Cancer Management and Research

Open Access Full Text Article

ORIGINAL RESEARCH

Development and Validation of Nomogram Models Incorporating the Inflammatory Nutritional Index CALLY for Predicting Survival in Locally Advanced Rectal Cancer After Neoadjuvant Chemoradiotherapy

Yichen Zhang[1,2,*], Zenghui Yang[2,*], Yuzhou Feng[1,2,*], Yifan Shi[2], Xiaoming Shen[2], Sen Gao[2], Tao Guo[1,2], Jing Cui[1,2], Chuanqing Bao[1,2]

[1]Wuxi School of Medicine, Jiangnan University, Wuxi, 214000, People's Republic of China; [2]Department of Gastrointestinal Surgery, Affiliated Hospital of Jiangnan University, Wuxi, 214000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Chuanqing Bao, Department of Gastrointestinal Surgery, Affiliated Hospital of Jiangnan University, Wuxi, 214000, People's Republic of China, Email wxbaocq@126.com

Background: Patients with locally advanced rectal cancer (LARC) have considerable rates of postoperative recurrence and metastasis, and existing scoring systems lack specificity. This study aims to establish and validate a prognostic model using inflammatory nutritional index CALLY for overall survival (OS) and progression-free survival (PFS) in patients with LARC following neoadjuvant chemoradiotherapy (NACRT), with the goal of enabling early risk assessment and intervention in LARC patients.

Methods: One hundred and thirty-one LARC patients were analyzed undergoing NACRT followed by surgery (January 2020–May 2024). The median follow-up was 27 months. LASSO regression and multivariate Cox analysis identified prognostic factors. Nomograms for 2-/3-year OS and PFS were constructed and validated using KM, time-dependent ROC curves, calibration plots, and decision curve analysis (DCA). Bootstrap method was used to internally verify the nomogram model.

Results: The study's multifactorial analysis revealed high CALLY were independently associated with improved OS (HR = 0.344, 95% CI: 0.133–0.893; P = 0.028) and PFS (HR = 0.492, 95% CI: 0.266–0.912; P = 0.024). OS nomogram (CALLY/CEA/CCI) achieved AUCs of 0.83 (2-year) and 0.76 (3-year). PFS nomogram (CALLY/PLR/CEA/CA724/vascular invasion) showed superior 3-year accuracy (AUC = 0.81) but lower 2-year accuracy (AUC = 0.71). Calibration curves confirmed good prediction-observation agreement. DCA revealed wider clinical applicability for 3-year PFS. Survival KM curve for OS suggested that high-risk patients had 8.25-fold higher mortality (95% CI: 3.05–22.30).

Conclusion: A prognostic nomogram of LARC patients after NACRT in terms of OS and PFS was established based on the inflammatory nutritional Index CALLY, in which the PFS model showed excellent long-term predictive accuracy and clinical utility, providing individualized risk stratification and advance intervention to guide adjuvant therapy.

Keywords: locally advanced rectal cancer, neoadjuvant chemoradiotherapy, prognostic model, inflammatory nutritional indices, nomogram

Introduction

The Global Cancer Statistics 2022 report indicated that there were nearly 20 million new cancer cases, including 1.9 million new colorectal cancer (CRC) cases, accounting for nearly one-tenth of cancer cases, making it the third most common malignant tumor in the world and the second leading cause of cancer-related deaths.[1] With advances in minimally invasive techniques, locally advanced colorectal cancer (LARC) patients may benefit from neoadjuvant therapy. However, in the presence of metastases, chances of survival are significantly reduced.[2] Most LARC patients

Received: 7 August 2025
Accepted: 19 November 2025
Published: 1 December 2025

were treated with total mesolectal excision (TME) and neoadjuvant chemoradiotherapy (NACRT) significantly improved the distant metastasis of the cancer.[3] The 5-year survival rate and cumulative incidence of 5-year local recurrence of 76% and 6%, respectively, with NACRT prior to TME reduced local recurrence, metastasis, and improved survival of patients with LARC.[4] This treatment achieved a high pathological complete remission rate (pCR) (44.3%), a high CRT compliance rate (98.8%), and significantly fewer postoperative complications than the TME group.[5] Therefore, NACRT, followed by resection of en bloc rectum and mesorectum, has become the standard of care for LARC.[3]

Different factors have a significant role in the stage reduction of LARC after NACRT-TME. Several studies have shown that from a radiation oncology point of view, radiomics column maps of MRI predict good response to NACRT,[6] and that short-term radiation therapy and long-term chemotherapy not only increase the local response to NACRT but also reduce the risk of systemic recurrence.[7] In terms of hematological indices, carcinoembryonic antigen (CEA), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-neutrophil index (PNI)[8] and CRP albumin-lymphocyte index (CALLY) were all recently proposed as novel inflammation-nutrition composite index.[9] CALLY has been shown to have a critical role in gastric, hepatic and pot-bellied cancers.[9–11] Regarding sarcopenia, which is characterized by loss of skeletal muscle mass (SMA), it is associated with progression-free survival (PFS) and overall survival (OS) in short-term CRC patients undergoing surgery.[12,13]

The above factors indicate that inflammatory nutritional indices are key determinants influencing cancer progression and prognosis and possess predictive capacity for postoperative PFS and OS in CRC patients. Unfortunately, no existing models are currently available to assess the risk of NACRT and postoperative outcomes in LARC, thereby limiting the provision of valuable post-treatment guidance. In this study, we developed nomograms combining clinical factors and inflammatory nutritional indices to comprehensively evaluate disease prognosis outcomes. It can predict the probability of recurrence or death in specific individuals, and its most important advantage is that it can assess the risk of clinical events independently based on patient and disease characteristics.[14] Nomograms can incorporate continuous variables and independent risk factors of the disease into prognosis, outperforming clinicians in assessing locally advanced tumors and is widely applicable in practice.[15]

Materials and Methods

Patients and Participants

This study retrospectively investigated patients with LARC who were treated with NACRT between January 2020 and May 2024 at Jiangnan University Hospital. The inclusion criteria were as follows: (1) patients with complete peripheral blood cell count data and serum CEA; (2) patients aged 18–79 years; (3) patients diagnosed with LARC after pathological histology, illnesses intestinal obstruction, distant metastases (lung/ovarian/peritoneal), or concurrent bone marrow transplantation during NACRT; patients who were unable to undergo surgery and opted for conservative treatment after NACRT; critically ill patients suffering from cardiac failure, renal failure, or other serious illnesses; and patients with incomplete follow-up data were excluded from the analysis (Figure 1). All patients were staged preoperatively with contrast-enhanced computed tomography of the abdomen and pelvis using MRI of the pelvis and contrast-enhanced computed tomography CT. Pathologic histology of all patients was staged, according to the 8th AJCC TNM. Clinical staging before the start of NACRT (cTNM) was compared with the pathology of the resected specimens after treatment (ypTNM), down to ypTNM stage 0-I as the criterion for grouping.[16] Owing to the specific nature of the disease, the sample size only met the minimum power requirement; however, multicenter studies on rare subgroups will be required in the future.

Treatment Strategies

All patients received a NACRT regimen consisting of a total radiation dose of 45 or 50.4 Gy and continuous infusion or oral (capecitabine) 5-fluorouracil chemotherapy-based chemotherapy. Radiotherapy was delivered in 25 fractions over 5 weeks.[17] Surgery was performed for at least 6 weeks after the last radiotherapy session. All cases were treated by open or laparoscopic surgery. Surgical approaches included Dixon’s procedure, colostomy, Hartmann’s procedure, and Miles’ procedure. Based on pre-NACRT imaging, if lateral pelvic lymph node (LLN) metastasis was suspected, lateral pelvic

