

The prognostic significance of nomogram-based pretreatment inflammatory indicators in patients with esophageal squamous cell carcinoma receiving intensity- modulated radiotherapy

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Abstract

Background: Currently, there is no objective prognostic index for patients with esophageal squamous cell carcinoma (ESCC) treated by intensity-modulated radiotherapy (IMRT). The current study aimed to develop a nomogram based on hematologic inflammatory indices for prognostic prediction and risk-stratification of patients with ECSS treated by IMRT.

Methods: 434 patients with treatment-naïve ESCC in Fujian Cancer Hospital between January 2012 and December 2016 were defined as the training cohort. In addition, 147 newly-diagnosed ESCC patients between January 2008 and December 2011 were used as the validation cohort. Independent predictors of overall survival (OS) identified by multivariate survival analysis were employed to establish a nomogram model. The predictive ability was evaluated by time-dependent receiver operating characteristic (ROC) curves, the concordance index (C-index), calibration plots, net reclassification index (NRI), and integrated discrimination improvement (IDI). Decision curve analysis (DCA) was performed to assess the clinical benefits of the nomogram model. The entire series was divided into three risk subgroups stratified by the total nomogram scores.

Results: On multivariate analyses, cTNM, primary gross tumor volume (GTVp), chemotherapy (CT), neutrophil-to-lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) were independent predictors of OS. Nomogram was developed incorporating these factors. The C-index for 5-year OS (0.627 and 0.629) and the AUC value of 5-year OS (0.706 and 0.719) in the training and validation cohorts (respectively) were superior to the 8th AJCC staging. Furthermore, the nomogram model presented higher NRI and IDI than the 8th AJCC staging ($P=0.001$; $P=0.001$, respectively). DCA showed greater clinical benefit of the nomogram model compared to 8th AJCC staging. Finally, according to the total nomogram score, patients with <84.8, 84.8–151.4, and >151.4 points were categorized into low-risk, intermediate-risk, and high-risk groups. Their 5-year OS rates were 44.0%, 23.6% and 8.9%, respectively. The C index was 0.625, which was higher than the 8th AJCC staging.

Conclusions: We developed a nomogram model for risk-stratification of ESCC patients receiving definitive IMRT. Our findings may provide a reference for individualized treatment.

Background

Esophageal cancer ranks seventh in morbidity and sixth in mortality around the world [1]. There are two main pathological subtypes of esophageal cancer, i.e., esophageal squamous cell carcinoma (ESCC) and adenocarcinoma. ESCC accounts for 90% of cases of esophageal cancer in China [2]. According to the National Comprehensive Cancer Network (NCCN) guidelines, curative resection is the cornerstone of treatment for ESCC; however, radical chemoradiotherapy is the primary treatment for locally advanced ESCC [3]. Unfortunately, ESCC patients receiving definitive radiotherapy have a poor prognosis with 5-year survival rates of only 25.3–39.2% [4, 5]. At present, the Union for International Cancer Control/American Joint Committee on Cancer (UICC/AJCC) staging system is widely used for prognostic assessment of

patients with ESCC. However, some patients with the same clinical stage and receiving similar treatment may show different outcomes [6, 7]. Therefore, there is a need to develop a more accurate prognostic model for ESCC patients treated by definitive radiotherapy, which may help inform personalized treatment strategies.

Several nomogram models have been shown to predict the prognosis of ESCC patients treated with definitive radiotherapy. In a study by Zhang et al. (2017) [8], C-reactive protein/albumin (CRP/Alb) ratio was found to be an independent predictor of OS in patients with thoracic ESCC undergoing standard definitive radiotherapy or chemoradiotherapy. Furthermore, a nomogram incorporating the CRP/Alb ratio effectively predicted the OS, and showed greater potential for clinical benefit than the AJCC staging system. In 2020, Xu et al.[9] reported a significant correlation of pretreatment lymphopenia with OS of ESCC patients undergoing definitive chemoradiotherapy. Additionally, the prediction of 3-year OS probability by the nomogram incorporating pre-treatment absolute lymphocyte count (ALC) showed good agreement with actual 3-year OS. Recently, hematologic inflammatory markers, such as CRP, neutrophil-to-lymphocyte ratio (NLR), and platelet lymphocyte ratio (PLR) have shown remarkable association with the prognosis of ESCC [10, 11]. In a recent study, pre-treatment NLR was found to predict long-term survival of patients with ESCC undergoing definitive chemoradiotherapy [7]. Moreover, a nomogram incorporating pre-treatment NLR showed greater predictive accuracy than the AJCC staging system.

