Preoperative C-reactive protein-albumin-lymphocyte index predicts survival outcomes in patients with stage I-III colorectal cancer: A retrospective cohort study

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Abstract. Colorectal cancer (CRC) is a major cause of cancer-related mortality worldwide. The present study aimed to investigate the value of the preoperative C-reactive protein-albumin-lymphocyte (CALLY) index in predicting recurrence-free survival (RFS) and overall survival (OS) rates in patients with stage I-III CRC. A retrospective analysis was conducted on 255 patients with stage I-III CRC who underwent radical resection. The optimal cutoff value of the CALLY index was determined by receiver operating characteristic curve analysis, and patients were stratified into high- and low-CALLY groups accordingly to assess its prognostic value for RFS and OS. The CALLY index had an area under the curve of 0.739 for predicting CRC prognosis. With a cutoff value of 6.790, patients in the high-CALLY group exhibited significantly better RFS and OS rates compared with those in the low-CALLY group. Multivariate Cox regression analysis confirmed CALLY as an independent prognostic factor. In conclusion, the preoperative CALLY index is an effective prognostic biomarker for predicting RFS and OS rates in patients with stage I-III CRC, demonstrating potential clinical utility.

Introduction

As the malignancy with the third highest incidence rate and the second highest rate of cancer-related deaths globally, colorectal cancer (CRC) accounts for 1.2 million new cases and ~600,000 fatalities annually (1,2). Epidemiological modeling predicts a notable increase in disease burden, with 2.5 million new CRC diagnoses forecast globally by 2035 (3). The epidemiological landscape of China is particularly concerning, as the country exhibits the world's highest absolute CRC burden due to its population size. Recent surveillance data from the National Cancer Center suggests that the incidence of CRC has increased to the extent that the disease is now the second most commonly occurring malignancy in China (4). Despite advancements in early diagnosis and treatment methods, the long-term survival rate and prognostic outcomes of patients with CRC still face challenges (5). Accurate prognosis assessment is crucial for formulating individualized treatment plans, predicting survival duration and optimizing patient management.

In recent years, numerous studies have shown that inflammatory response, nutritional status and immune function play pivotal roles in cancer initiation, progression and outcomes (6-8). Therefore, identifying biomarkers that can comprehensively reflect a patient's inflammatory, nutritional and immune status holds significant importance for improving the prognostic assessment of patients with CRC. The preoperative hematological parameters of patients with cancer can reflect their inflammatory, immune and nutritional statuses. Thus, multiple inflammation indices derived from hematological examinations have been demonstrated to be closely associated with cancer prognosis. Key validated prognostic indicators include the neutrophil-to-lymphocyte ratio (NLR) (9), the platelet-to-lymphocyte ratio (10), the lymphocyte-to-monocyte ratio (11), the fibrinogen-to-albumin ratio (12), the derived NLR (dNLR) (13), the mean corpuscular volume-to-lymphocyte ratio (14), the systemic inflammation response index (15), the systemic immune-inflammation index (16), the prognostic nutritional index (PNI) (17), the cumulative inflammation index (18), the prognostic inflammatory and nutritional index (19), the hemoglobin, albumin, lymphocyte and platelet score (20) and pan-immune-inflammation values (21). Recently, the C-reactive protein (CRP)-albumin-lymphocyte (CALLY) index, an emerging immune-nutrition scoring system, has garnered increasing attention from researchers (22). The CALLY index, integrating CRP, albumin and lymphocyte levels, provides a comprehensive assessment of a patient's inflammatory, nutritional and immune status.

Multiple studies have confirmed that the CALLY index serves as an independent prognostic factor in patients with gastric cancer and that it can predict prognosis (23-25). Conversely, relatively limited evidence exists in the literature regarding the association between the CALLY index

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and prognosis in patients with CRC. Given this context, the present study was designed to evaluate the prognostic value of the CALLY index in patients with stage I-III CRC. Through retrospective analysis of clinicopathological data and preoperative hematological parameters of patients who underwent radical resection, the study sought to determine whether the CALLY index could serve as an independent predictor for both recurrence-free survival (RFS) and overall survival (OS) rates, thereby potentially offering a novel biomarker for prognostic assessment in CRC.

Patients and methods

Patients. The present retrospective study analyzed clinicopathological data and preoperative laboratory hematological parameters (measured within 1 week before surgery) from patients with stage I-III CRC who underwent radical resection (R0) at Jingdezhen First People's Hospital (Jingdezhen, China) between January 2012 and March 2020. All consecutive patients meeting the eligibility criteria during this period were initially screened. The inclusion criteria were as follows: i) Histologically confirmed primary CRC; ii) no neoadjuvant therapy; and iii) R0 resection with curative intent. Exclusion criteria eliminated patients with: i) Synchronous/metachronous malignancies; ii) hematological disorders; iii) preoperative infection/immunodeficiency; iv) incomplete data; v) non-radical resection; and vi) receival of neoadjuvant therapy. All data were extracted from the hospital's maintained database.

