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The prognostic value of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in colorectal cancer and colorectal anastomotic leakage patients: a retrospective study

Nuo Xu[1], Jian-Xin Zhang[2], Jia-Jie Zhang[3], Zhuo Huang[2], Lian-Chun Mao[2], Zhi-Yong Zhang[2*] and Wei-Dong Jin[2*]

Abstract

Objective The purpose of this study was to investigate the influence and predictive value of preoperative peripheral blood neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) index on the prognosis of colorectal anastomotic leakage (CAL) patients.

Methods This study retrospectively analyzed the clinical data of 1016 patients who underwent radical resection for colorectal cancer at a single center between January 1, 2007 and December 31, 2023. In this study, NLR and PLR were analyzed before surgery. Kaplan–Meier survival analysis was performed according to the postoperative survival status of the patients. Nomogram and calibration curve were established by proportional hazards model (COX) to verify its predictive value.

Results A total of 890 patients with colorectal cancer, 102 patients with CAL, and 788 patients with non- anastomotic leakage (AL) colorectal cancer were enrolled for a median follow-up of 96 months (quartile range 33–133). In this study, COX regression analysis showed that preoperative NLR and PLR could predict the prognosis of CAL patients, and the optimal cut-off points of NLR and PLR were 2.89 and 157.62, respectively. Kaplan–Meier survival curve results showed that 5-year overall survival (OS) and disease-free survival (DFS) in the low NLR and PLR group were significantly higher than those in the high NLR and PLR group. OS and DFS were divided into high, low NLR and PLR groups. Finally, based on COX model, a nomogram analysis was conducted to analyze the risk factors affecting OS and DFS, and the accuracy and practicality of the model were verified by calibration curve and decision curve.

Conclusion Preoperative NLR and PLR can predict the long-term prognosis of colorectal cancer (CRC) and CAL patients, and patients with NLR ≥ 2.89 and PLR ≥ 157.62 have poor survival prognosis. Nomogram and calibration curve analysis will further improve the accuracy of OS and DFS prediction.

*Correspondence:
Zhi-Yong Zhang
ptwkzzy@163.com
Wei-Dong Jin
jwdong1972@163.com
Full list of author information is available at the end of the article

Keywords Colorectal cancer, Anastomotic leakage, Neutrophil-to-lymphocyte ratio, Platelet-to-lymphocyte ratio, Prognostic value

Introduction

Colorectal cancer (CRC) is a prevalent malignant tumor of the digestive system, posing a significant threat to public health and imposing a considerable social burden. In the past few years, CRC incidence and mortality rates have been increasing, ranking it as the third most common malignant tumor [1].Currently, CRC diagnosis primarily relies on colonoscopy and pathological biopsy. However, due to the lack of early-stage clinical symptoms, it is often easily overlooked by patients. Treatment mainly includes surgery, endoscopic therapy, chemotherapy, radiotherapy, and immunotherapy [2–4].

The systemic inflammatory response significantly contributes to tumor development and is essential in the formation and dissemination of various malignancies [5]. As research advances, increasing evidence suggests that markers of the systemic inflammatory response hold prognostic significance for multiple types of cancer [6]. Numerous studies have proposed using inflammatory biomarkers to predict anti-tumor immune response, cancer progression, and patient survival [7–12]. The inflammatory response is generally indicated by preoperative expression of inflammatory factors, with leukocytes, neutrophils, lymphocytes, and monocytes becoming the most commonly used inflammation indicators [13–15]. Among various inflammation markers, many studies have shown that elevated neutrophil-to-albumin ratio (NAR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) are important prognostic factors for cancer [16, 17]. An increased systemic immune-inflammation index, frequently attributed to elevated levels of neutrophils and platelets alongside reduced lymphocyte counts, reflects a heightened inflammatory response and a compromised immune response. This condition suggests an elevated risk of tumor recurrence and a worse prognosis [18]. Additionally, the presence of tumor cells affects platelets, leading to cancer-associated thrombosis. Due to this stimulation, platelets release numerous growth regulators that promote tumor development, angiogenesis, and metastasis [19]. Yang et al. [20]. Research has shown that high serum neutrophil counts correlate with overall survival(OS) and disease-free survival(DFS) in metastatic CRC patients with Ras wild-type. Increasing experimental and clinical evidence suggests that platelet activation acts as a chemotactic factor for cancer cells, creating favorable conditions for metastasis development. Moreover, platelets enhance the survival of cells with significant metastatic potential while they are transported through the bloodstream [21]. A reduction in lymphocyte levels is often linked to leukocytosis and thrombocytosis, which may allow tumor cells to escape immune surveillance and protect themselves from cytotoxic T cell responses [22].

