostic nutrition index; AMC, absolute monocyte count; TNM, tumor/node/metastasis; ESCC, esophageal squamous cell carcinoma.

the nomogram (red line) had a higher net benefit than that of TNM staging (green line) to predict OS (Figure S2). The clinical impact curve also indicated that the nomogram had good net benefits for the identification of severe ESCC patients (Figure S3). In Table 4, the IDI suggested that the predictive accuracy of the nomogram was better than those of other evaluation systems, including TNM staging (IDI > 0). Furthermore, the NRI showed the accuracy of the nomogram had improvements of 17.6%, 38.8%, and 34.9% when predicting 1-, 3-, and 5-y OS, respectively. To conclude, the DCA, NRI, and IDI indicated a better net benefit and predictive accuracy of the newly constructed model.

Table 3 C-Index for the Prediction of OS

Factor	C-Index (95% CI)	*P* value
PNI	0.613 (0.509–0.716)	
AMC	0.618 (0.499–0.737)	
TNM stage	0.681 (0.565–0.798)	
Nomogram	0.790 (0.688–0.893)	
Nomogram vs PNI		0.002
Nomogram vs AMC		<0.001
Nomogram vs TNM		0.026

Abbreviations: OS, overall survival; PNI, prognostic nutrition index; AMC, absolute monocyte count; TNM, tumor node metastasis.

Construction of Risk Stratification Based on Nomogram

Based on cutoff value (67 for OS) of the total points determined by the X-tile program, we subdivided patients into low- and high-risk groups, and applied a Kaplan–Meier survival analysis to assess their survival. In our cohort, compared with patients in the low-risk group, patients in the high-risk one had shorter OS ($P < 0.01$; Figure 4). This stratification demonstrated that the newly

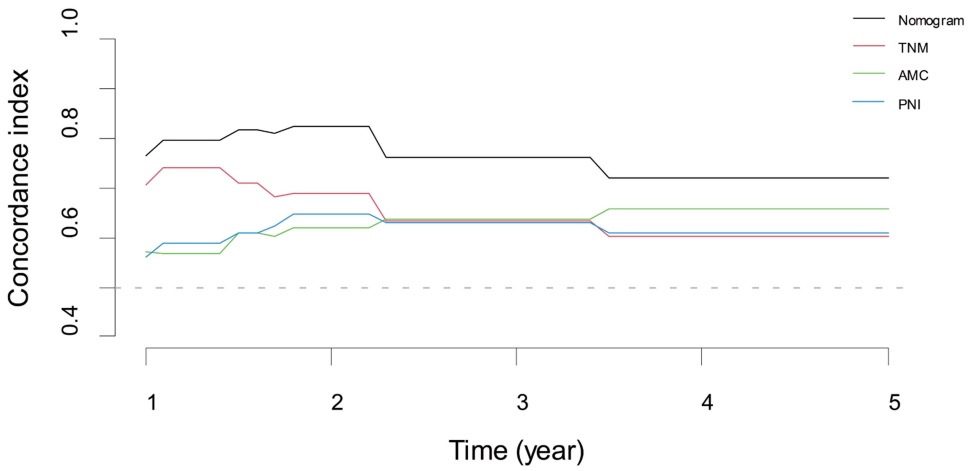

Figure 3 Harrell's concordance index based on the predictions of the nomogram.

constructed nomogram could effectively separate OS for the two proposed risk groups.

Discussion

NCRT before surgery has been a focus of research for ESCC treatment in recent years. Owing to the high malignancy potential, patients who only receive surgery trend to relapse. NCRT can increase the rate of radical resections and reduce locoregional recurrences.[43–45] Multidisciplinary comprehensive treatment can prolong the survival time of patients, but the prognosis is still poor.

In the present study, we analyzed individual clinical features and hematological markers and successfully established a prognostic nomogram to predict OS for ESCC treated with NCRT followed by surgery with the use of univariate analysis and multivariate cox proportional hazards regression. The effects of inflammation and nutrition on the prognosis of ESCC patients with NCRT were analyzed, which provided reference for the treatment of esophageal cancer. This nomogram shows better predictive accuracy and discriminative ability in the prognosis of ESCC patients treated with NCRT followed by surgery when compared to traditional TNM staging. Our prognostic nomogram efficiently stratified those patients into high-risk and low-risk subgroups with significant differences in OS.