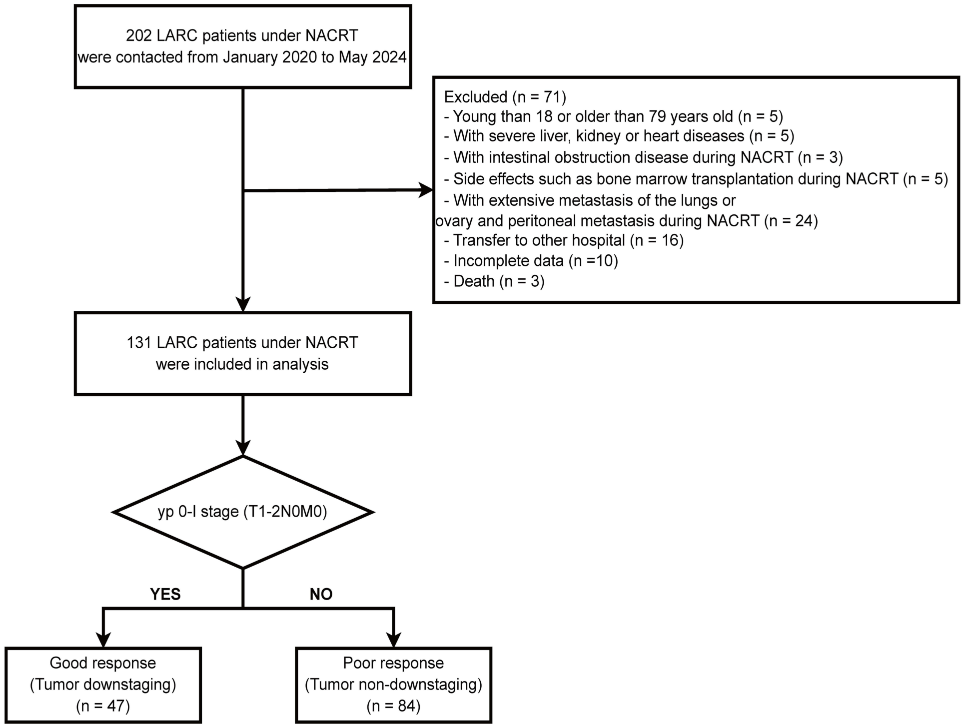

Figure 1 Study flow chart.
Abbreviations: LARC, locally advanced colorectal cancer; NACRT, neoadjuvant chemoradiotherapy.

lymph node dissection was performed concurrently. Adjuvant chemotherapy was considered for all patients regardless of pathological results. The regimen used for adjuvant chemotherapy was as follows: the Roswell Park regimen of intravenous 5-FU plus LV, oral UFT plus l-LV, or oral capecitabine plus oxaliplatin, capecitabine plus oxaliplatin.[18]

Date Collection

The following data were collected: (1) Baseline clinical variables: gender, age, Diabetes, Hypertension, body mass index (BMI), Charlson comorbidity index (CCI), nutritional risk screening 2002 (NRS2002) score and L3 skeletal muscle cross-sectional area (L3SM). (2) pre-NACRT, serologic parameters within 24 hours of admission: platelet count, lymphocyte count, neutrophil count, monocyte count, albumin count, C-reactive protein (CRP), CEA, carbohydrate antigen 19–9 (CA199) et al (3) Pathological information: TNM stage before and after NACRT, vascular invasion and nerve invasion et al (4) Follow-up data: overall survival (OS) and progression-free survival (PFS) (months). We calculated L3SMI, NLR, PLR, LMR, PNI and CALLY according to the following formula.

Slice-Omatic, version 5.0 (TomoVision, Magog, Canada) was used to analyse L3SM on CT images. Muscle tissue unit thresholder ranged from −29 HU to 150 HU. L3SMI (cm^2/m^2) = total area of all skeletal muscle at the L3 level (cm^2)/height^2 (m^2).[19,20] CALLY index = (albumin level in g/L) × (lymphocyte count in/μL)/(CRP level in mg/L) × 10.[21] The formulas for the remaining inflammatory nutritional indices were presented in Supplementary Table S1.

Complication Assessment

Postoperative complications following LARC radical surgery are defined as medical or surgical complications occurring within 30 days postoperatively. The Claven-Dindo system is used for grading (Supplementary Table S2), with grade ≥ IIIa classified as severe postoperative complications.[22] CCI includes all postoperative adverse events, which are weighted according to severity and comprehensively calculated (www.assessurgery.com) to derive the corresponding score (0–100 points, with 0 points indicating no complications and 100 points indicating death).[23,24]

Endpoints and Follow-Up

All patients were followed by telephone and in the clinic. The endpoints event defined as any form of tumour recurrence, metastasis or death, with a follow-up deadline of May 2025. The primary endpoint of this study was OS, defined as the time interval from the date of randomization to death from any cause. The secondary endpoint was PFS, defined as the time from the start of treatment to the first imaging-confirmed disease progression or death from any cause.

Establishment and Validation of Prognostic Models

LASSO regression was used for preliminary analysis, and the selected variables were further screened using univariate Cox analysis to identify potential risk factors affecting survival. After identifying the potential risk factors, we performed backward multivariate analysis to select the optimal model. Based on the results of the multivariate Cox, statistically significant variables ($P < 0.05$) were included in the nomogram to predict 2-year and 3-year survival rates after NACRT and surgery. The predictive performance of the nomogram model was assessed using time-dependent receiver operating characteristics (ROC), bootstrap method and calibration curves. Time-dependent ROC were used to evaluate discriminatory ability. Bootstrap method was used to repeat 500 times for internal validation of the nomogram model. Calibration curves were used to compare the probabilities predicted by the nomogram with actual outcomes. Kaplan–Meier curves (KM) was used to validate the risk stratification ability of the nomogram model. Finally, the net benefit of the model was assessed using decision curve analysis (DCA).

Statistical Analysis

Statistical analysis was performed using SPSS 27.0 software. For continuous variables, normality was tested using the Kolmogorov–Smirnov test. Compliance was expressed as mean ± standard deviation (SD) for continuous variables and as median M [P25, P75] for non-continuous variables. For categorical variables, categorical information was presented as numbers and percentages (n,%). Comparisons between groups were performed using independent samples *t*-tests, non-parametric rank-sum tests, and chi-square (χ^2) tests. ROC curves were plotted, and the Youden index was calculated to identify the optimal cutoff value for the inflammatory nutritional index in predicting survival. LASSO regression was used for preliminary screening of potential risk factors, followed by Cox proportional hazards models for univariate and multivariate analysis. Forest plots were created using the Dream Cloud statistical platform (https://mengte.pro/forest_plot), and the model was visualized using a nomogram. The calibration curve, bootstrap method and DCA were used to evaluate the model. All analyses were conducted using R (version 4.5.0; http://www.r-project.org/), with a two-sided $P < 0.05$ indicating statistical significance.

Results

Baseline Characteristics and ROC Curves That Affect the Survival

The baseline characteristics of LARC patients included in this retrospective study are presented in Table 1. The median OS and PFS for all patients were 27 months and 26 months, respectively. The 2-year and 3-year OS rates were 93.9% and 79.3%, respectively. The 2-year and 3-year PFS rates were 76.7% and 52.8%, respectively. Among the 131 patients (95 male, 36 female), the median age of LARC patients was 62 years [IQR: 55, 70]. According to the 8th AJCC TNM classification, postoperative histopathology showed that ypTNM stage 0-I was defined as a good response, and ypTNM stage II–IV was defined as a poor response. Moreover, according to postoperative pathology findings, the results showed that six inflammatory nutritional indices, the quantitative indicator CCI for complications occurring within 30 days postoperatively in 101 LARC patients (77.1%); histological differentiation, with moderate differentiation (71.7%); and no vascular invasion (77.9%) were significantly associated with tumor downstaging. All patient characteristics are listed in Table 1.

According to ROC analyses, the optimal cutoffs for predicting survival using L3SMI, PLR, NLR, LMR, CALLY, and PNI were 43.44, 152.09, 2.83, 3.09, 1.47, and 45.85, respectively. The optimal inflammatory nutritional index for predicting survival was CALLY (AUC = 0.736, 95% CI: 0.609–0.863; $P < 0.001$). All inflammatory nutritional indices are listed in Figure 2 and Table 2.