Treatment and follow-up. The disease staging was determined using the eighth edition of the American Joint Committee on Cancer Tumor-Node-Metastasis (TNM) classification (26). Comorbidities was defined as pre-existing comorbidities, including cardiovascular diseases, pulmonary diseases, diabetes mellitus, chronic kidney disease and chronic liver disease. Postoperative anastomotic leakage specifically referred to anastomotic leakage occurring within 30 days after surgery. Postoperative adjuvant therapy primarily comprised chemotherapy, radiotherapy and other treatment modalities based on these core therapeutic approaches. Patients with stage II or III CRC received postoperative adjuvant therapy when deemed clinically appropriate based on their overall health status. Postoperative surveillance included contrast-enhanced computed tomography scans performed at minimum every 6 months and blood tests conducted every 3 months. Patients were followed up regularly through outpatient visits or telephone interviews every 3 months beginning on postoperative day 1 until the study endpoint, defined as either patient death or March 31, 2025, whichever occurred first. For outcome assessment, RFS time was calculated as the time from surgery to CRC recurrence, last follow-up or death, while OS time was defined as the time from surgery to death from any cause or last follow-up for surviving patients.

Determination of inflammatory markers. All calculations for inflammatory markers are presented in Table I, with the CALLY index calculated as follows: Albumin (g/dl) x lymphocyte count (n/μl)/[CRP (mg/dl) x10^4] (22).

Statistical analysis. All statistical analyses were performed using R software (version 4.3.3; R Foundation for Statistical Computing). The following R packages were employed: pROC (version 1.18.5) for receiver operating characteristic (ROC) curve analysis, with the area under the curve (AUC) calculated to determine the optimal cutoff value using the Youden index; survival (version 3.6.4) and survminer (version 0.4.9) for survival analyses; and rstatix (version 0.7.2) for statistical testing. Based on the optimal cutoff, the patients were stratified into high-CALLY and low-CALLY groups. Continuous variables with normal distribution are expressed as mean ± standard deviation (SD) and compared using independent samples t-tests, while non-normally distributed continuous variables are presented as median (Q_1-Q_3) and analyzed using Wilcoxon rank-sum tests. Categorical variables are reported as n (%) and were compared using χ^2 tests or Fisher's exact tests, as appropriate. All tests were two-sided, with $P<0.05$ considered to indicate a statistically significant difference. Univariate and multivariate Cox proportional hazards regression models were constructed using the survival package to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) for RFS and OS. Variables with values of $P<0.05$ upon univariate analysis were included in the multivariate model. Survival probabilities were estimated using Kaplan-Meier curves, with between-group differences assessed by log-rank tests.

Ethical approval. The present study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee at Jingdezhen First People's Hospital (approval no. jdzyykt202514). The requirement for informed consent was waived due to the retrospective nature of the study and data anonymization.

Results

Patient characteristics. The present study consecutively screened 309 patients with stage I-III CRC undergoing radical resection (Fig. 1). After applying exclusion criteria (n=42) and accounting for loss to follow-up (n=12), the final cohort comprised 255 patients. ROC curve analysis evaluated the prognostic performance of 14 inflammatory markers for clinical outcomes in stage I-III CRC. The CALLY index demonstrated superior discriminative ability, with an AUC of 0.739 (95% CI, 0.702-0.773), significantly outperforming all other biomarkers (Fig. 2). Stratified by the CALLY cutoff of 6.790 (Table I), the cohort comprised 160 low-CALLY (<6.790) and 95 high-CALLY (≥6.790) patients (Table II). The low-CALLY group was associated with more aggressive tumor biology, characterized by higher rates of poorly differentiated histology (26.25 vs. 6.32%; P<0.001), advanced T4 stage (71.25 vs. 49.47%; P<0.001), nodal metastasis (N1-2: 74.38 vs. 16.84%; P<0.001), and stage III disease (73.12 vs. 16.84%; P<0.001). Clinically, these patients more frequently required adjuvant therapy (75.62 vs. 45.26%; P<0.001), alongside significantly worse RFS (38.33±19.03 vs. 52.93±15.57 months; P<0.001) and OS (44.01±16.22 vs. 54.26±13.46 months; P<0.001) times that were visually substantiated by pronounced separation in Kaplan-Meier curves (Figs. 3 and 4). Notably, elevated CA125 (23.08 vs. 10.14%; P=0.005) and CA19-9

Table I. Inflammatory marker names, formulae and optimal cut-off values.

Marker	Calculation formula	Optimal cutoff value
C-reactive protein-albumin-lymphocyte index	Albumin (g/dl) x lymphocyte count (/μl)/[CRP (mg/dl) x10^4]	6.790
Derived neutrophil-to-lymphocyte ratio	Neutrophils/(white blood cells-neutrophils)	2.320
Fibrinogen-to-albumin ratio	Fibrinogen (g/l)/albumin (g/l) x100	0.095
Hemoglobin, albumin, lymphocyte and platelet scores	Hemoglobin (g/l) x albumin (g/l) x lymphocytes/platelets	35.130
Cumulative inflammatory index	(Corpuscular volume x width of erythrocyte distribution x neutrophils)/(lymphocytes x1,000)	7.275
Lymphocyte-to-monocyte ratio	Lymphocyte/monocyte	2.890
Ratio between the mean corpuscular volume and lymphocytes	Corpuscular volume/lymphocytes	72.310
Neutrophil-to-lymphocyte ratio	Neutrophil/lymphocytes	3.225
Prognostic immune and nutritional index	[Albumin (g/dl) x0.9]-[monocytes (mm^3) x 0.0007]	3.255
Pan-immune-inflammatory values	Neutrophils x monocytes x platelets/lymphocytes	391.72
Platelet-to-lymphocyte ratio	Platelets/lymphocytes	135.980
Prognostic nutritional index	Albumin (g/l) + 5 x lymphocytes (10^9/l)	45.825
Systemic immune-inflammation index	Platelets x neutrophils/lymphocytes	532.985
Systemic inflammatory response index	Neutrophils x monocytes/lymphocytes	2.390

(24.79 vs. 14.49%; P=0.038) were more prevalent in the high-CALLY group despite its less advanced pathology. No significant intergroup differences existed in terms of age, sex, tumor location, surgical approach, blood loss, comorbidities , anastomotic leakage and tumour size P>0.05), while the median (Q_1-Q_3) CALLY values robustly distinguished the cohorts [low-CALLY, 2.62 (1.62-4.64) vs. high-CALLY, 12.97 (9.88-17.16); P<0.001]. Collectively, low CALLY status is associated with advanced disease, intensified treatment needs and inferior survival, graphically validated by stratified survival analyses, positioning it as a significant prognostic integrator of inflammatory-nutritional imbalance in CRC.