Colorectal anastomotic leakage (CAL) is the most severe complication after CRC surgery, with documented prevalence rates between 7 and 15%. The occurrence of anastomotic leakage (AL) affects postoperative functional recovery, local recurrence, and long-term survival rates [23]. In recent years, several studies have proposed predictive models and risk scores for rectal cancer [24]. Preoperative predictive models of inflammation indicators, such as C-reactive protein and procalcitonin, have been proven to be risk factors for postoperative AL [25]. Most predictive models currently rely on individual inflammation indicators.However, combining multiple inflammation indicators may provide a more accurate prediction of AL incidence.NLR has been researched as a predictive marker for CAL [26]. Presently, the predictive value of preoperative NLR and PLR for postoperative colorectal cancer has been confirmed [27, 28].A previous high-quality meta-analysis reported that increased NLR is associated with poorer overall survival and recurrence-free survival in CRC patients [29]. Liu et al. reported that CRC patients with a change from low pre-treatment NLR levels to high post-treatment NLR levels had worse OS and progression-free survival compared to those with a change from high to low NLR levels [30]. Furthermore, previous studies have reported that increased preoperative NLR is associated with increased perioperative complications in colorectal surgery and has a trend towards AL occurrence [31]. Currently, there is limited research on preoperative predictive factors for CAL prognosis, and studies on preoperative NLR and PLR predicting CAL prognosis are also lacking. Additionally, In this study, the prediction model of OS and DFS of CAL patients at 1, 3 and 5 years and calibration curve were constructed to provide theoretical basis for improving perioperative treatment and reducing the risk of complications.

Materials and methods

Study population

This study adheres to the STROBE guidelines [32]. This study was a retrospective analysis of clinical data from 1,016 patients who underwent radical surgery for colorectal cancer at the Central Theatre General Hospital of

the Chinese People's Liberation Army between January 1, 2007, and December 31, 2023.

Inclusion and exclusion criteria

The inclusion criteria: preoperative pathological confirmation of colorectal cancer; radical colorectal cancer surgery; and complete clinical data. The exclusion criteri: patients with grade A anastomotic leakage without special clinical management; patients with hematological diseases; patients with primary tumors in other parts of the body; preoperative neoadjuvant radiotherapy; clinically diagnosed infectious diseases or other conditions causing systemic inflammation prior to surgery; and patients who could not be followed up or had missing data. Ultimately, 890 colorectal cancer patients and 102 patients with colorectal anastomotic leakage were included after applying the inclusion and exclusion criteria.

Study methods

Data source

Baseline patient information was obtained from the medical record system. We collected data on patients' age, gender, body mass index (BMI), length of hospital stay, follow-up duration, history of smoking and alcohol consumption, diabetes mellitus, hypertension, coronary artery disease, history of abdominal surgery, history of intestinal lesions, surgical procedure, intraoperative placement of drains, postoperative adjuvant therapy, tumor site, tumor size, degree of tumor differentiation, AJCC 9th edition TNM staging [33], presence or absence of anastomotic leakage, leukocyte count, neutrophil count, platelet count, lymphocyte count, hemoglobin, albumin, carcinoembryonic antigen levels, and the calculation of NLR and PLR ratios. This retrospective study complied with the requirements of the ethics committee, and informed consent was obtained from the patients. The study was approved by the Ethics Committee of the General Hospital of the Central Theater Command of the Chinese People's Liberation Army [(2023) Lun Audit Zi (092–01) No.].