Table 1 Baseline Data and Clinicopathologic Features

Variables	Total (N =131)	Good Response (N = 47)	Poor Response (N = 84)	*P* value
Gender				0.045*
Male	95(72.5%)	39(83.0%)	56(66.7%)	
Female	36(27.5%)	8(17.0%)	28(33.3%)	0.485
Age (Year)	62.00(55.00, 70.00)	63.00(57.00, 70.00)	62.00(55.00, 69.00)	
Diabetes				0.739
None	97(74.0%)	34(72.3%)	63(75.0%)	
Yes	34(26.0%)	13(27.7%)	21(25.0%)	
Hypertension				0.150
None	75(57.3%)	23(48.9%)	52(61.9%)	
Yes	56(42.7%)	24(51.1%)	32(38.1%)	
BMI (Kg/m^2)	9.68 ± 3.11	9.93 ± 3.15	8.88 ± 2.98	0.009*
NRS2002	2.00(1.00, 3.00)	2.00(1.00, 2.00)	2.00(1.00, 3.00)	0.444
CCI	8.70(8.70, 20.90)	8.70(0.00, 20.90)	20.90(8.70, 20.90)	0.026*
HB (g/L)	127.00(115.00, 137.00)	129.00(123.00, 149.00)	125.00(106.75, 135.00)	0.003*
CEA (μg/L)	4.24(2.07, 7.84)	4.55(1.77, 7.45)	4.14(2.40, 8.24)	0.715
CA199 (U/L)	9.45(5.30, 21.80)	9.30(5.40, 20.99)	9.68(5.23, 24.05)	0.611
CA724 (U/L)	1.81(1.10, 3.59)	1.70(1.11, 2.78)	1.83(1.09, 4.52)	0.382
L3SMI	42.77(39.38, 48.65)	45.15(41.80, 55.84)	41.63(38.37, 46.90)	<0.001*
PLR	152.50(118.46, 198.89)	128.26(101.60, 164.00)	164.01(121.28, 220.22)	0.001*
NLR	2.37(1.77, 3.07)	2.21(1.75, 2.65)	2.47(1.82, 3.42)	0.037*
LMR	2.50 ± 1.58	2.23 ± 1.49	2.52 ± 1.59	0.019*
CALLY	3.92(2.21, 6.69)	5.71(3.55, 9.47)	2.77(1.48, 4.99)	<0.001*
PNI	30.50 ± 5.53	25.41 ± 5.04	31.80 ± 5.64	0.018*
Pathological features				
Fistula				0.434
None	36(27.5%)	11(23.4%)	25(29.8%)	
Yes	95(72.5%)	36(76.6%)	59(70.2%)	
Recovery time (Day)	13.00(10.00, 16.00)	11.00(10.00, 15.00)	13.50(11.00, 16.00)	0.118
Histological differentiation				0.002*
Low	20(15.3%)	1(2.1%)	19(22.6%)	
Middle	94(71.7%)	36(76.6%)	58(69.1%)	
High	17(13.0%)	10(21.3%)	7(8.3%)	
Histological type				0.716
Tubular adenocarcinoma	89(67.9%)	31(66.0%)	58(69.0%)	
Adenocarcinoma	42(32.1%)	16(34.0%)	26(31.0%)	
Vascular invasion				0.005*
None	102(77.9%)	43(91.5%)	59(70.2%)	
Yes	29(22.1%)	4(8.5%)	25(29.8%)	
Nerve invasion				0.725
None	98(74.8%)	36(76.6%)	62(73.8%)	
Yes	33(25.2%)	11(23.4%)	22(26.2%)	
Microsatellite stabilization				0.170
MSI-L	3(2.3%)	1(2.1%)	2(2.4%)	
MSI-H	6(4.6%)	0(0.0%)	6(7.1%)	
MSI-S	122(93.1%)	46(97.9%)	76(90.5%)	
Her-2 (+)				0.960
0	64(48.9%)	23(48.9%)	41(48.8%)	
1	46(35.1%)	17(36.2%)	29(34.5%)	
2	21(16.0%)	7(14.9%)	14(16.7%)	

(*Continued*)

 https://doi.org/10.2147/CMAR.S555346

Table 1 (Continued).

Variables	Total (N =131)	Good Response (N = 47)	Poor Response (N = 84)	*P* value
EGFR (+)				0.357
0	24(18.3%)	12(25.5%)	12(14.3%)	
1	41(31.3%)	15(31.9%)	26(31.0%)	
2	61(46.6%)	19(40.4%)	42(50.0%)	
3	5(3.8%)	1(2.1%)	4(4.8%)	

Note: *Indicate P < 0.05.
Abbreviations: CCI, charlson comorbidity index; CA199, carbohydrate antigen 19–9; CA724, carbohydrate Antigen 72–4; PLR, platelet to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PNI, prognostic nutrition index; CALLY, C-reactive protein-albumin-lymphocyte index; L3SMI, L3 Skeletal Muscle Index.

LASSO Regression Screening for Prognostic Factors of OS and PFS in LARC

By comparing the clinical characteristics of LARC patients undergoing NACRT and whether the tumor stage was downgraded post-surgery (Table 1), multiple potential prognostic factors were identified, including gender, age, diabetes, hypertension, BMI, NRS2002 score, CCI, and 19 other indicators. These factors were included in LASSO regression analysis, and the optimal assessment indicator for OS was achieved when the harmonic parameter log(λ) was 0.033. Ultimately, 17 variables were selected: gender, age, BMI, NRS2002, CCI, CEA, N stage, L3SMI, PLR, NLR, LMR, CALLY, PNI, histological differentiation, vascular and nerve invasion, and Her-2 (Figure 3A and B). These clinical characteristics were found to be associated with OS in LARC patients. Similarly, the optimal assessment indicator for PFS was achieved when the harmonic parameter log(λ) was 0.084, and ultimately 7 variables were selected that were associated with PFS: CEA, CA724, PLR, CALLY, histological differentiation, vascular invasion, and nerve invasion (Figure 3C and D).

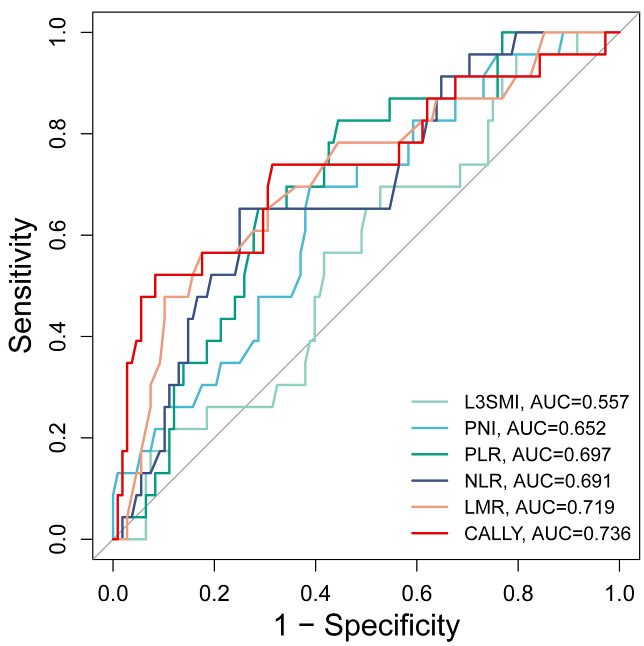

Figure 2 Receiver operating characteristic curves of inflammatory nutritional indices for predicting survival. The highest area under curve (AUC) value for survival is CALLY (0.736).
Abbreviations: L3SMI, L3 Skeletal Muscle Index; PNI, prognostic nutrition index; PLR, platelet to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; CALLY, C-reactive protein-albumin-lymphocyte index.

 https://doi.org/10.2147/CMAR.S555346

Table 2 AUC Values from the ROC Analysis of Inflammatory Nutritional Indices for Predicting Survival

Variables	Cut-Off Points	AUC	*P* value	95% CI
L3SMI	43.435	0.557	0.39	0.435–0.680
PNI	45.85	0.652	0.023*	0.534–0.769
PLR	152.085	0.697	0.003*	0.590–0.805
NLR	2.825	0.691	0.004*	0.576–0.806
LMR	3.085	0.719	0.001*	0.599–0.838
CALLY	1.47	0.736	<0.001*	0.609–0.863

Notes: *Indicate P < 0.05.
Abbreviations: L3SMI, L3 Skeletal Muscle Index; PNI, prognostic nutrition index; PLR, platelet to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; CALLY, C-reactive protein-albumin-lymphocyte index.

Prognostic Prediction of the CALLY Index in LARC

We performed Cox regression analysis using the variables selected through Lasso regression analysis. The results of univariate and multivariate Cox regression analysis were presented in Figure 4. Multivariate analysis of OS showed (Figure 4A) that elevated levels of high CALLY (HR = 0.344, 95% CI: 0.133–0.893; P = 0.028) reduced the risk of OS by 65.6%. For the PFS multivariate analysis results (Figure 4B), high CALLY (HR = 0.492, 95% CI: 0.266–0.912; P = 0.024) reduced the risk of PFS by 50.8%. Additionally, we found that CEA is not only a risk factor for OS (HR = 1.004, 95% CI: 1.001–1.007; P = 0.014) but also PFS (HR = 1.005, 95% CI: 1.002–1.008; P < 0.001).