Prognostic significance of CALLY in CRC survival. Stratification based on the CALLY index revealed significant survival disparities among the patients with CRC. Kaplan-Meier analysis showed that the high-CALLY group (≥6.790) had superior RFS (79.6 vs. 32.1%; log-rank P<0.001; Fig. 3) and OS (80.0 vs. 38.8%; log-rank P<0.001; Fig. 4) rates compared with the low-CALLY group (<6.790).

COX regression analysis of 5-year RFS rate in patients with CRC. Univariate and multivariate Cox regression analyses established CALLY as an independent predictor of RFS in CRC (Table III). In the univariate analysis, high CALLY exhibited a strong association with improved RFS (HR, 0.22; 95% CI, 0.14-0.35; P<0.001), outperforming conventional biomarkers including CA19-9 (HR, 1.57; 95% CI, 1.04-2.38; P=0.032), CA125 (HR, 2.05; 95% CI, 1.36-3.07; P<0.001) and CEA (HR, 1.45; 95% CI, 1.01-2.06; P=0.041). After adjusting for clinicopathological confounders in multivariate analysis, CALLY retained independent significance (HR, 0.56; 95% CI, 0.35-0.90; P=0.016), while among the other factors, only nodal metastasis (N1-2 vs. N0: HR, 6.71; 95% CI, 4.17-10.81; P<0.001), poor differentiation (moderate/poor vs. well: HR, 2.79; 95% CI, 1.88-4.16; P<0.001), advanced TNM stage (I vs. II-III: HR 2.59, 1.03-6.51; P=0.043) and elevated CA19-9 (>30 vs. ≤30 U/ml: HR, 1.69; 95% CI, 1.06-2.71; P=0.028) remained significant. Notably, tumor size (P=0.114), blood loss (P=0.100), CEA (0.213), CA125 (0.755), advanced T stage (P=0.056) and adjuvant therapy (P=0.082) lost statistical significance after adjustment.

COX regression analysis of 5-year OS rate in patients with CRC. Univariate and multivariate Cox regression analyses established CALLY as an independent predictor of OS in CRC (Table IV). Upon univariate analysis, high CALLY exhibited a profound protective effect on OS, with an HR of 0.26 (95% CI, 0.16-0.43; P<0.001), outperforming all other variables including nodal metastasis (HR, 7.95; 95% CI, 4.79-13.18; P<0.001), poor differentiation (HR, 3.69; 95% CI, 2.50-5.45; P<0.001) and elevated CA19-9 (HR, 1.74; 95% CI, 1.14-2.65; P=0.010). Following multivariate adjustment for clinicopathological confounders, CALLY retained robust independent significance (HR, 0.47; 95% CI, 0.27-0.82; P=0.008), while nodal metastasis (HR, 5.41; 95% CI, 2.93-9.98; P<0.001), poor differentiation (HR, 2.42; 95% CI, 1.54-3.81; P<0.001) and elevated CA19-9 (HR, 1.61; 95% CI, 1.02-2.57; P=0.043) remained significant, alongside advanced TNM stage (HR, 1.74; 95% CI, 1.03-2.95; P=0.040). Conventional biomarkers (CEA and CA125), anatomical factors (T stage), and treatment variables (adjuvant therapy) lost statistical significance (P>0.05) after adjustment, along with tumor size (P=0.121) and intraoperative blood loss (P=0.154), which were significant in the univariate analysis.