With the continuous improvement of diagnosis and treatment methods, many malignant tumors have gradually become a controllable chronic disease. Malnutrition in patients with upper gastrointestinal malignancies is frequent due to increased metabolic demand and loss of nutrition.[46] Meanwhile, the increase of inflammatory cytokines associated with cancer can also lead to malnutrition in cancer patients. The nutrients available in tumor microenvironment plays a dominant role in defining cancer cell metabolism.[47,48] In fact, although tumor metabolism is highly heterogeneous, some tumors have been proved to develop metabolic dependence on glutamine and other nutrients. Availability of nutrients depends on the flow of plasma nutrients from systemic circulation to tumor cells.[49] PNI, calculated using serum albumin levels and total lymphocyte count in peripheral blood, was established by Japanese scholar and originally used to evaluate the nutritional and immune status of patients undergoing gastrointestinal surgery.[50] In recent years, it has gradually become a new index to judge the prognosis of malignant tumors.[51–53] Many recent studies reveal that there is an association between PNI and survival in various cancers, including colorectal cancer,[54] gastric cancer,[55] lung cancer,[56–59] etc. Uniformly, this study shows that the PNI level is the independent influencing factor of patients' OS. Therefore, nutritional evaluation should be carried out before salvage in patients with NCRT, and the nutritional status of patients with nutritional risk or malnutrition should be improved actively in order to improve long-term survival.

Currently, it has been well established that inflammation has a strong link with cancer development through proliferative responses, invasion, and metastasis.[60] Tumour cells produce various cytokines that attract leukocytes. The inflammatory component of developing tumors may include different leukocyte populations, such as neutrophils, dendritic cells, lymphocytes, etc. In the presence of granulocyte-macrophage colonization stimulating factor (GM-CSF) and interleukin (IL)-4, Monocytes differentiate into immature dendritic cells.[61] Dendritic cells migrate to

Table 4 Predictive Improvement of the Nomogram

	1-Year				3-Year				5-Year			
	NRI %	*P* value	IDI %	*P* value	NRI %	*P* value	IDI %	*P* value	NRI %	*P* value	IDI %	*P* value
OS												
Nomogram vs PNI	40.8	0.110	6.5	0.154	38.3	0.074	13.8	0.028	30.3	0.182	17.2	0.026
Nomogram vs AMC	38.3	0.044	8.3	0.016	30.0	0.118	14.0	0.018	11.9	0.655	9.7	0.192
Nomogram vs TNM	17.6	0.286	3.4	0.384	38.8	0.030	13.7	0.014	34.9	0.138	13.3	0.022

Abbreviations: OS, overall survival; NRI, net reclassification improvement; IDI, integrated discrimination improvement; PNI, prognostic nutrition index; AMC, absolute monocyte count; TNM, tumor node metastasis.

inflammatory peripheral tissues to capture antigens and migrate to lymph nodes to activate T lymphocytes after maturation. Monocytes seem to be recruited during the whole process of tumor progression, including the early stages of tumor growth and the establishment of distant metastasis.[62–64] Many studies suggest that a high AMC was associated with tumor poor OS,[65–68] which was also reflected in our study. Here we show that 1-, 3- and 5-years survival and median survival time in high AMC groups were 87.0%, 21.1%, 5.7% and 19 months, respectively. But for the low AMC group, 1-, 3- and 5-years survival and median survival time were 80.0%, 35.7%, 11.4% and 23 months, respectively. There is a significant statistical difference between the two groups (p = 0.019). Similarly, Han et al[69] also found that compared with the preoperative low AMC group, patients with high AMC had poor DFS (high and low: 27.5% vs 39.0%, P = 0.015) and OS (high and low: 31.1% vs 44.8%, P = 0.009); Preoperative AMC were independent prognostic factors of ESCC for DFS (P = 0.025) and OS (p = 0.015), respectively. These findings may reflect that AMC could be regarded as a substitute biomarker of systemic inflammation, which contributes to tumor progression.

Besides, although some pathological factors such as pathologically complete response (pCR), marginal status and lymph node status are not involved in our modeling process, their influence on the prognosis of esophageal cancer still deserves our great attention. The study indicates approximately 30% of patients receiving NCRT followed by surgery have a pCR.[4] It has also been found that early tumors show pCR more often than later tumors after NCRT, which may be due to lower tumor burden.[70] Compared to patients with residual disease in the resection specimen, patients with pCR have a better overall survival.[71,72] The resection margin is considered as an important factor in the surgical treatment of esophageal cancer.[73] Dexter et al studied 135 patients who received esophagogastrectomy and reported that presence of tumor within 1 mm of the circumferential margin was a significant and independent predictor of survival. This was found to be more significant in patients with a low nodal metastatic burden.[73] Some retrospective reports imply that lymph node status is also an essential prognostic factor regardless of whether patients received NCRT.[74–76] However, there is still controversy because of the lack of prospective evidence and the numbers of patients in these studies.