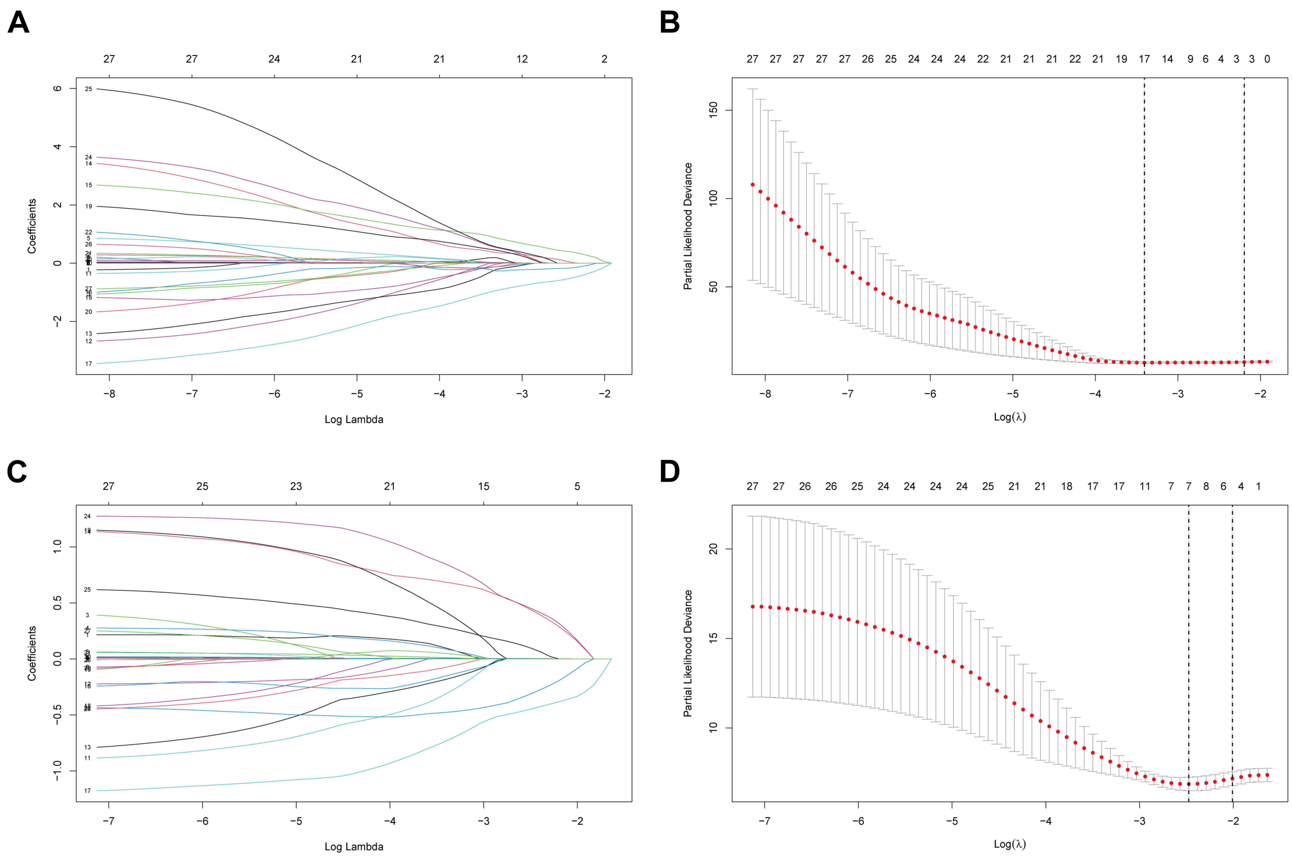

Figure 3 A LASSO binary Cox regression model based on the minimum Lambda value was used to screen predictive indices for overall survival (OS) and progression-free survival (PFS) in LARC patients. (**A**) LASSO coefficient parameter for the 28 variables predicting OS. Vertical lines are drawn at the values selected by 10-fold cross-validation in (**B**). As the λ value decreases, the model's compression increases, enhancing its ability to select important variables. (**B**) 10-fold cross-validation results for predicting OS. The values between the two dashed lines represent the positive and negative standard deviation ranges of log(λ). The left dashed line indicates the value of the harmonic parameter log(λ) when the model error is minimized. When log(λ) = 0.033, 17 variables were selected. (**C**) LASSO coefficient parameters for the 28 variables predicting PFS. Vertical lines are drawn at the values selected in the 10-fold cross-validation in (**D**). As the λ value decreases, the model's accuracy also decreases. (**D**) 10-fold cross-validation results for predicting PFS. When log(λ) = 0.084, 7 variables were selected.

https://doi.org/10.2147/CMAR.S555346

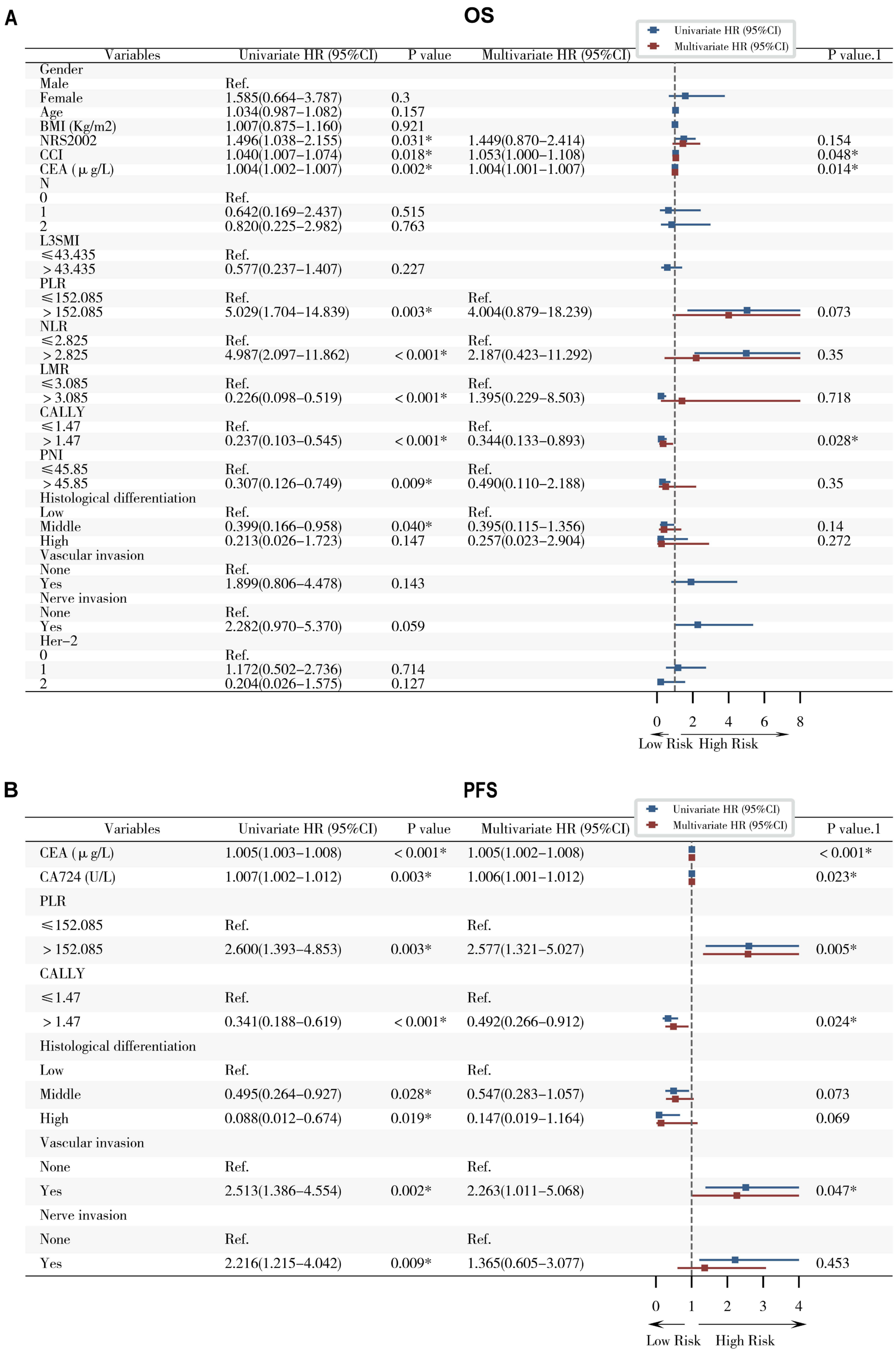

Figure 4 Multivariate Cox regression forest plot analyzing the survival prognosis of LARC patients based on the LASSO regression model. (**A**) Forest plot obtained from univariate and multivariate Cox regression analysis with OS as the outcome. (**B**) Forest plot obtained from univariate and multivariate Cox regression analysis with PFS as the outcome.

Notes: *Indicate P < 0.05.