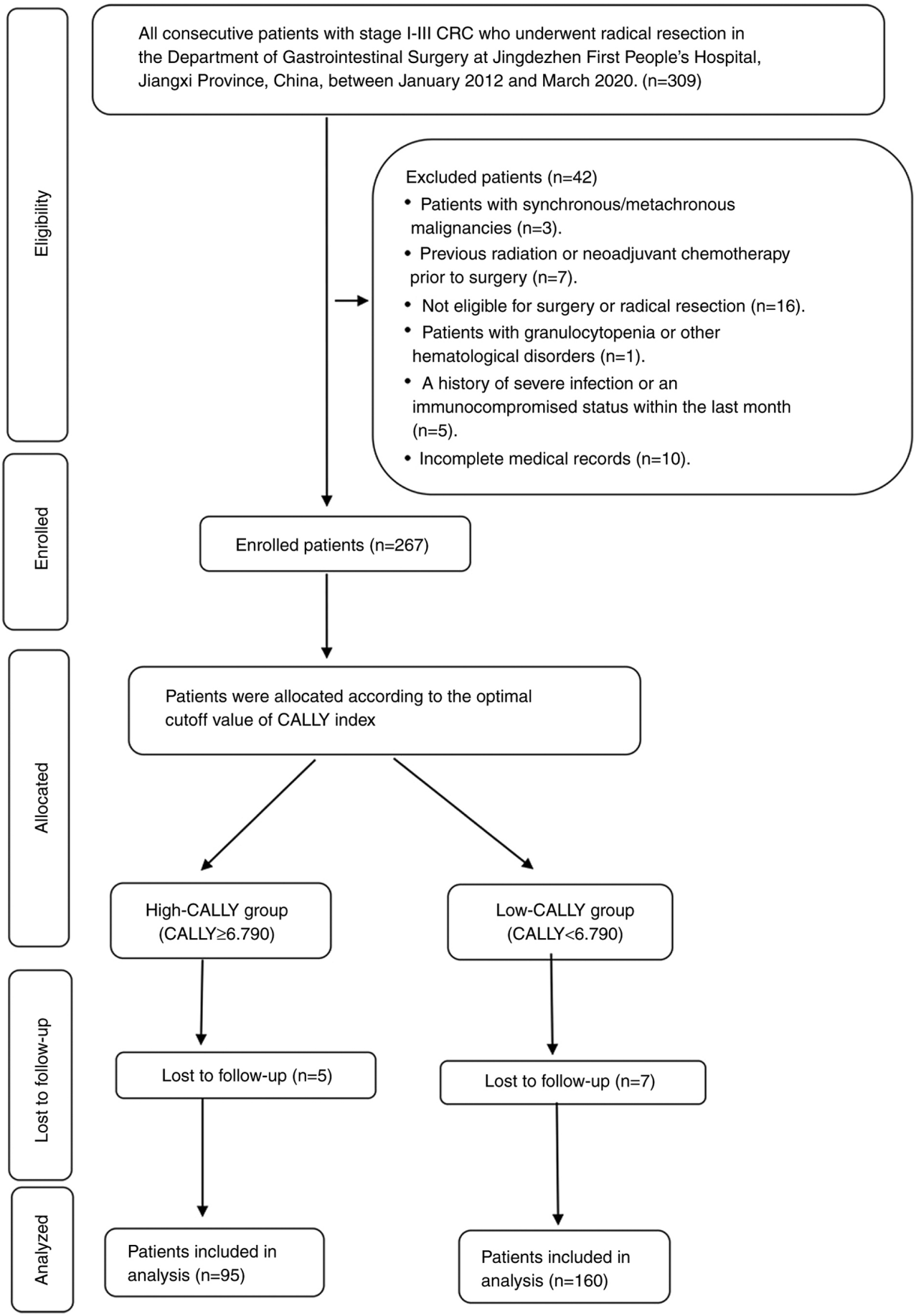

Figure 1. Patient screening flowchart for patients with stage I-III CRC undergoing radical resection. CRC, colorectal cancer; CALLY, C-reactive protein-albumin-lymphocyte.