However, for patients with ESCC receiving definitive radiotherapy, the current nomogram based on hematological inflammatory indices has some shortcomings. For one, previous prognostic nomogram models did not incorporate or only incorporate a single inflammatory biomarker [7–9]. Hence, further exploration of the prognostic value of more inflammatory indicators in ESCC patients treated with definitive radiotherapy is a key imperative. Secondly, previous studies evaluated the discriminative ability of the nomogram model mainly by consistency index (C-index) and area under subject operating characteristic curve (AUC) [12, 13]. Net reclassification index (NRI) and integrated discrimination improvement (IDI) have rarely been used to compare the predictive performance of the nomogram model and the staging system [14, 15]. Collectively, these studies indicate a need to generate a novel nomogram for a more accurate prediction of the outcomes of ESCC patients undergoing definitive radiotherapy.

The aim of the current study was to develop a nomogram model to facilitate more accurate risk-stratification of ESCC patients receiving definitive radiotherapy or chemoradiotherapy. Our findings may facilitate more reliable prognostic prediction and individualized treatment for these patients.

Materials And Methods

Patients

This retrospective study was approved by the Institutional Review Board of the Fujian Cancer Hospital (No. K2021-129-01). The primary series of this clinical study included 434 consecutive patients with newly-diagnosed ESCC, which was defined as the training cohort. The eligibility criteria were as follows:

(1) patients with a histological or cytological diagnosis of ESCC; (2) definitive intensity-modulated radiation therapy (IMRT) with or without chemotherapy; (3) availability of complete pre-treatment clinical and laboratory data; (4) no history of another malignancy. The exclusion criteria were: (1) patients with any other primary malignancy; (2) patients who received conventional radiotherapy. In addition, another set of 147 patients who were screened using the above criteria from January 2008 to December 2011 was taken as the validation set.

As explained in our previously published study, two experienced thoracic radiation oncologists plotted GTVp from pre-treatment chest computed tomography (CT) images [16]. Clinical TNM staging was performed according to the eighth edition of the Union for International Cancer Control/American Joint Committee on Cancer (UICC/AJCC) staging criteria for esophageal cancer.

Peripheral blood differential cell counts and the related indices

As part of routine clinical workup, the baseline neutrophil, lymphocyte, platelet, and monocyte counts were obtained before definitive radiotherapy or chemotherapy. NLR was defined as neutrophil count divided by lymphocyte count. LMR was calculated as lymphocyte count divided by the monocyte count. PLR was calculated as platelet count divided by lymphocyte count. For transformation of continuous variables (including NLR, LMR, and PLR) into categorical variables, receiver operating characteristic (ROC) curve analysis was performed to identify threshold values for survival using the area under the curve. The optimal cut-off values of NLR, LMR, and PLR were 2.0, 3.0, and 160, respectively.

Treatment and follow-up

All patients in the present study were treated with definitive IMRT. The median dose was 61.50 Gy (range, 40–70 Gy) (dose per fraction: 1.8–2.1 Gy). The contents of IMRT, as described in our previous studies, include the total volume of the clinical target volume and primary tumor (GTVp), organs at risk (OAR) of radiotherapy, the target dose and dose limit of OAR [17]. 415 (71.4%) of 581 patients received chemotherapy including platinum- or taxane-based regimens with a median of 2 cycles.

The schedule for follow-up of patients is described in our previous study. In brief, the follow-up was performed once every three months within the first 2 years after definitive IMRT, subsequently every 6 months within years 3 to 5, and annually thereafter. The primary endpoint of the study was OS, which was defined as the period from the date of histological diagnosis to the date of death due to any cause or last follow-up. The last follow-up was October 2021.

Statistical Analyses

All statistical analyses were performed using IBM SPSS statistical software version 26.0 and R version 9.0.0 (<http://www.r-project.org>). ROC curve was used to determine the optimal threshold of continuous parameters for predicting survival based on the Youden index. The OS rates were estimated using the Kaplan-Meier method and between-group differences were assessed using the log-rank test. To identify

independent prognostic factors for OS, univariate and multivariate analyses of baseline indicators were performed using Cox proportional hazards regression.

Subsequently, a prognostic nomogram model based on these independent predictors was established to predict 1-, 3-, and 5-year OS. The discriminative ability of the nomogram model was evaluated by the C-index and the AUC of the ROC curve. The corrected C-index was calculated by 1000 resampling bootstrap. The accuracy of the nomogram model was verified by plotting a calibration curve, which was a comparison of the nomogram-predicted survival probability and actually observed survival outcome. Furthermore, NRI and IDI were calculated to assess the degree of predictive performance optimization by comparing the nomogram model with the 8th AJCC staging. Decision curve analysis (DCA), based on net benefits, was applied to measure clinical usefulness of the nomogram model. Finally, on the basis of the total scores calculated by nomogram, the entire study population (including the training and validation cohort) were divided into three risk groups (low-, intermediate-, and high-risk) using X-tile software (<http://www.tissuearray.org/rimmlab/>). Two-sided *P* values < 0.05 were considered indicative of statistical significance.