Abbreviations: LARC, locally advanced colorectal cancer; CCI, Charlson comorbidity index; CA724, carbohydrate Antigen 72–4; L3SMI, L3 Skeletal Muscle Index; PLR, platelet to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PNI, prognostic nutrition index; CALLY, C-reactive protein-albumin-lymphocyte index.

 https://doi.org/10.2147/CMAR.S555346

Development and Evaluation of Nomograms Based on CALLY

To develop a quantitative method for predicting the prognosis of LARC, we implement nomogram prediction models for OS and PFS based on the results of multivariate Cox analysis, including CALLY, CEA, and CCI (HR = 1.053, 95% CI: 1.000–1.108; P = 0.048) to predict the 2-year and 3-year OS of patients (Figure 5A), and CALLY, PLR (HR = 2.577, 95% CI: 1.321–5.027; P = 0.005), CEA, CA724 (per-unit increase HR = 1.006, 95% CI: 1.001–1.012; P = 0.023) and vascular invasion (HR = 2.263, 95% CI: 1.011–5.068; P = 0.047) to predict the 2-year and 3-year PFS of patients (Figure 6A). To utilize the nomogram, a vertical line is drawn from each variable's value to the points axis, with total points calculated as the sum of all individual risk scores.

Model performance was evaluated using time-dependent ROC curves, calibration analyses, decision curve analysis (DCA) and bootstrap resampling method. The AUCs for 2- and 3-year OS predictions were 0.83 and 0.76, respectively (Figure 5B). However, the PFS model showed higher 3-year accuracy (AUC = 0.81), but lower 2-year accuracy (AUC = 0.71) compared to the OS model, respectively (Figure 6B). Calibration curves display the better consistency between predicted survival probabilities from the nomogram and the OS/PFS at 2- and 3-years (Figures 5C and 6C), indicating improved reliability in longer-term predictions. Furthermore, DCA shows that under the comparison of curve areas, the 3-year PFS model is much higher than that of the 2-year-3-year OS model (Figure 5D and E), which suggests that the value of the net benefit of the PFS model is much greater than that of the OS model, and even more strikingly, the 3-year PFS model exceeds the default strategy in terms of net benefit when the decision threshold exceeds 0.93 (Figure 6D and E). These results suggest that the PFS model improves the accuracy of long-term prognostic stratification and increases clinical value as the time horizon increases. At the same time, we performed internal validation of the models using the bootstrap resampling method 500 times and obtained the resampled ROC of the OS and PFS models: AUC = 0.866 (95% CI: 0.862–0.869) (Figure 7A); 0.861 (95% CI: 0.858–0.864) (Figure 7B). In summary, the nomogram model for PFS can better predict the value.

Survival Curves Based on the Nomograms

Patients were divided into low-risk and high-risk groups based on their survival status. Kaplan-Meier analysis showed that the two survival curves were significantly separated (Log rank test, P < 0.001). The OS and PFS rates indicated that the high-risk group had an 8.25 times higher risk of death (95% CI: 3.05–22.30) and a 6.98 times higher risk (95% CI:

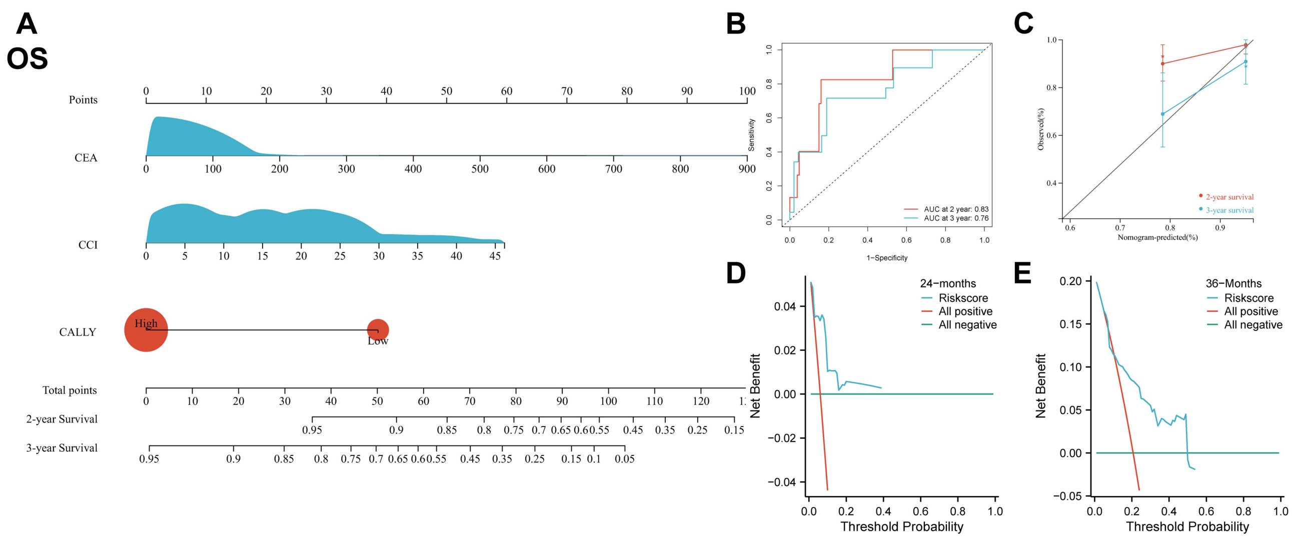

Figure 5 Comprehensive evaluation of the NACRT and postoperative OS prediction model for LARC patients: nomogram, calibration curve, and clinical decision curve (DCA). (**A**) Nomogram to predict 2-year and 3-year OS for LARC patients. (**B**) Time-ROC curves for 2-year and 3-year OS prediction based on the nomogram. (**C**) Calibration curves for 2-year and 3-year OS prediction based on the nomogram. The 45-degree diagonal line represents ideal prediction. (**D** and **E**) DCA of risk scores for OS prediction based on the nomogram. The net benefit, calculated by adding true positives and false positives, corresponds to the measurement value on the Y-axis; the X-axis represents the threshold probability. (**D**) 2-, (**E**) 3-year DCA for OS prediction based on the nomogram.

Abbreviations: LARC, locally advanced colorectal cancer; NACRT, neoadjuvant chemoradiotherapy; CCI, Charlson comorbidity index; CALLY, C-reactive protein-albumin-lymphocyte index.

 https://doi.org/10.2147/CMAR.S555346

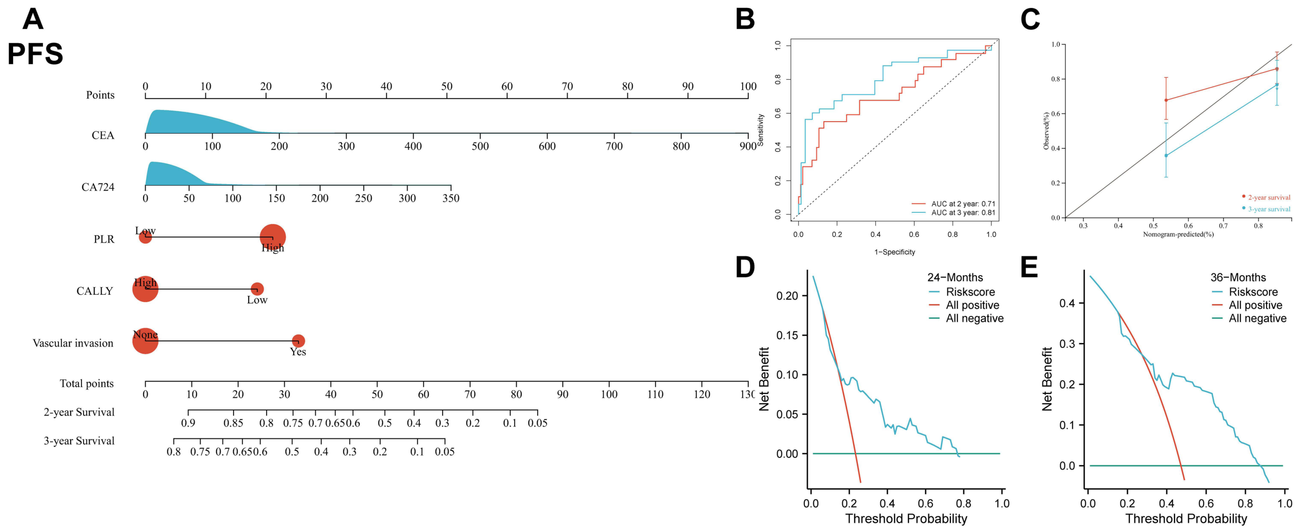

Figure 6 Comprehensive evaluation of the NACRT and postoperative PFS prediction model for LARC patients: nomogram, calibration curve, and clinical decision curve (DCA). (**A**) Nomogram to predict 2-year and 3-year PFS for LARC patients. (**B**) Time-ROC curves for 2-year and 3-year PFS prediction based on the nomogram. (**C**) Calibration curves for 2-year and 3-year PFS prediction based on the nomogram. The 45-degree diagonal line represents ideal prediction. (**D** and **E**) DCA of risk scores for PFS prediction based on the nomogram. The net benefit, calculated by adding true positives and false positives, corresponds to the measurement value on the Y-axis; the X-axis represents the threshold probability. (**D**) 2-, (**E**) 3-year DCA for PFS prediction based on the nomogram.
Abbreviations: LARC, locally advanced colorectal cancer; NACRT, neoadjuvant chemoradiotherapy; CA724, carbohydrate Antigen 72–4; PLR, platelet to lymphocyte ratio; CALLY, C-reactive protein-albumin-lymphocyte index.