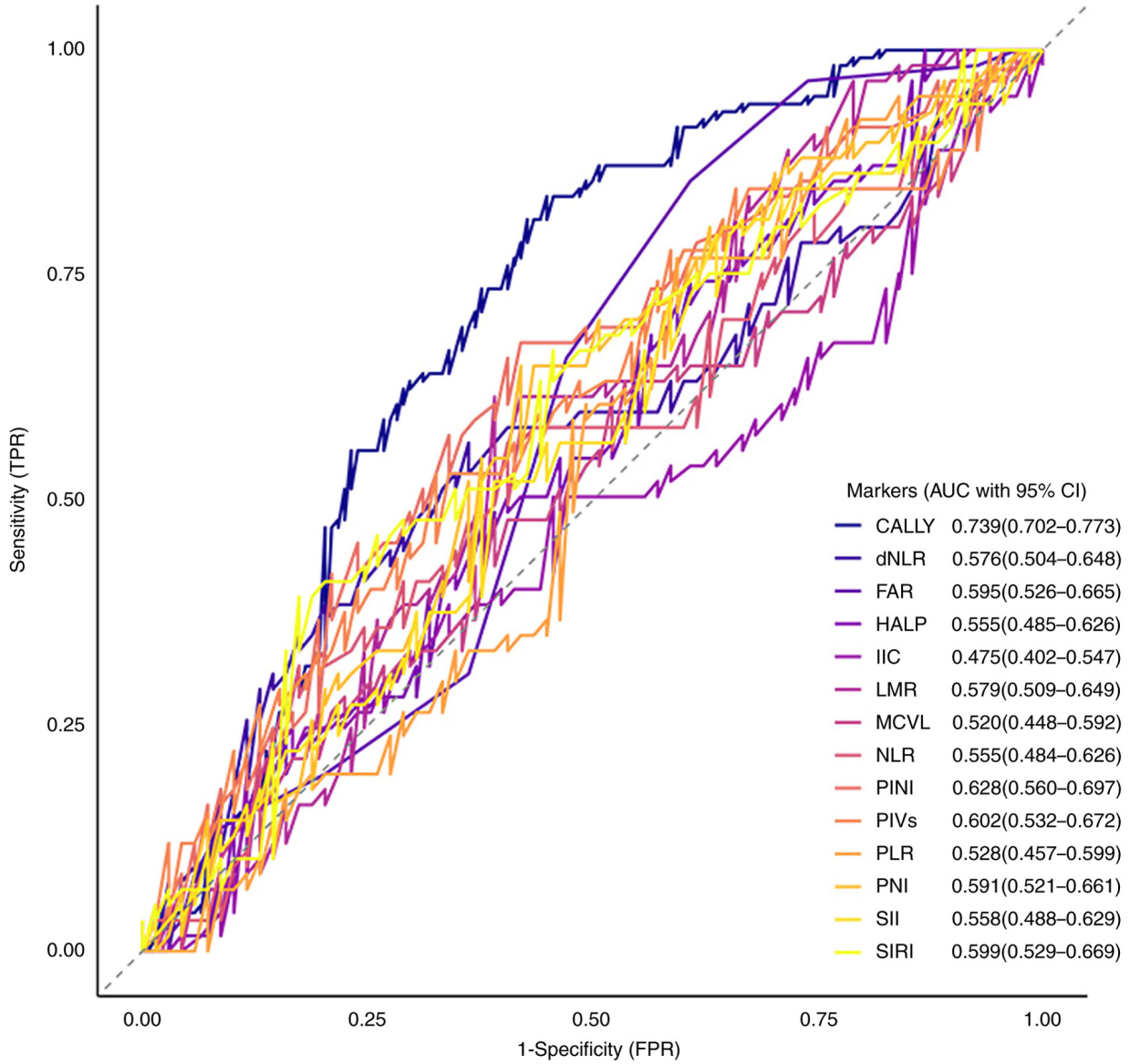

Figure 2. Receiver operating characteristic curve and AUC for the inflammatory markers. CALLY, C-reactive protein-albumin-lymphocyte; AUC, area under the curve; CI, confidence interval; TPR, true-positive rate (sensitivity); FPR, false-positive rate (1-specificity).

Discussion

The CALLY index derives its prognostic power from quantifying a pathophysiological triad that orchestrates CRC progression through tumor microenvironment (TME)-specific mechanisms. Elevated CRP levels reflect activation of interleukin-6/Janus kinase/signal transducer and activator of transcription 3 signaling, which expands myeloid-derived suppressor cells (MDSCs) that spatially exclude cytotoxic T lymphocytes from tumor nests, a hallmark of 'immune-excluded' CRC subtypes (27,28). Concurrently, hypoalbuminemia disrupts gut barrier integrity, permitting translocation of procarcinogenic microbiota (for example, *Fusobacterium nucleatum*) that activate transforming growth factor-β signaling (29,30). This further amplifies MDSC-mediated immunosuppression by inducing regulatory T cell differentiation and programmed death-ligand 1 (PD-L1) upregulation on tumor-associated macrophages (31). Lymphopenia completes this vicious cycle by depleting $CD103^+$ tissue-resident memory T cells critical for controlling microsatellite-stable CRC (32). Collectively, these processes establish an immunosuppressive TME favoring metastasis.

In gastric cancer research, Hashimoto *et al* (33) demonstrated that the high-CALLY group (cut-off value: 3.28) exhibited a significantly higher proportion of early-stage cases (stage I: 71.5%; P=0.019) and lower venous invasion rates compared with the low-CALLY group. These findings align closely with the present study, where the high-CALLY group (≥6.790) displayed superior tumor biological characteristics, including significantly reduced rates of poor differentiation (6.32 vs. 26.25%), T4 invasion (49.47 vs. 71.25%), lymph node metastasis (N1-2 stage: 16.84 vs. 74.38%) and stage III disease (16.84 vs. 73.12%) (all P<0.001). Paradoxically, despite the favorable prognosis, the high-CALLY group showed elevated levels of CA125 (23.08 vs. 10.14%) and CA19-9 (24.79 vs. 14.49%). This apparent contradiction

Table II. Clinicopathological characteristics of colorectal cancer patients by CALLY score group.

Variables	Total (n=255)	CALLY		P-value
		Low (n=160)	High (n=95)	
Age, years	62.58±12.49	62.34±12.87	62.98±11.90	0.695
Sex				0.927
Male	144 (56.47)	90 (56.25)	54 (56.84)	
Female	111 (43.53)	70 (43.75)	41 (43.16)	
Tumor location				0.808
Colon	149 (58.43)	95 (59.38)	54 (56.84)	
Rectum	106 (41.57)	65 (40.63)	41 (43.16)	
Surgical approach				0.662
Open	173 (67.84)	114 (71.25)	59 (62.11)	
Laparoscopic	82 (32.16)	46 (28.75)	36 (37.89)	
Tumor size ≥3.5 cm				0.077
No	95 (37.25)	53 (33.13)	42 (44.21)	
Yes	160 (62.75)	107 (66.88)	53 (55.79)	
Blood loss, ml[a]	50.00 (50.00-100.00)	50.00 (50.00-100.00)	50.00 (50.00-100.00)	0.093
Comorbidities				0.062
No	201 (78.82)	132 (82.50)	69 (72.63)	
Yes	54 (21.18)	28 (17.50)	26 (27.37)	
Anastomotic leakage				0.437
No	240 (94.12)	152 (95.00)	88 (92.63)	
Yes	15 (5.88)	8 (5.00)	7 (7.37)	
Pathological pattern				<0.001
Well	18 (7.06)	10 (6.25)	8 (8.42)	
Moderate	189 (74.12)	108 (67.50)	81 (85.26)	
Poor	48 (18.82)	42 (26.25)	6 (6.32)	
T stage				<0.001
I	2 (0.78)	0 (0.00)	2 (2.11)	
II	57 (22.35)	21 (13.13)	36 (37.89)	
III	35 (13.73)	25 (15.6)	10 (10.53)	
IV	161 (63.14)	114 (71.25)	47 (49.47)	
N stage				<0.001
0	120 (47.06)	41 (25.63)	79 (83.16)	
I	103 (40.39)	92 (57.50)	11 (11.58)	
II	32 (12.55)	27 (16.88)	5 (5.26)	
TNM stage				<0.001
I	42 (16.47)	4 (2.50)	38 (40.00)	
II	80 (31.37)	39 (24.38)	41 (43.16)	
III	133 (52.16)	117 (73.13)	16 (16.84)	
P-adjuvant therapy				<0.001
No	91 (35.69)	39 (24.38)	52 (54.74)	
Yes	164 (64.31)	121 (75.63)	43 (45.26)	
RFS, months	43.76±19.14	38.33±19.03	52.93±15.57	<0.001
OS, months	47.83±16.01	44.01±16.22	54.26±13.46	<0.001
CEA ≥5 ng/ml				0.031
No	166 (65.10)	120 (75.00)	46 (48.42)	
Yes	89 (34.90)	40 (25.00)	49 (51.58)	
CA19-9 ≥30 U/ml				0.038
0	206 (80.78)	140 (87.50)	66 (69.47)	
1	49 (19.22)	20 (12.50)	29 (30.53)	

Table II. Continued.