Results

Clinical characteristics and survival

The baseline clinical characteristics of 581 patients in the whole cohort are summarized in Table 1. There were more males than females (ratio, 2.40:1) and the median age of patients was 65 years (range, 41–91). 37.8% patients were aged ≥ 70 years. In 51.9% of all patients, the primary tumor was located in the middle esophagus. Most patients were staged as locally-advanced. The threshold value of GTVp and tumor length were retrospectively defined as 30 cm³ and 5 cm in our previous studies [17, 18].

Table 1
Clinical characteristics and inflammatory indicators of patients with esophageal squamous cell carcinoma

	Whole cohort (n = 581)	Training cohort (n = 434)	Validation cohort (n = 147)
Gender			
Male	410 (70.6)	303 (69.8)	107 (72.8)
Female	171 (29.4)	131 (30.2)	40 (27.2)
Age (years)			
< 70	361 (62.2)	268 (61.9)	93 (63.3)
≥ 70	219 (37.8)	165 (38.1)	54 (36.7)
Tumor location			
Cervical	50 (8.6)	40 (9.2)	10 (6.8)
Upper thoracic	172 (29.6)	137 (31.6)	35 (23.8)
Middle thoracic	300 (51.6)	215 (49.5)	85 (57.8)
Lower thoracic	56 (9.6)	39 (9.0)	17 (11.6)
Unknown	3 (0.5)	3 (0.7)	
Clinical T stage			
T1	1 (0.2)	1 (0.2)	
T2	45 (7.7)	22 (5.1)	23 (15.6)
T3	186 (32.0)	125 (28.8)	61 (41.5)
T4	349 (60.1)	286 (65.9)	63 (42.9)
Clinical N stage			
N0	167 (28.7)	120 (27.6)	47 (32.0)
N1	218 (37.5)	162 (37.3)	56 (38.1)
N2	168 (28.9)	128 (29.5)	40 (27.2)
N3	28 (4.8)	24 (5.5)	4 (2.7)
Clinical M stage			
No	467 (80.4)	350 (80.6)	117 (79.6)

Abbreviations: GTVp, primary gross tumor volume; AJCC, American Joint Committee on Cancer; NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PLR, platelet-to-lymphocyte ratio

	Whole cohort (n = 581)	Training cohort (n = 434)	Validation cohort (n = 147)
Yes	114 (19.6)	84 (19.4)	30 (20.4)
8th AJCC stage			
II	85 (14.6)	55 (12.7)	30 (20.4)
III	126 (21.7)	76 (17.5)	50 (34.0)
IVA	256 (44.1)	219 (50.5)	37 (25.2)
IVB	114 (19.6)	84 (19.4)	30 (20.4)
GTVp (cm ³)			
< 30	231 (39.8)	179 (41.2)	52 (35.4)
≥ 30	350 (60.2)	255 (58.8)	95 (64.6)
Tumor length (cm)			
≤ 5	321 (55.2)	247 (56.9)	74 (50.3)
> 5	260 (44.8)	187 (43.1)	73 (49.7)
Chemotherapy			
No	166 (28.6)	120 (27.6)	46 (31.3)
Yes	415 (71.4)	314 (72.4)	101 (68.7)
NLR			
≤ 2.0	254 (43.7)	191 (44.0)	63 (42.9)
> 2.0	327 (56.3)	243 (56.0)	84 (57.1)
LMR			
< 3.0	158 (27.2)	110 (25.3)	48 (32.7)
≥ 3.0	423 (72.8)	324 (74.7)	99 (67.3)
PLR			
< 160.0	417 (71.8)	314 (72.4)	103 (70.1)
≥ 160.0	164 (28.2)	120 (27.6)	44 (29.9)

Abbreviations: GTVp, primary gross tumor volume; AJCC, American Joint Committee on Cancer;NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PLR, platelet-to-lymphocyte ratio

In the training cohort, 340 (21.7%) patients had died and the median survival was 21.8 months (range, 1.6–117.3). In the validation cohort, 127 (13.6%) patients had died and the median survival was 20.8

months (range, 2.2–164.4). The 5-year OS rate in the whole series was 26.0% (26.7% in the training cohort and 23.8% in the validation cohort).