Sample source

Fasting blood samples were collected from the elbow vein early in the morning on the second day after patient

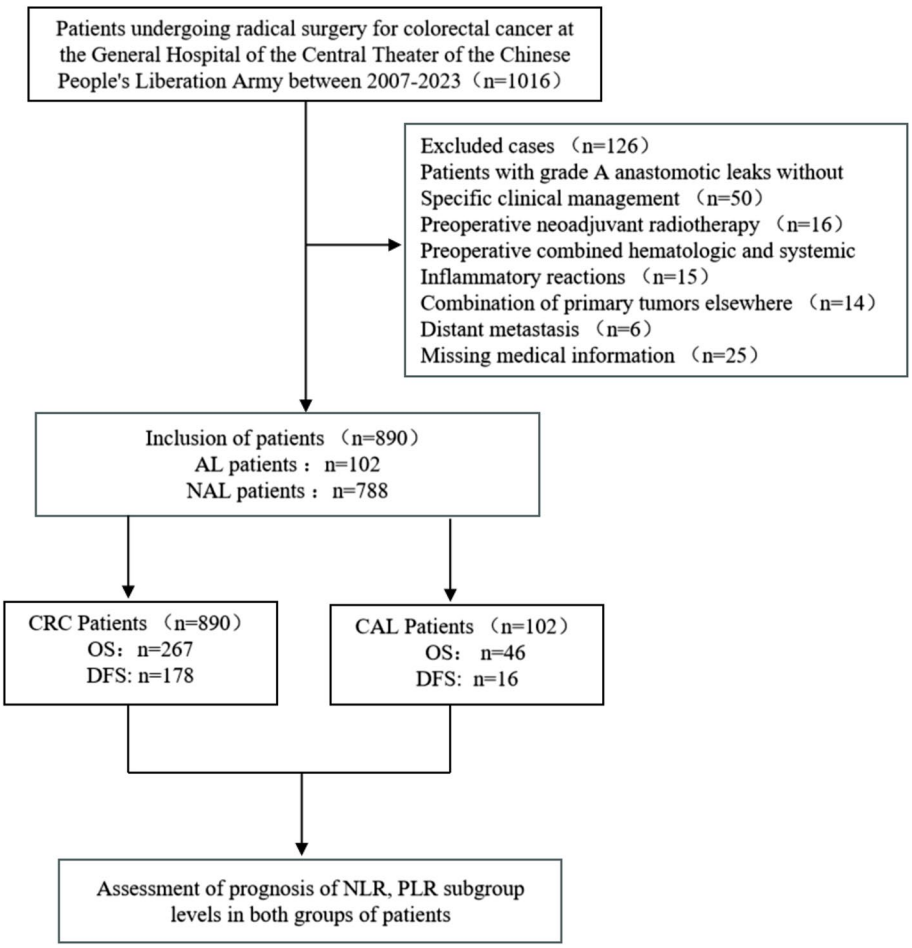

Fig. 1 Flowchart of patients included for analysis

Table 1 Patient clinical characteristics($n = 890$)