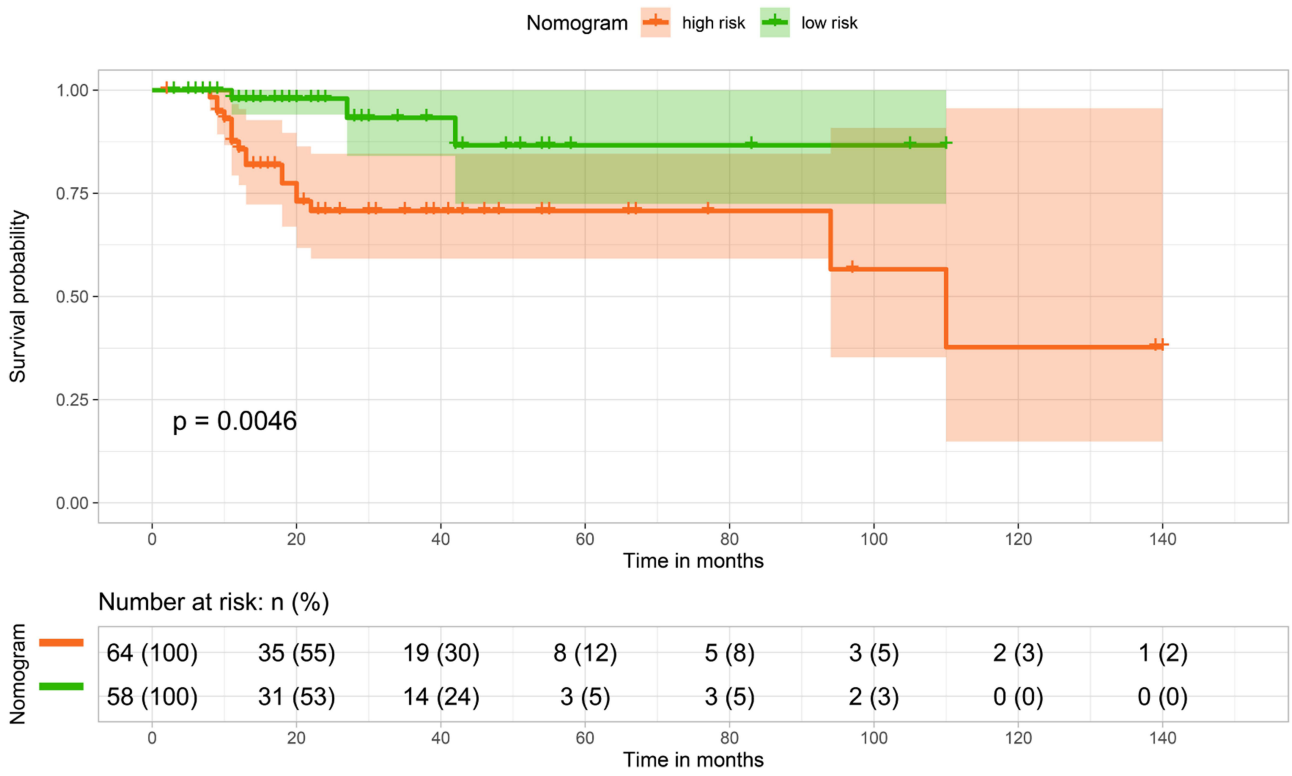

Figure 4 Kaplan–Meier curves for overall survival based on the predictions of the nomogram.

This study has the following advantages: (1) Compared to previous studies,[77–79] multiple potential prognostic factors were assessed, thus to increase prognostic accuracy and the C-index of the prognostic nomogram. (2) Compared with the traditional TNM staging system, the new nomogram improved the prognostic prediction ability and accuracy. Although this nomogram might represent a helpful survival prediction tool to assist in therapy decisions, some limitations should not be ignored: (1) At present, we only analyzed small size sample from a single cancer center. A large-scale multi-center verification of results will be needed in the future. (2) For further research, continuous variables need to be transformed into categorical variables based on the cut-off values. There were some limitations in choosing the cut-off values for continuous variables. (3) Our endpoint was OS, and further research on the disease-free survival (DFS) should also be conducted. (4) There may be some changes in the selection of patients for these treatments at this hospital over the study period. We should consider adjusting for year of treatment as a variable in our multivariate model to account for these potential changes. Despite the above-mentioned shortcomings, the prognostic nomogram is effective and may be useful in predicting the outcomes of ESCC treated with NCRT followed by surgery.

Conclusion

In our study, we established and provided a multiparametric prognostic nomogram derived from nutrition- and inflammation-related indicators that showed favorable performance when compared to traditional TNM staging for individualized OS estimation. If further validation in multi-center, large-scale trial studies could be completed, this simple, precise and understandable prognostic model may serve as a potential tool for clinicians in the prognostic prediction of ESCC treated with NCRT followed by surgery.

Abbreviations

NCRT, neoadjuvant chemoradiotherapy; ESCC, esophageal squamous cell carcinoma; EC, esophageal cancer; OS, overall survival; TNM, tumor node metastasis; BMI, body mass index; PNI, prognostic nutrition index; SII, systemic immune-inflammation index; WBC, white blood cell; RBC, red blood cell; HB, hemoglobin; PLT, platelet count; AMC, absolute monocyte count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; PLR,

platelet lymphocyte ratio; NLR, neutrophil lymphocyte ratio; LMR, lymphocyte monocyte ratio; NRI, net reclassification improvement; IDI, integrated discrimination improvement.

Ethics Statement

Our study was approved by The Shantou University Medical Ethics Committee (approval no. SUMC2011XM-0066). All patients provided written informed consent prior to enrollment in the study.

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Disclosure

The authors declare that they have no competing interest.

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