Nomogram model construction and validation

On univariate analyses, age, tumor location, cT stage, cN stage, cTNM stage, GTVp, CT, NLR, LMR, and PLR were identified as prognostic factors for the training cohort. On multivariate analyses, cTNM, GTVp, CT, NLR, and PLR were independent predictors of prognosis (Table 2). Based on the above independent prognostic factors, a nomogram model was developed to predict 1-, 3-, and 5-year OS rates (Fig. 1). Firstly, internal validation was performed to assess the predictive ability of the nomogram model in the training cohort. The discriminative ability of the nomogram model was measured by calculating the C-index. The C-index for 5-year OS was 0.627 (95% CI: 0.597–0.658) (Table 3), and the AUC value of the ROC curve for 5-year OS was 0.706 (95% CI: 0.653–0.760) (Fig. 2A). The calibration curve for 5-year OS showed that the observed clinical outcomes were in accordance with the predicted outcomes (Fig. 2B).

Table 2 Multivariable analysis for overall survival in training cohort

	HR	95% CI	<i>P</i> value
8th AJCC stage	1.372	1.205–1.562	<0.001
Chemotherapy	0.625	0.492–0.794	<0.001
GTVp	1.543	1.231–1.935	<0.001
NLR	1.328	1.041–1.693	0.022
PLR	1.473	1.147–1.892	0.002

Abbreviations: HR, hazard ratio; CI, confidence interval; GTVp, primary gross tumor volume; AJCC, American Joint Committee on Cancer; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio

Finally, the predictive ability of the constructed nomogram model was assessed in the validation cohort. The C-index for 5-year OS was 0.629 (95% CI: 0.578–0.676) and the 5-year AUC value was 0.719 (95% CI: 0.605–0.833) in the validation cohort, which were higher than those for the training cohort (Figure 2C). The calibration curve of 5-year OS was found to have good consistency (Figure 2D).

Comparing the predictive accuracies of the nomogram and the 8th AJCC staging

As shown in Table 3, the C-index for the nomogram model was higher than the AJCC staging in the training cohort (0.627 vs. 0.567) as well as in the validation cohort (0.629 vs. 0.605). In addition, time-

dependent ROC analyses showed that the AUC for the AJCC staging was inferior to the AUC for the nomogram model in the training cohort (0.605 vs. 0.706) as well as in the validation cohort (0.662 vs. 0.719).

In terms of the improvement in predictive performance, the NRI of the nomogram model increased by 30.9% and 17.1% in the training and validation cohorts, respectively (all $P < 0.05$). Furthermore, the IDI of the nomogram model increased by 8.0% and 5.5% in the training and validation cohorts, respectively (all $P < 0.05$). Finally, DCA, as a novel method to assess the clinical usefulness, suggested a greater net clinical benefit of nomogram compared to the 8th AJCC staging, as displayed in Figure 3.

Table 3 Discriminatory ability of the nomogram model versus AJCC stage

	C-index	AUC	NRI	IDI
	(95% CI)	(95% CI)	(<i>P value</i>)	(<i>P value</i>)
TC	0.627	0.706	-	-
Nomogram	(0.597–0.658)	(0.653–0.760)		
TC	0.567	0.605	-	-
AJCC stage	(0.578–0.656)	(0.550–0.660)		
VC	0.629	0.719	-	-
Nomogram	(0.578–0.676)	(0.618–0.620)		
VC	0.605	0.662	-	-
AJCC stage	(0.576–0.678)	(0.557–0.767)		
TC Nomogram	-	-	0.309	0.08
vs. AJCC stage			$p < 0.00$	$p < 0.00$
VC Nomogram	-	-	0.171	0.055
vs. AJCC stage			$P = 0.01$	$P = 0.01$

Abbreviation: TC, training cohort; VC, validation cohort; C-index, concordance index; CI, confidence interval; NRI, net reclassification index; IDI, integrated discrimination improvement.

Risk-groups categorization

According to the total points of nomogram, all patients were divided into three risk subgroups using the X-tile software (Figure 4). Of these, 28.6% patients with <84.8 points were classified as low-risk group, 48.2% patients with 84.8–151.4 points were classified as intermediate-risk group, and 23.2% patients with >151.4 points were classified as high-risk group. The 5-year OS rates in the three groups were 44.0%, 23.6%, and 8.9%, respectively (Figure 4A). The C-index was 0.625 (95% CI: 0.599-0.651), as shown in Supplemental table 1. According to the 8th AJCC staging, the whole cohort was divided into stage II, stage III, stage IVA, stage IVB, and the proportion of patients in each group were 14.6%, 21.7%, 44.1%, and 19.6%, respectively. The 5-year OS rates in these groups were 47.1%, 23.8%, 25.4%, and 14.0%, respectively (Figure 4B). The C-index was 0.574 (95% CI: 0.549–0.600) (Supplemental table 1). The results demonstrated markedly better discrimination ability of the nomogram model in terms of C-index ($P<0.001$).