Variables	All patients ($n = 890$)	AL patients ($n = 102$)	Non-AL patients($n = 788$)	$t/Z/\chi^2$	*P*
Age(years)	68.66 ± 12.66	68.88 ± 12.86	68.63 ± 12.64	0.843	0.198
BMI(kg/m^2)	23.05 ± 3.18	23.03 ± 3.81	23.04 ± 3.18	0.978	0.028
Hospitalization (day)	22.51 ± 11.71	37.22 ± 16.21	20.60 ± 9.46	10.355	< 0.001
Gender					
Male	532(59.8)	74(72.55)	458(58.12)	7.818	0.005
Female	358(40.2)	28(27.45)	330(41.88)		
Smoking					
Yes	125(14.0)	28(27.45)	97(12.31)	18.062	< 0.001
No	765(86.0)	74(72.55)	691(87.70)		
Alcohol					
Yes	84(9.4)	14(13.73)	70(8.88)	2.477	0.115
No	806(90.6)	88(86.27)	718(91.12)		
Diabetes					
Yes	70(7.9)	16(15.69)	54(6.85)	9.725	0.002
No	820(92.1)	86(84.31)	734(93.15)		
Hypertension					
Yes	202(22.7)	33(32.35)	169(21.45)	6.122	0.013
No	688(77.3)	69(67.65)	619(78.55)		
Cardiovascular disease					
Yes	62(7.0)	11(10.78)	51(6.47)	2.591	0.107
No	828(93.0)	91(89.22)	737(93.53)		
Abdominal operation					
Yes	171(19.2)	41(40.20)	130(16.50)	32.677	< 0.001
No	719(80.8)	61(59.80)	658(83.50)		
Intestinal polyps					
Yes	151(17.0)	56(54.90)	95(12.06)	117.684	< 0.001
No	739(83.0)	46(45.10)	693(87.94)		
Chemotherapy					
Yes	480(53.9)	49(48.04)	431(54.70)	1.610	0.204
No	410(46.1)	53(51.96)	357(45.30)		
Surgical options					
laparoscopy	667(74.9)	52(50.98)	615(78.05)	35.230	< 0.001
open	223(25.1)	50(49.02)	173(21.95)		
Drainage tube					
Yes	625(70.22)	101(99.02)	90(88.24)	17.872	< 0.001
No	265(29.78)	1(0.98)	12(11.76)		
Tumor location					
descending colon	124(13.9)	15(14.71)	109(13.83)	3.750	0.153
sigmoid colon	274(30.8)	23(22.55)	251(31.85)		
rectum	492(55.3)	64(62.75)	428(54.31)		
Tumor diameter					
< 5 cm	503(56.5)	55(53.92)	448(56.85)	0.316	0.574
≥ 5 cm	387(43.5)	47(46.08)	340(43.15)		
Tumor differentiation grade					
Poor	6(0.7)	2(1.96)	4(0.51)	3.973	0.137
Medium	849(95.4)	98(96.08)	751(95.30)		
High	35(4.3)	2(1.96)	33(4.19)		

Table 1 (continued)

Variables	All patients ($n=890$)	AL patients ($n=102$)	Non-AL patients($n=788$)	$t/Z/\chi^2$	*P*
TNM Stage					
I	241(27.1)	20(19.61)	221(28.05)	10.531	0.015
II	340(38.2)	53(51.96)	288(36.55)		
III	217(24.4)	24(23.53)	201(25.51)		
IV	83(9.3)	5(4.90)	78(9.90)		
CEA(ng/mL)					
≥ 5	402(45.17)	47(46.08)	355(45.05)	0.039	0.844
< 5	488(54.83)	55(53.92)	433(54.95)		
Leukocyte (10^9/L)	6.25 ± 2.68	6.32 ± 2.53	6.24 ± 2.71	0.742	0.330
Neutrophil (10^9/L)	4.10 ± 3.32	4.51 ± 3.52	3.95 ± 2.11	1.227	0.223
Platelet (10^9/L)	221.98 ± 83.31	236.75 ± 87.97	220.06 ± 82.55	1.776	0.079
Lymphocyte (10^9/L)	1.62 ± 0.67	1.48 ± 0.60	1.63 ± 0.68	-2.454	0.016
Hemoglobin (g/L)	117.44 ± 21.91	118.12 ± 22.92	117.35 ± 21.79	0.338	0.736
Albumin (g/dL)	38.61 ± 4.95	38.12 ± 4.02	38.68 ± 5.05	-1.402	0.164
NAR(10^9/L)	0.11 ± 0.06	0.12 ± 0.09	0.10 ± 0.06	2.117	0.037
NLR(10^9/L)	3.05 ± 2.88	3.65 ± 3.19	2.98 ± 2.83	2.116	0.037
PLR(10^9/L)	0.11 ± 0.06	0.11 ± 0.06	0.10 ± 0.06	16.651	< 0.001