Variables	Total (n=255)	CALLY		P-value
		Low (n=160)	High (n=95)	
CA125 ≥25 U/ml				0.005
No	214 (83.92)	146 (91.25)	68 (71.58)	
Yes	41 (16.08)	14 (8.75)	27 (28.42)	
CALLY[a]	4.93 (2.16-10.53)	2.62 (1.62-4.64)	12.97 (9.88-17.16)	<0.001

[a]Data are presented as median (1st quartile-3rd quartile), mean ± standard deviation or n (%). TNM, Tumor-Node-Metastasis; RFS, recurrence-free survival; OS, overall survival; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 199; CA125, carbohydrate antigen 125; CALLY, C-reactive protein-albumin-lymphocyte index; P-adjuvant therapy, postoperative adjuvant therapy, specifically referring to radiotherapy and chemotherapy.

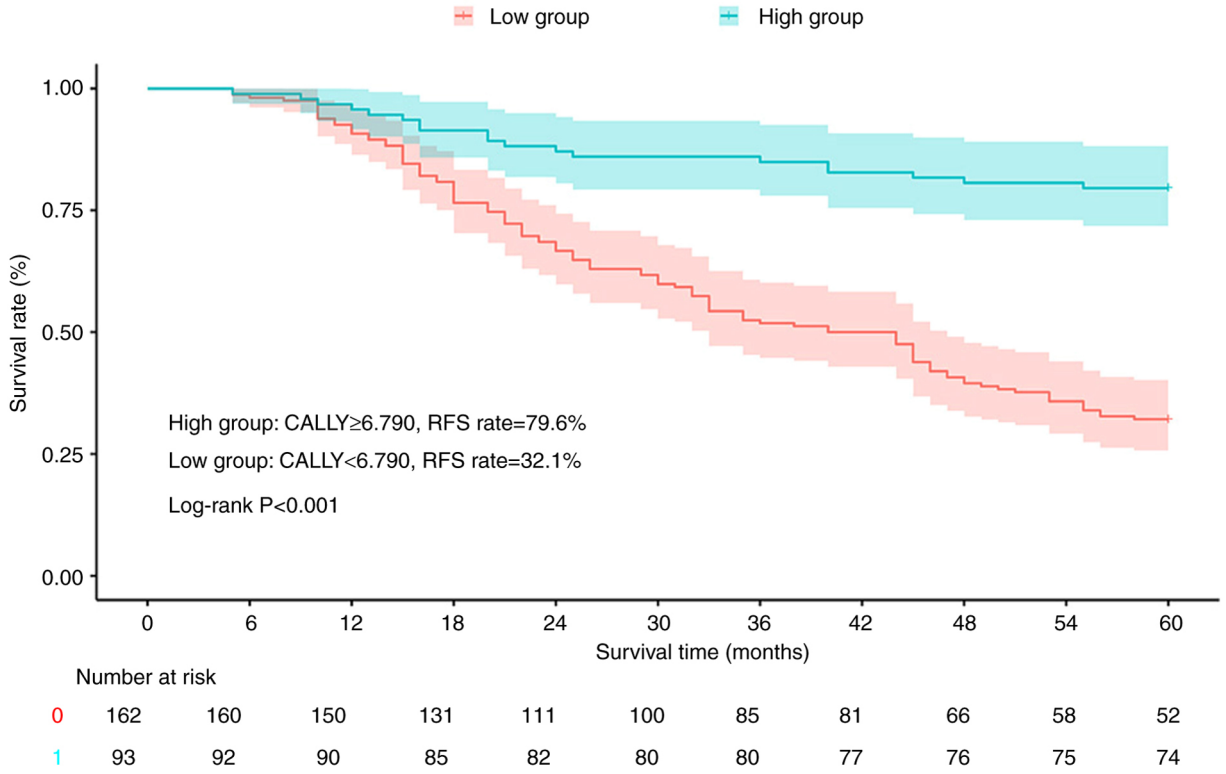

Figure 3. Kaplan-Meier analysis of RFS in patients with colorectal cancer stratified by CALLY index. CALLY, C-reactive protein-albumin-lymphocyte; RFS, recurrence-free survival.

may be explained by enhanced immunoediting mechanisms, such as intact lymphocyte function, mediated through antibody-dependent cellular cytotoxicity, which efficiently eliminates antigen-expressing tumor cells, leading to the release of tumor-associated antigens (e.g., CA125/CA19-9) into the bloodstream (34,35). Single-cell sequencing further reveals that specific T-cell subsets (for example, tissue-resident memory T cells) may modulate biomarker release dynamics by regulating immune checkpoint molecules such as PD-L1 (36). Future studies should explore the combined prognostic value of serial CALLY measurements and tumor markers.