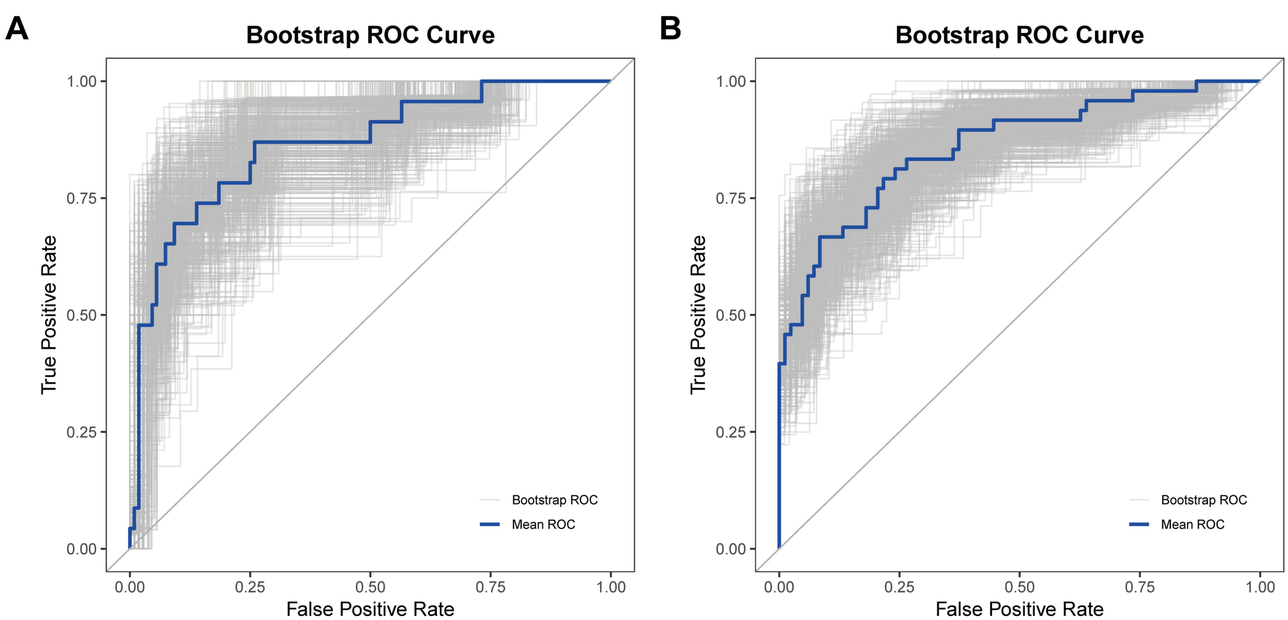

Figure 7 Bootstrap resampling 500 times for internal validation of the model. (**A**) Bootstrap resampling of the OS model 500 times, AUC = 0.866 (95% CI: 0.862–0.869); (**B**) Bootstrap resampling of the PFS model 500 times, AUC = 0.861 (95% CI: 0.858–0.864).

3.75–12.99) compared to the low-risk group (Figure 8A and C). These results, along with the model, confirmed the clinical applicability of the nomogram. In addition, Kaplan-Meier curves for OS and PFS were plotted for CALLY (Figure 8B and D), showing that the risk of death in the low CALLY group was 3.99 times higher than that in the high CALLY group (95% CI: 1.437–10.80) and 2.89 times higher (95% CI: 1.335–6.259), respectively. In summary, compared to individual factors, the nomogram model can better predict OS and PFS.

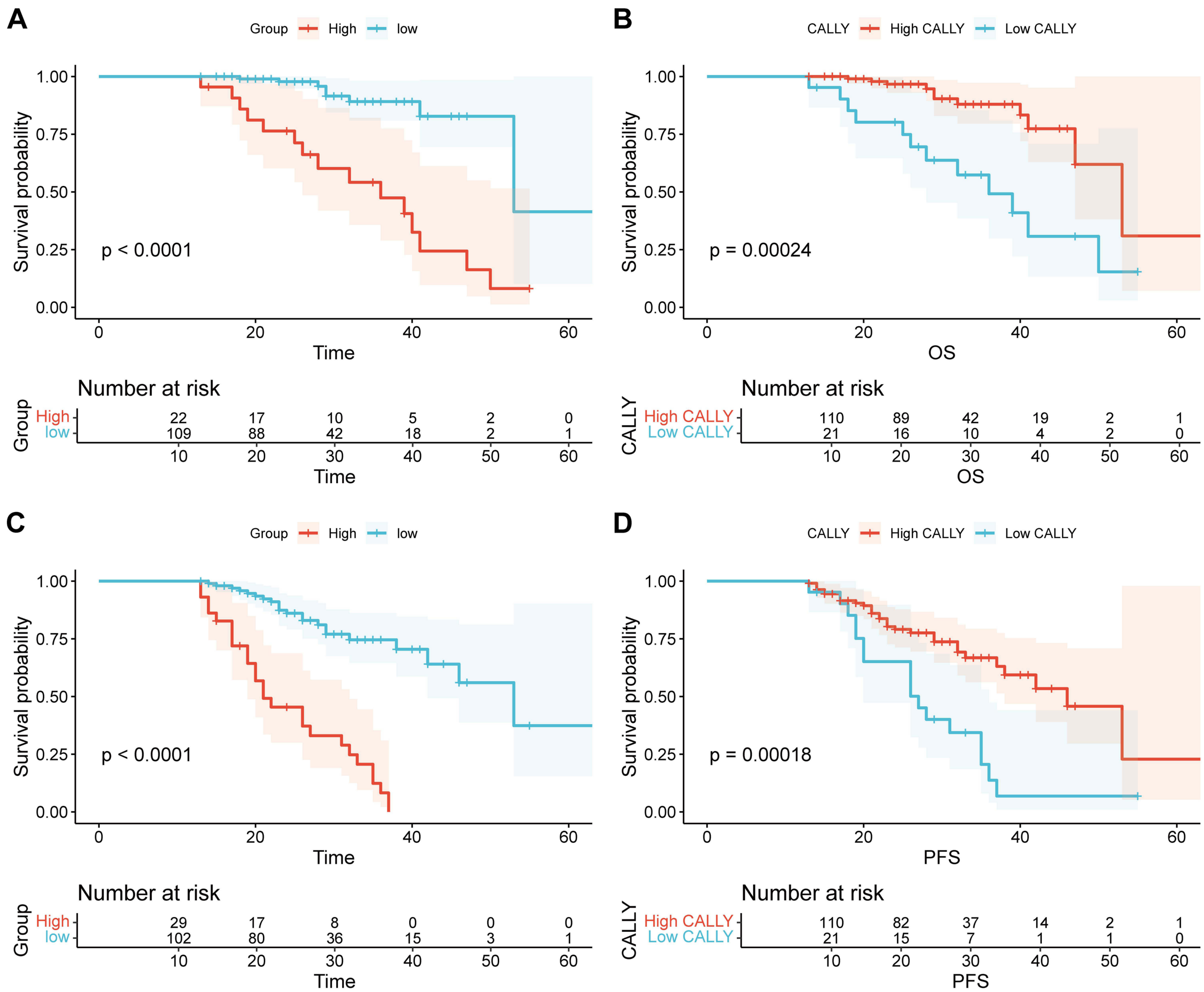

Figure 8 Kaplan-Meier survival analysis based on nomogram risk groups and CALLY. (**A**) Nomogram risk stratification for predicting OS. The 5-year mortality risk in the high-risk group was 8.25 times higher than that in the low-risk group. (**B**) The effect of CALLY levels on OS. The mortality risk in the low CALLY group was 3.99 times higher than that in the high CALLY group. (**C**) Nomogram risk stratification for predicting PFS. The 5-year mortality risk in the high-risk group is 6.98 times higher than that in the low-risk group. (**D**) The impact of CALLY levels on PFS. The mortality risk in the low CALLY group is 2.89 times higher than that in the high CALLY group.
Abbreviations: CALLY, C-reactive protein-albumin-lymphocyte index.