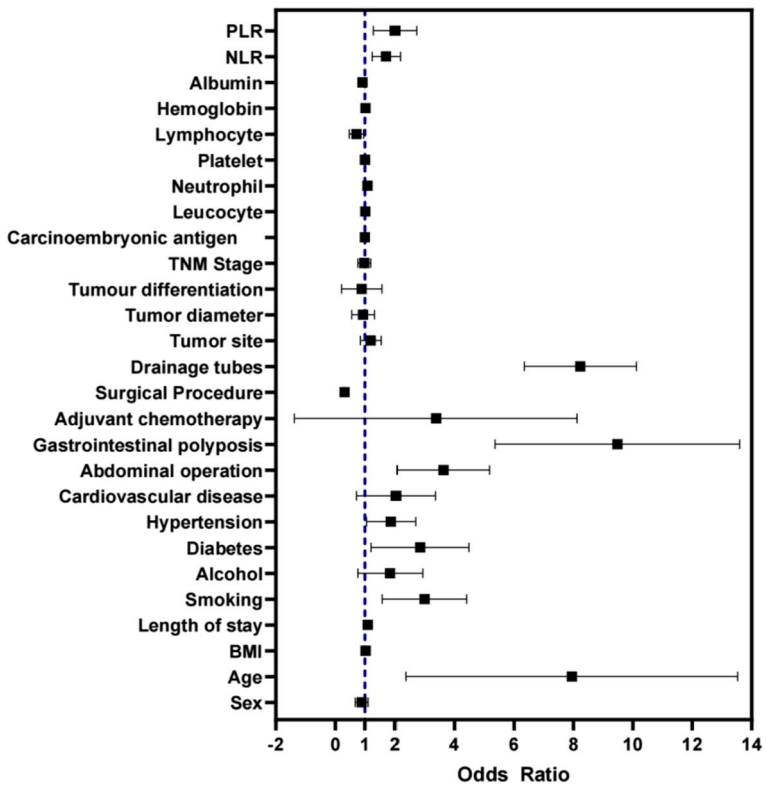

Fig. 2 Forest plot of clinical features in AL and NAL

admission. These samples were sent for testing to the Laboratory Department of the General Hospital of the Central Theatre of Operations. The setup, layout, equipment, and facilities of the clinical laboratory department complied with the Measures for the Administration of Clinical Laboratories in Healthcare Institutions. The

neutrophil, platelet, and lymphocyte counts obtained from these blood samples were utilized to compute the NLR and PLR. Specifically, NLR was determined by dividing the absolute neutrophil count by the absolute lymphocyte count, while PLR was calculated by dividing the absolute platelet count by the absolute lymphocyte count.

Grouping method

Patients were categorized according to the calculated cut-off points for NLR and PLR, and their clinical characteristics were analyzed to assess statistical significance.

Surgery

Surgical options were determined based on the tumor's location, including: 1. radical transverse colon resection with colonic end-to-end anastomosis;2. radical (extended) left hemicolectomy with colon-colonic end-to-end anastomosis;3.radical(extended) right hemicolectomy with colon-colonic end-to-end anastomosis;4. radical sigmoid resection with colorectal end-to-end anastomosis;5. anterior proctocolectomy with either colorectal end-to-end anastomosis or colon-anal canal end-to-end anastomosis.All surgical patients received postoperative abdominal (pelvic) drainage. The surgeries were conducted by experienced general surgeons, each with over five years of expertise in colorectal tumor surgery, to ensure adherence to standard surgical practices.