Discussion

To the best of our knowledge, the current study represents a novel research to successfully build a prognostic nomogram model and risk-stratification system incorporating multiple hematologic inflammatory indices for patients with ESCC receiving definitive IMRT based on a large cohort. In this study, cTNM, GTVp, CT, NLR, and PLR were first identified as independent prognostic indicators by multivariate Cox regression analysis in the training cohort. A nomogram was developed based on these five independent factors to predict OS, and verified in the validation cohort as well. The nomogram model was found to be better than the AJCC staging in predicting OS and clinical survival benefits. Lastly, depending on the nomogram total scores, the entire cohort was divided into low-, intermediate-, and high-risk subgroups. This risk stratification was found to be superior than AJCC clinical staging in predicting OS. Collectively, these results suggest that the nomogram model is a useful for risk stratification and for predicting survival of patients with ESCC treated with radical IMRT.

In this study, several hematological inflammatory indices including NLR and PLR were found to independently impact the prognosis besides other common factors, such as cTNM, GTVp, and CT. Of note, several studies have demonstrated a close correlation of NLR and PLR with prognosis of patients with several other kinds of malignancies including gastric cancer, non-small cell lung cancer, and colorectal carcinoma [19-21]. Moreover, some studies have also demonstrated a significant association of pre-treatment elevated PLR and NLR with poorer prognosis and deeper tumor invasive depth in patients with ESCC [22, 23]. This phenomenon may be attributable to the potential involvement of systemic inflammatory response in the migration, invasion, and metastasis of malignant cells in various

tumors, including ESCC [24]. Therefore, inclusion of NLR and PLR in the nomogram model may help improve the prognostic assessment of patients with ESCC receiving definitive IMRT.

We evaluated the predictive performance of the nomogram model using a variety of indices, including accuracy, discrimination ability, and clinical validity. Calibration, which is generally used to evaluate the accuracy of nomogram, refers to the agreement between the observed and estimated probabilities of the occurrence of an event or outcome [25]. In this study, the calibration curves between the OS predicted by nomogram and the actual OS showed a good agreement in both the training and validation cohorts. In addition, the C-index and the ROC curve are most commonly used to assess the discrimination of the nomogram model [26]. In the training cohort, the C-index and AUC values for 5-year OS were 0.627 and 0.706, respectively, showing good differentiation and predictive ability for OS. Moreover, the C-index and AUC values for 5-year OS were 0.629 and 0.719 in the validation cohort, respectively, confirming the reproducibility and stability of the nomogram model. Hence, the constructed nomogram model presented a good predictive performance.

To further compare the predictive ability of the nomogram model with that of the AJCC staging, 4 evaluation indicators including AUC, C-index, NRI, and IDI were employed. AUC value and C-index were used as the basic reference indicators to estimate the improvement of predictive performance of the nomogram model as compared to the AJCC staging [26]. In our study, the AUC values and C-index of the nomogram in the training and validation cohorts were superior to those of the AJCC staging. In recent years, NRI and IDI have been strongly recommended for evaluating and comparing the distinctive ability between the two prediction models [14]. NRI was originally applied for quantitative evaluation of the improvement in classification performance of the new model over the original model, while the IDI was employed to assess the changes in risk differentials [26]. In our study, the NRI and IDI of the AJCC staging were significantly inferior to those of the nomogram, suggesting better predictive ability of the nomogram model for OS.

DCA was developed to determine whether use of predictive models to inform clinical decision-making does more harm than good, and to further evaluate the clinical applicability of predictive models [27]. In our study, the nomogram offered a higher net benefit than the AJCC staging at any given threshold, indicating a better clinical application value of the constructed nomogram. It is noteworthy that the clinical net benefit of GTVp was almost the same as that of the clinical AJCC staging. GTVp has been shown to be an independent predictor of survival in patients with ESCC treated with definitive radiotherapy [16, 28]. Larger GTVp always means greater tumor load, and a greater proportion of tumor radioresistant hypoxic cells and clonogenic cells, which causes poor survival [28]. This explains the markedly superior net benefit of the nomogram incorporating hematological inflammatory indices, GTVp, cTNM, and CT compared to the AJCC staging.