Discussion

The 5-year survival rate and 5-year cumulative local recurrence rate for LARC patients are 76% and 6%.[4] The most effective treatment currently available involves NACRT followed by radical resection, with adjuvant chemotherapy administered subsequently. This approach improves preoperative tumor response rates and reduces postoperative local metastasis rates.[25] In short-term efficacy analyses, NACRT did improve the R0 resection rate and 3-year OS, but the distant metastasis rate remained high, and improvements in 5-year OS and disease-free survival (DFS) were not significant.[26] Therefore, as Okamura reported,[27] early identification of LARC with poor postoperative outcomes following NACRT, combined with adaptive treatment strategies, may improve the likelihood of tumor recurrence in the short term. While the Okamura model for esophageal cancer achieved an initial AUC of 0.679 with 1000 bootstrap validations of 0.670,[27] our nomogram demonstrates substantially improved discriminative ability in the LARC-specific context: initial 2-year AUC 0.830 further enhanced to 0.866 after 500 bootstraps (Figure 7A). This represents a relative improvement in predictive accuracy over current standards. We concluded that the model could enhance the treatment of NACRT patients by rapidly identifying high risk and then intervening with treatment regimens. In our study, we used OS and PFS as outcomes and analyzed 131 LARC patients using

Lasso-Cox regression, screening out 3 and 5 variables respectively to establish two nomogram models predicting 2-year and 3-year outcomes. These indicators include tumor burden markers (CEA, CA724), inflammatory-nutritional markers (CALLY, PLR), and postoperative pathological and complication status (CCI, vascular invasion). The nomograms based on the inflammatory-nutritional index CALLY can rapidly stratify patients into risk groups prior to NACRT, thereby enabling individualized treatment.

Inflammation can promote carcinogenesis by inducing gene mutations, inhibiting apoptosis, stimulating angiogenesis and cell proliferation.[28] Mark Schmitt et al[29] demonstrated that even in the absence of exogenous carcinogens, inflammation itself can trigger tumor development by inducing DNA damage, and that part of the mechanism involves the release of innate immunity cells excessive reactive oxygen species leading to increased oxidative stress. CALLY, as an inflammatory nutritional index, has been reported to aid in the prognosis of various cancers.[9–11] It consists of CRP, serum albumin, and lymphocytes, playing a crucial role in inflammation, nutrition, and immunity in CRC.[21] CRP and Alb are commonly used clinical markers for inflammation or nutrition. Previous studies had shown that elevated CRP levels indicated more severe inflammatory states and were closely associated with cancer prognosis.[30] Similarly, nutritional status should not be overlooked during cancer development. Inflammation can induce cancer, affecting metabolic processes and reducing the absorption and utilization of nutrition.[31] Disease progression often leads to reduced food intake, and LARC may exhibit malnutrition or hypoproteinemia.[32] This was highly consistent with our data: reduced CALLY values (reflecting elevated CRP and reduced albumin/lymphocytes) were independently associated with significant deterioration in 2- and 3-years OS and PFS. More importantly, our statistical analyses showed that CALLY demonstrated greater discriminatory power and comprehensive value in predicting the long-term survival prognosis of patients with LARC undergoing NACRT compared with CRP or Alb alone.

Surgery is a crucial step in the treatment of LARC-NACRT, and postoperative complications within 30 days can directly impact clinical outcomes and subsequent comprehensive treatment.[33] Slankamenac et al[34] first proposed the CCI scoring system in 2013, with a range of 0–100 points, offering a broader and more discriminative grading range for complications. David et al[35] reported that each one-point increase in CCI was associated with a 1.02-fold increase in risk, suggesting that CCI was an independent risk factor for postoperative outcomes in CRC. These findings were also validated in the present study, where CCI was closely associated with OS. Higher CCI scores (HR = 1.053, 95% CI: 1.000–1.108, P = 0.048) were associated with higher OS risk, indicating that patients with poorer baseline health status have a higher risk of postoperative mortality. Unlike CALLY, CCI is not a dynamic laboratory index but a clinical indicator reflecting the overall physiological reserve. Its value lies in its ability to indirectly reflect patients' tolerance to treatment and postoperative recovery capacity, thereby predicting the prognosis of comprehensive treatment in the later stages.

Prognostic nomograms demonstrated superior versatility and efficiency in large-scale NACRT.[36] Our nomogram, integrating clinical serological markers, neoadjuvant strategies, postoperative pathology, genetic testing, and complication data effectively predicted OS and PFS in patients with LARC. Validation confirmed robust discriminatory performance that time-dependent ROC and bootstrap-validated AUC were all above 0.8. Additionally, calibration curves demonstrated close alignment with true outcomes, while DCA showed significant net benefit. It should be emphasized that the primary strength of models lies in their robust prediction of short-to-mid-term outcomes (AUC = 0.83 for 2-year OS), while extrapolation beyond 3 years remains limited by the current median follow-up of 27 months. Furthermore, based on the risk scores derived from the model, the high-risk group exhibited the worst prognosis. The risk stratification provided by this model directly guides precision treatment decisions. Low-risk patients can be exempted from chemotherapy, reducing treatment toxicity while lowering healthcare expenditures. Conversely, high-risk patients can initiate PD-L1 targeted therapy earlier, improving quality of life and optimizing survival benefits. At initial diagnosis, clinicians can rapidly assign risk scores using our designed scoring system to generate risk stratification reports, supporting multidisciplinary consultation decisions. Critically, our models' advantages lie in clinical accessibility: it used routinely available clinical data, unlike costly multi-omics approaches (eg, radiomics, metagenomics, transcriptomics) that require specialized infrastructure. However, several limitations were presented in our study. First, this was a single-center design with a small sample size and potential selection bias. Second, median follow-up duration of 27 months, necessitating longer-term validation. Third, lack of dynamic perioperative biomarker monitoring. Finally, the models required further external validation in multi-center prospective cohorts to confirm clinical practicality.

Conclusion

In this study, we used nomograms to intuitively construct a prediction model of OS and PFS in patients with LARC by the inflammatory nutritional index CALLY. Higher CALLY levels were an independent protective factor for survival. Although the nomogram of OS showed strong discrimination, the PFS model not only presented a higher 3-year predictive accuracy but was more extensive in terms of clinical utility. All these results highlighted the prognostic value of CALLY in the treatment of LARC, and secondly, the nomogram of PFS could provide an individualized risk assessment before NACRT in patients and provide valuable guidance for clinical decision-making.

Data Sharing Statement

Data generated and analysed during the current study is not publicly available, due to patient confidentiality and hospital research site requirements. However, they can be obtained from the corresponding author, Chuanqing Bao, if reasonably requested.

Ethics Approval and Informed Consent

The Ethics Committee of Jiangnan University approved the study (JNU202306011RB15), and our study complied with the Declaration of Helsinki. Patients' medical records were anonymized and de-identified before analysis. Since this study was a retrospective study using medical records from previous clinical visits and patients were recruited from across the country, the written informed consent form could not be signed in person. However, to ensure the legality of the study, we obtained consent from patients by telephone recording during telephone follow-up visits. If a patient was unable to speak or had died during the follow-up visit, consent was obtained from the family member.

Acknowledgments

We thank all the participants involved in this study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research was supported by Wuxi Municipal Health Commission Major Project (Grant: Z202213). Author Chuanqing Bao has received research support from the Wuxi Municipal Health Commission.