The prognostic role of the CALLY index in advanced CRC has been established. Furukawa *et al* (37) demonstrated its superiority in metastatic settings, showing a 2.8-fold increased mortality risk in patients with colorectal liver metastasis (95% CI, 1.6-4.9; P<0.001) compared with conventional NLR/PNI biomarkers. The present study extends these findings to stage I-III CRC through three key analytical approaches. First, in a head-to-head comparison of 14 prognostic markers, the CALLY index achieved the highest discriminative power (AUC, 0.739). Second, multivariable Cox models confirmed its independence from TNM stage and age (OS: HR, 2.15; 95% CI, 1.16-3.98; P=0.015; and

Table III. Univariate and multivariate analysis for recurrence-free survival (RFS) in patients with colorectal cancer patients.

	Univariate analysis		Multivariate analysis	
Variables	HR (95% CI)	P-value	HR (95% CI)	P-value
Sex (female vs. male)	0.85 (0.60-1.20)	0.352	-	-
Age (≥60 vs. <60 years)	0.80 (0.56-1.14)	0.211	-	-
Tumor location (rectum vs. colon)	0.90 (0.63-1.28)	0.564	-	-
Surgical approach (laparoscopic vs. open)	0.20 (0.03-1.42)	0.107	-	-
Tumor size (≥3.5 vs. <3.5 cm)	1.78 (1.22-2.61)	0.003	1.51 (0.90-2.54)	0.114
Blood loss (≥100 vs. <100 ml)	2.53 (1.56-4.08)	<0.001	1.83 (0.89-3.76)	0.100
Predisease (yes vs. no)	0.72 (0.46-1.13)	0.156	-	-
Anastomotic leakage (yes vs. no)	0.58 (0.24-1.42)	0.236	-	-
Pathological pattern (moderate and poor vs. well)	3.76 (2.58-5.48)	<0.001	2.79 (1.88-4.16)	<0.001
T stage (I and II vs. III and IV)	3.29 (1.89-5.73)	<0.001	1.75 (0.98-3.12)	0.056
N stage (0 vs. I and II)	7.88 (4.95-12.54)	<0.001	6.71 (4.17-10.81)	<0.001
TNM stage (I vs. III and III)	12.04 (3.83-37.87)	<0.001	2.59 (1.03-6.51)	0.043
P-adjuvant therapy (yes vs. no)	3.77 (2.40-5.92)	<0.001	1.59 (0.94-2.69)	0.082
CEA (>5 vs. ≤5 ng/ml)	1.45 (1.01-2.06)	0.041	0.76 (0.49-1.17)	0.213
CA125 (>25 vs. ≤25 U/ml)	2.05 (1.36-3.07)	<0.001	0.92 (0.54-1.56)	0.755
CA19-9 (>30 vs. ≤30 U/ml)	1.57 (1.04-2.38)	0.032	1.69 (1.06-2.71)	0.028
CALLY (high vs. low)	0.22 (0.14-0.35)	<0.001	0.56 (0.35-0.90)	0.016

TNM, Tumor-Node-Metastasis; P-adjuvant therapy, postoperative adjuvant therapy, specifically referring to radiotherapy and chemotherapy; HR, hazard ratio; CI, confidence interval; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 199; CA125, carbohydrate antigen 125; CALLY, C-reactive protein-albumin-lymphocyte index.

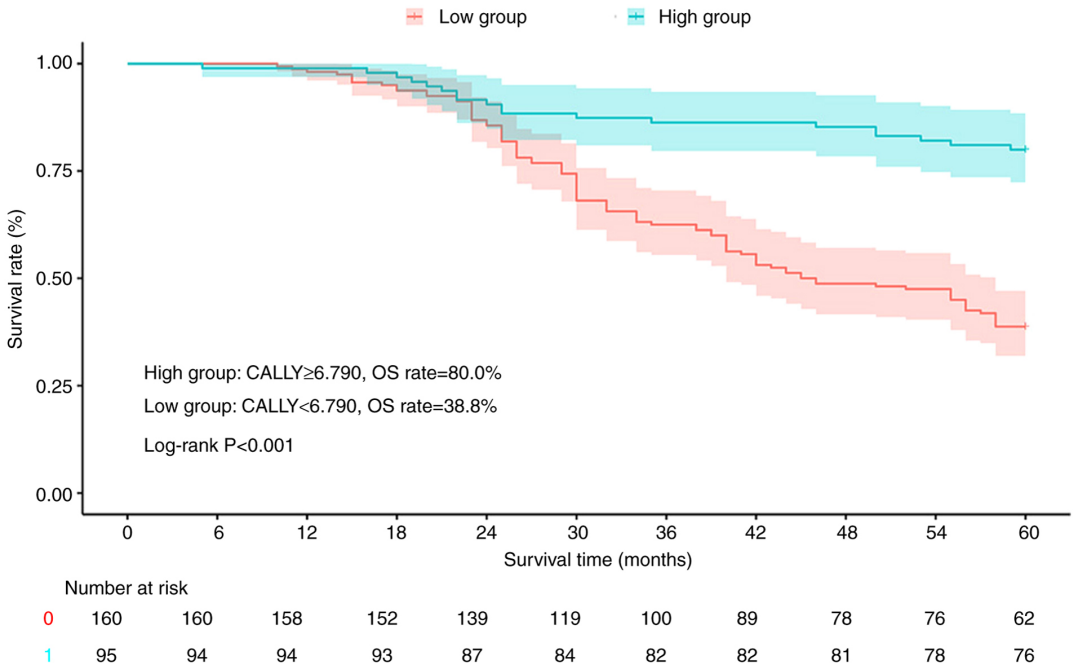

Figure 4. Kaplan-Meier analysis of OS in patients with colorectal cancer stratified by CALLY index. CALLY, C-reactive protein-albumin-lymphocyte; OS, overall survival.