Finally, risk stratification system was formed depending on the total nomogram scores using the X-tile software. In the study population, 28.6%, 48.2%, and 23.2% of patients were categorized into low-, moderate-, and high-risk subgroups, whereas the proportion of patients in AJCC stages II, III, IVa, and IVb

were 14.6%, 21.7%, 44.1%, and 19.6%, respectively. This indicated a more balanced patient distribution among the three risk subgroups as compared to that among the clinical AJCC stage. Moreover, this risk stratification showed a significantly higher C-index than the clinical AJCC stage, suggesting that the nomogram had a better discrimination ability for risk stratification. Patients in the high-risk group require more intensive therapies: (1) adjuvant chemotherapy; (2) targeted drugs [29]; or (3) immunotherapy. In particular, immunotherapy has developed rapidly in recent years and has been actively explored and applied to patients with ESCC [30, 31]. Studies have demonstrated that the combination of immunotherapy and radiotherapy can synergistically promote anti-tumor activity in vitro, thus effectively controlling local lesions and distant micrometastases [32, 33]. Therefore, radiotherapy plus immunotherapy may improve the treatment efficacy for high-risk ESCC patients. In addition, for patients in the low-risk group, it may be appropriate to reduce the radiation dose or chemotherapy cycles to decrease not only the side effects of radiotherapy combined with adjuvant chemotherapy, but also the treatment cost.

Nevertheless, several limitations of our study should be considered. First, we did not analyze all inflammatory parameters, as some inflammatory mediators such as procalcitonin, C-reactive protein, interleukin-1, interleukin-6, and tumor necrosis factor were not routinely examined at our institution. In addition, this was a retrospective, single-center study and our results may have been influenced by confounders. Further prospective, multicenter studies are required to verify the precision of the nomogram model. Finally, we did not evaluate the dynamic changes in hematological indicators before and after treatment. Such an analysis may help improve the prognostic capability of the nomogram and improve the risk stratification of patients.

Conclusions

We successfully established a nomogram based on pretreatment inflammatory indices for predicting OS, and developed a risk stratification system for ESCC patients receiving IMRT, which was superior to the AJCC staging. Our study may provide a useful clinical reference for prognostic prediction and individualized treatment.

Abbreviations

ESCC: Esophageal squamous cell carcinoma

IMRT: Intensity-modulated radiotherapy

OS: Overall survival

ROC: Receiver operating characteristic

AUC: Area under the curve

C-index: Concordance statistics

NRI: Net reclassification index

IDI: Integrated discrimination improvement

DCA: Decision curve analysis

GTVp: Primary gross tumor volume

CT: Chemotherapy

NLR: Neutrophil-to-lymphocyte ratio

PLR: Platelet lymphocyte ratio

NCCN: National Comprehensive Cancer Network

UICC/AJCC: Union for International Cancer Control/American Joint Committee on Cancer

CRP/Alb: Reactive protein/albumin ratio

ALC: Absolute lymphocyte count

LMR: Lymphocyte-to-monocyte ratio

CI: Confidence level

HR: Hazard ratio

TC: Training cohort

VC: Validation cohort

Declarations

Ethics approval and consent to participate

This study is a retrospective observational study and was conducted in accordance with the relevant guidelines, regulations, and the Declaration of Helsinki. The methods and procedures for this study were approved by the Institutional Review Board of the Fujian Cancer Hospital (No. K2021-129-01). Each patient provided written informed consent before treatment, and the information was anonymized before

analysis. Consecutive patients with new diagnoses of ESCC and treated in Fujian Cancer Hospital from January 2008 to December 2016 were retrospectively reviewed.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YX and JC participated in the design of the study. ZX and HK performed the experiments and the statistical analysis, drafted the manuscript, and assisted with the manuscript preparation. BL, CL, YZ, and LW drafted the manuscript and helped with the manuscript preparation. LY, YY, LC, and MY assisted with experiments performance and statistical analysis. YX examined and revised the manuscript. All authors read and approved the final manuscript.