Disclosure

The authors declare no potential conflicts of interest.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clin*. 2024;74(3):229–263. doi:10.3322/caac.21834
2. Klekowski J, Chabowski M, Krzystek-Korpacka M, et al. The utility of lipidomic analysis in colorectal cancer diagnosis and prognosis—a systematic review of recent literature. *Int J Mol Sci*. 2024;25(14). doi:10.3390/ijms25147722
3. Shadmanov N, Aliyev V, Bakir B, et al. The shifting and evolving neoadjuvant treatments and surgical platforms on oncological outcomes and sphincter preservation in distal rectal cancer: a 23-year retrospective experience. *J Gastrointest Cancer*. 2025;56(1):177. doi:10.1007/s12029-025-01303-y
4. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med*. 2004;351(17):1731–1740.
5. Serra-Aracil X, Pericay C, Badia-Closa J, et al. Short-term outcomes of chemoradiotherapy and local excision versus total mesorectal excision in T2-T3ab, N0, M0 rectal cancer: a multicentre randomised, controlled, Phase III trial (the TAU-TEM study). *Annals Oncol*. 2023;34(1):78–90. doi:10.1016/j.annonc.2022.09.160

6. Cheng Y, Luo Y, Hu Y, et al. Multiparametric MRI-based Radiomics approaches on predicting response to neoadjuvant chemoradiotherapy (nCRT) in patients with rectal cancer. *Abdom Radiol*. 2021;46(11):5072–5085. doi:10.1007/s00261-021-03219-0
7. Smith HG, Nilsson PJ, Shogan BD, et al. Neoadjuvant treatment of colorectal cancer: comprehensive review. *BJS Open*. 2024;8(3). doi:10.1093/bjsopen/zrae038
8. Armstrong J, Balasubramanian I, Brannigan A, et al. A multicentre cohort study assessing the utility of routine blood tests as adjuncts to identify complete responders in rectal cancer following neoadjuvant chemoradiotherapy. *Int J Colorectal Dis*. 2022;37(4):957–965. doi:10.1007/s00384-022-04103-z
9. Iida H, Tani M, Komeda K, et al. Superiority of CRP-albumin-lymphocyte index (CALLY index) as a non-invasive prognostic biomarker after hepatectomy for hepatocellular carcinoma. *HPB*. 2022;24(1):101–115. doi:10.1016/j.hpb.2021.06.414
10. Toda M, Musha H, Suzuki T, et al. Impact of C-reactive protein-albumin-lymphocyte index as a prognostic marker for the patients with undergoing gastric cancer surgery. *Front Nutr*. 2025;12. doi:10.3389/fnut.2025.1556062
11. Xi P, Huang G, Huang K, et al. The prognostic significance of the CALLY index in ampullary carcinoma: an inflammation-nutrition retrospective analysis. *J Inflamm Res*. 2025;18:621–635. doi:10.2147/jir.S495815
12. van Vugt JLA, Coebergh van den Braak RRJ, Lalmahomed ZS, et al. Impact of low skeletal muscle mass and density on short and long-term outcome after resection of stage I-III colorectal cancer. *Eur J Surg Oncol*. 2018;44(9):1354–1360. doi:10.1016/j.ejso.2018.05.029
13. Li Z, Yan G, Liu M, et al. Association of perioperative skeletal muscle index change with outcome in colorectal cancer patients. *J Cachexia Sarcopenia Muscle*. 2024;15(6):2519–2535. doi:10.1002/jcsm.13594
14. Huang Z, Chen S, Yin S, et al. Development and validation of a nomogram for predicting the risk of developing gastric cancer based on a questionnaire: a cross–sectional study. *Front Oncol*. 2024;14. doi:10.3389/fonc.2024.1351967
15. Gou M, Qian N, Zhang Y, et al. Construction of a nomogram to predict the survival of metastatic gastric cancer patients that received immunotherapy. *Front Immunol*. 2022;13. doi:10.3389/fimmu.2022.950868
16. Nagtegaal ID, Glynne-Jones R. How to measure tumour response in rectal cancer? An explanation of discrepancies and suggestions for improvement. *Cancer Treatment Rev*. 2020;84. doi:10.1016/j.ctrv.2020.101964.
17. Matsuda T, Sumi Y, Yamashita K, et al. Outcomes and prognostic factors of selective lateral pelvic lymph node dissection with preoperative chemoradiotherapy for locally advanced rectal cancer. *Int J Colorectal Dis*. 2018;33(4):367–374. doi:10.1007/s00384-018-2974-1
18. Horie K, Matsuda T, Yamashita K, et al. Sarcopenia assessed by skeletal muscle mass volume is a prognostic factor for oncological outcomes of rectal cancer patients undergoing neoadjuvant chemoradiotherapy followed by surgery. *Eur J Surg Oncol*. 2022;48(4):850–856. doi:10.1016/j.ejso.2021.10.018
19. Utsumi M, Inagaki M, Kitada K, et al. Combination of sarcopenia and systemic inflammation-based markers for predicting the prognosis of patients undergoing pancreaticoduodenectomy for pancreatic cancer. *PLoS One*. 2024;19(6):e0305844. doi:10.1371/journal.pone.0305844
20. Jin J, Xiong G, Peng F, et al. The ratio of skeletal muscle mass to body mass index combined with inflammatory immune markers to stratify survival of pancreatic cancer after pancreatoduodenectomy. *Eur J Surg Oncol*. 2024;50(7):108355. doi:10.1016/j.ejso.2024.108355
21. Yang M, Lin S-Q, Liu X-Y, et al. Association between C-reactive protein-albumin-lymphocyte (CALLY) index and overall survival in patients with colorectal cancer: from the investigation on nutrition status and clinical outcome of common cancers study. *Front Immunol*. 2023;14. doi:10.3389/fimmu.2023.1131496
22. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications. *Annals Surg*. 2009;250(2):187–196. doi:10.1097/SLA.0b013e3181b13ca2
23. Yamashita S, Sheth RA, Niekamp AS, et al. Comprehensive complication index predicts cancer-specific survival after resection of colorectal metastases independent of RAS mutational status. *Annals Surg*. 2017;266(6):1045–1054. doi:10.1097/sla.0000000000002018
24. Tahiri M, Sikder T, Maimon G, et al. The impact of postoperative complications on the recovery of elderly surgical patients. *Surg Endoscopy*. 2015;30(5):1762–1770. doi:10.1007/s00464-015-4440-2
25. Aliyev V, Shadmanov N, Piozzi GN, et al. Comparing total mesorectal excision with partial mesorectal excision for proximal rectal cancer: evaluating postoperative and long-term oncological outcomes. *Updates Surg*. 2024;76(4):1279–1287. doi:10.1007/s13304-024-01926-z
26. Zhang Z-T, Xiao -W-W, Li L-R, et al. Neoadjuvant chemoradiotherapy versus neoadjuvant chemotherapy for initially unresectable locally advanced colon cancer: short-term outcomes of an open-label, single-centre, randomised, controlled, Phase 3 trial. *eClinicalMedicine*. 2024;76. doi:10.1016/j.eclinm.2024.102836
27. Okamura A, Watanabe M, Okui J, et al. Development and validation of a predictive model of therapeutic effect in patients with esophageal squamous cell carcinoma who received neoadjuvant treatment: a nationwide retrospective study in Japan. *Annals Surg Oncol*. 2022;30(4):2176–2185. doi:10.1245/s10434-022-12960-9
28. Kundu J, Surh Y. Inflammation: gearing the journey to cancer. *Mutation Res /Rev Mutation Res*. 2008;659(1–2):15–30. doi:10.1016/j.mrrev.2008.03.002
29. Schmitt M, Greten FR. The inflammatory pathogenesis of colorectal cancer. *Nat Rev Immunol*. 2021;21(10):653–667. doi:10.1038/s41577-021-00534-x
30. Zhu M, Ma Z, Zhang X, et al. C-reactive protein and cancer risk: a pan-cancer study of prospective cohort and Mendelian randomization analysis. *BMC Med*. 2022;20(1). doi:10.1186/s12916-022-02506-x
31. Martínez-Escribano C, Arteaga Moreno F, Pérez-López M, et al. Malnutrition and increased risk of adverse outcomes in elderly patients undergoing elective colorectal cancer surgery: a case-control study nested in a cohort. *Nutrients*. 2022;14(1). doi:10.3390/nu14010207
32. Kim WR, Han YD, Min BS. C-reactive protein level predicts survival outcomes in rectal cancer patients undergoing total mesorectal excision after preoperative chemoradiation therapy. *Annals Surg Oncol*. 2018;25(13):3898–3905. doi:10.1245/s10434-018-6828-4
33. Warps AK, Tollenaar RAEM, Tanis PJ, et al. Postoperative complications after colorectal cancer surgery and the association with long-term survival. *Eur J Surg Oncol*. 2022;48(4):873–882. doi:10.1016/j.ejso.2021.10.035
34. Slankamenac K, Nederlof N, Pessaux P, et al. The comprehensive complication index. *Annals Surg*. 2014;260(5):757–763. doi:10.1097/sla.0000000000000948
35. Ortiz-López D, Marchena-Gómez J, Nogués-Ramía E, et al. Utility of a new prognostic score based on the Comprehensive Complication Index (CCI®) in patients operated on for colorectal cancer (S-CRC-PC score). *Surg Oncol*. 2022;42. doi:10.1016/j.suronc.2022.101780
36. Ribeiro U. Nomogram for predicting pathologic response following neoadjuvant chemotherapy or chemoradiotherapy in patients with esophageal cancer. *Annals Surg Oncol*. 2023;30(4):1945–1947. doi:10.1245/s10434-023-13133-y