RFS: HR, 2.34; 95% CI, 1.32-4.15; P=0.003). Most notably, Kaplan-Meier analysis revealed significant survival disparities, with low-CALLY patients exhibiting 23.8 and 31.6% absolute reductions in 5-year OS (58.3 vs. 82.1%; P=0.008) and RFS (45.2 vs. 76.8%; P<0.001), respectively. This tripartite validation, spanning ROC performance, regression stability and survival curve divergence, solidifies the CALLY index as a pan-stage prognostic tool.

Table IV. Univariate and multivariate analysis for overall survival in patients with colorectal cancer.

	Univariate analysis		Multivariate analysis	
Variables	HR (95% CI)	P-value	HR (95% CI)	P-value
Sex (female vs. male)	0.77 (0.53-1.11)	0.158	-	-
Age (≥60 vs. <60 years)	0.81 (0.56-1.17)	0.263	-	-
Tumor location (rectum vs. colon)	0.86 (0.59-1.25)	0.440	-	-
Surgical approach (laparoscopic vs. open)	0.20 (0.03-1.42)	0.107	-	-
Tumor size (≥3.5 vs. <3.5 cm)	2.28 (1.50-3.47)	<0.001	1.57 (0.89-2.76)	0.121
Blood loss (≥100 vs. <100 ml)	2.94 (1.81-4.78)	<0.001	2.01 (0.77-5.25)	0.154
Predisease (yes vs. no)	0.75 (0.47-1.20)	0.230	-	-
Anastomotic leakage (yes vs. no)	0.66 (0.27-1.63)	0.372	-	-
Pathological pattern (moderate and poor vs. well)	3.69 (2.50-5.45)	<0.001	2.42 (1.54-3.81)	<0.001
T stage (I and II vs. III and IV)	4.65 (2.35-9.18)	<0.001	1.44 (0.63-3.30)	0.394
N stage (0 vs. I and II)	7.95 (4.79-13.18)	<0.001	5.41 (2.93-9.98)	<0.001
TNM stage (I vs. III and III)	15.56 (3.84-63.01)	<0.001	1.74 (1.03-2.95)	0.040
P-adjuvant therapy (yes vs. no)	4.27 (2.58-7.06)	<0.001	1.64 (0.95-2.85)	0.077
CEA (>5 vs. ≤5 ng/ml)	1.61 (1.11-2.32)	0.011	0.90 (0.58-1.38)	0.622
CA125 (>25 vs. ≤25 U/ml)	1.82 (1.19-2.81)	0.006	1.01 (0.60-1.71)	0.971
CA19-9 (>30 vs. ≤30 U/ml)	1.74 (1.14-2.65)	0.010	1.61 (1.02-2.57)	0.043
CALLY (high vs. low)	0.26 (0.16-0.43)	<0.001	0.47 (0.27-0.82)	0.008

P-adjuvant therapy, postoperative adjuvant therapy, specifically referring to radiotherapy and chemotherapy; HR, hazard ratio; CI, confidence interval; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 199; CA125, carbohydrate antigen 125; CALLY, C-reactive protein-albumin-lymphocyte index.

The present study has several limitations that warrant consideration. First, the single-center retrospective design and relatively limited sample size may introduce selection bias, highlighting the need for future multicenter studies with larger cohorts to validate the findings. Second, the proposed CALLY cutoff value was derived from a single institutional dataset, necessitating external validation through collaborative multicenter research to confirm its generalizability across diverse populations. Specifically, the lack of an independent external cohort for validating the optimal cutoff (6.790) and prognostic performance limits the immediate clinical translatability of the findings. Future studies should prioritize multi-institutional collaboration to establish population-adjusted thresholds. Third, the exclusive reliance on single-timepoint preoperative measurements precluded assessment of dynamic changes in CALLY values, suggesting that prospective studies incorporating serial measurements would provide more comprehensive insights into its clinical utility. Fourth, the absence of key prognostic confounders in the analysis, including molecular subtypes (RAS/BRAF mutation status), microsatellite instability status, perioperative nutritional support and postoperative complications, may have influenced survival outcomes independent of the CALLY index. Finally, the analysis did not incorporate circulating tumor DNA or other molecular residual disease markers, which could potentially miss early micrometastatic signals.

The present study establishes the CALLY index as a simple yet effective prognostic marker for patients with stage I-III CRC after radical resection. Key findings demonstrate its ability to: i) Independently predict RFS and OS rates; ii) stratify patients by tumor aggressiveness; and iii) complement traditional TNM staging. As a composite of routine blood parameters, this multifaceted marker, integrating inflammatory, nutritional and immune indicators, enhances clinical relevance while offering cost-effectiveness and immediate clinical implementability. Although further validation is warranted, the CALLY index may guide personalized management by identifying high-risk patients requiring intensified surveillance, ultimately optimizing CRC therapeutic decisions.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JL and SZ were responsible for the study conceptualization and methodology. JL and XH were responsible for visualization, validation, investigation and data curation. JL provided

resources and wrote the original draft manuscript. SZ helped to review and edit the manuscript, and supervised the study. JL, XH and SZ were responsible for project administration. JL and SZ confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee at The Jingdezhen First People's Hospital (Jingdezhen, China; approval no. jdzyykt202514). The requirement for informed consent was waived due to the retrospective nature of the study and data anonymization.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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