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Figures

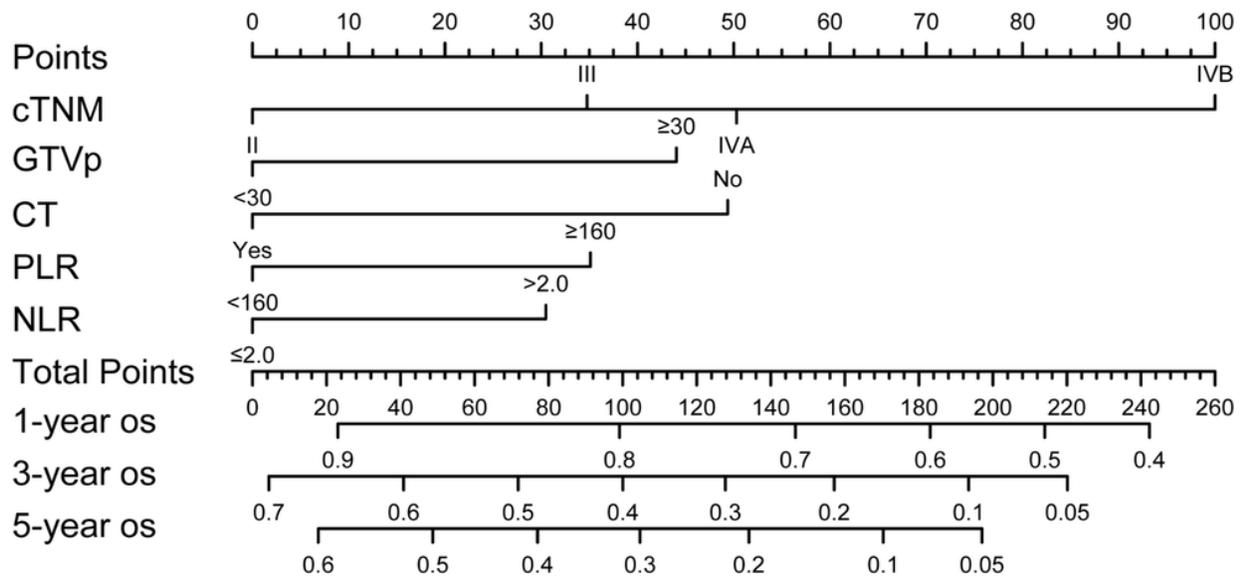


Figure 1

Nomogram model for prediction of 1-, 3-, and 5-year overall survival (OS) in ESCC patients in the training cohort.

Figure 2

(A) Receiver operating characteristic (ROC) curves by nomogram for 3-year and 5-year OS in the primary cohort (PC) (red line: 3-year OS; blue line: 5-year OS); (B) Calibration curve for 5-year OS prediction according to the PC nomogram; (C) ROC curves by nomogram for 3-year and 5-year OS validation cohort (VC) (red line: 3-year OS; blue line: 5-year OS); (D) Calibration curve for predicting 5-year OS according to the VC nomogram.

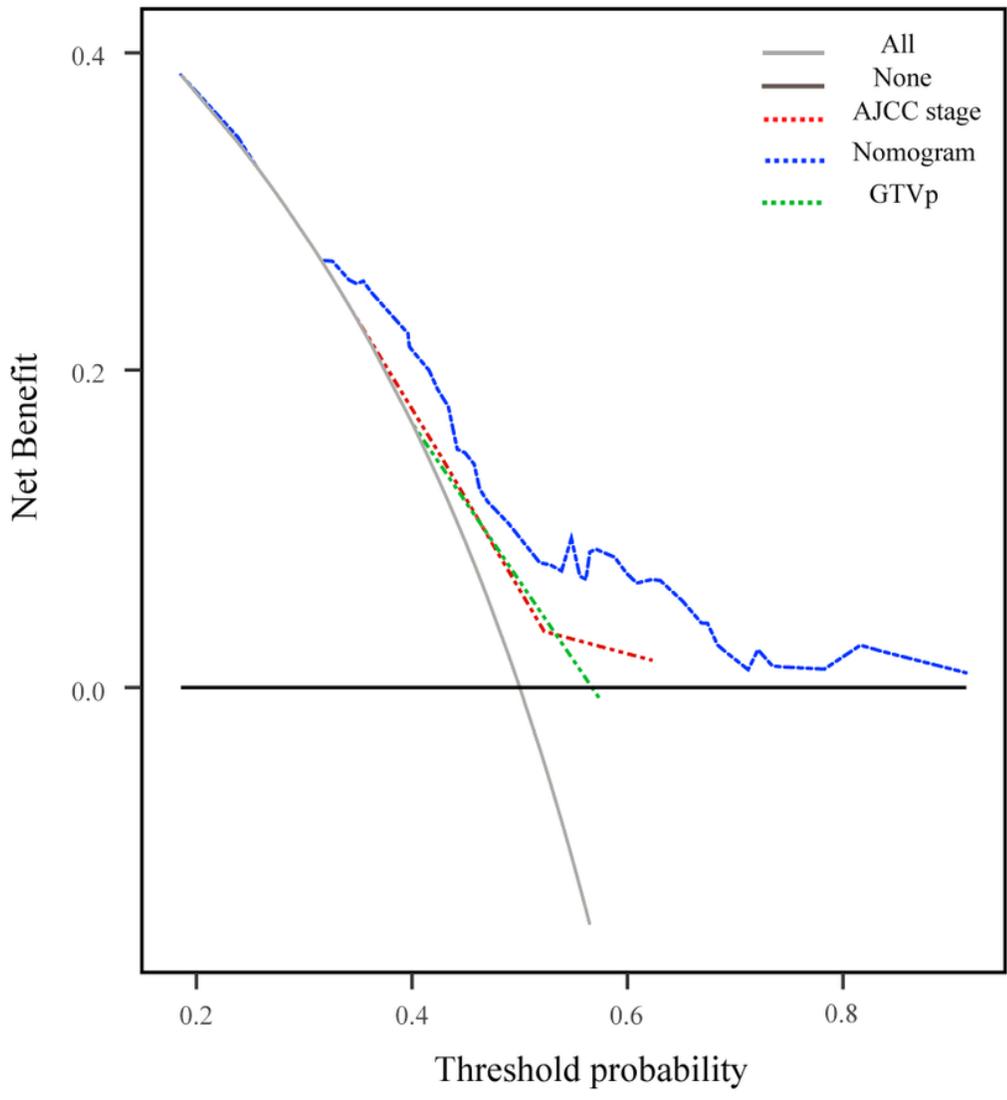


Figure 3

Decision curve analysis of the nomogram (blue line), the AJCC stage (red line), and GTVp (green line) for 5-year OS in the primary cohort (PC).

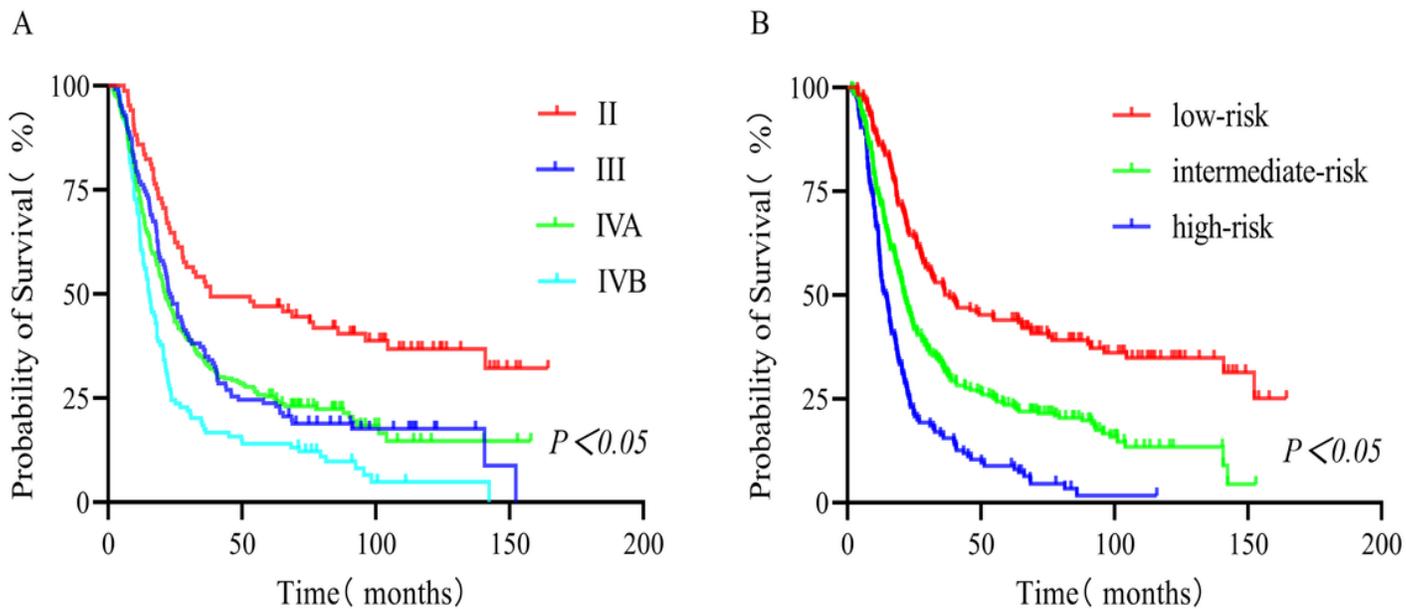


Figure 4

Kaplan–Meier overall survival (OS) curves for (A) groups disaggregated by the AJCC stage and (B) risk group based on the nomogram model in the entire cohort.

Supplementary Files

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- [Supplementaltable1.docx](#)