Definition of AL and diagnostic criteria

Patients follow-up A total of 1,016 eligible patients from the Central Theatre General Hospital were included in this study. One hundred patients were lost to follow-up (9.84% loss rate), 36 patients had missing data, and 890 patients had complete data collection. Postoperative follow-up was conducted regularly over a 5-year period,

Table 2 Logistic regression analysis of CAL patients ($n = 102$)

Variable		Univariate analysis		Multivariate analysis	
		OR(95%CI)	*P*	OR(95%CI)	*P*
Age(years)	(≥ 60/ < 60)	1.002 (0.985–1.018)	0.847		
BMI(kg/m^2)		1.015 (0.952–1.082)	0.654		
Hospitalization (day)	(≥ 25.5/ < 25.5)	1.093 (1.074–1.112)	< 0.001	1.095 (1.072–1.118)	< 0.001
Gender	(Male/Female)	1.904 (1.205–3.008)	0.006	1.750 (0.987–3.101)	0.055
Smoking	(Yes/No)	2.770 (1.705–4.502)	< 0.001	1.307 (0.730–2.340)	0.368
Alcohol	(Yes/No)	1.632 (0.882–3.018)	0.119		
Diabetes	(Yes/No)	2.529 (1.387–4.612)	0.002	1.248 (0.615–2.533)	0.539
Hypertension	(Yes/No)	1.752 (1.119–2.743)	0.014	0.818 (0.488–1.373)	0.448
Cardiovascular disease	(Yes/No)	1.747 (0.879–3.472)	0.112		
Abdominal operation	(Yes/No)	3.402 (2.195–5.273)	< 0.001	2.162 (1.303–3.588)	0.003
Intestinal polyps	(Yes/No)	8.881 (5.690–13.859)	< 0.001	4.504 (2.777–7.306)	< 0.001
Chemotherapy	(Yes/No)	0.766 (0.507–8.857)	0.205		
Surgical options	(Yes/No)	0.293 (0.192–0.447)	< 0.001	0.313 (0.163–0.600)	< 0.001
Drainage tube	(Yes/No)	7.763 (6.626–10.314)	< 0.001	5.636 (3.441–9.970)	0.002
Tumor location	(Descending/ Sigmoid/ Rectum)	1.162 (0.864–1.563)	0.321		
Tumor diameter	(≥ 5/ < 5)	0.888 (0.587–1.344)	0.574		
Tumor differentiation	(Poor/ Medium/ High)	0.363 (0.110–1.198)	0.096		
TNM Stage	(I/II/III/IV)	0.960 (0.768–1.199)	0.719		
CEA(ng/mL)		1.000 (0.994–1.006)	0.944		
Leukocyte (10^9/L)		1.011 (0.939–1.088)	0.771		
Neutrophil (10^9/L)		1.086 (1.010–1.168)	0.027	1.329 (0.855–2.064)	0.206
Platelet (10^9/L)		1.002 (1.000–1.004)	0.080	1.008 (1.001–1.014)	0.022
Lymphocyte (10^9/L)		0.687 (0.486–0.969)	0.033	0.605 (0.336–1.090)	0.095
Hemoglobin (g/L)		1.016 (1.003–1.029)	0.015	1.003 (0.991–1.015)	0.617
Albumin (g/dL)		0.914 (0.818–1.022)	0.114		
NLR(10^9/L)		1.790 (1.206–2.129)	0.031	0.171 (0.218–0.562)	0.022
PLR(10^9/L)		1.803 (1.401–2.805)	0.001	1.605 (1.001–2.009)	0.022

with visits at 3-month intervals during the first 2 years, 6-month intervals in the third year, and annual intervals thereafter. The follow-up included systematic physical examinations, blood tests (routine and biochemical), tumor markers, chest CT, abdominal and pelvic enhanced CT, and annual colonoscopy for 5 consecutive years. Patients were followed up for 4 to 203 months (mean: 89 months, median: 96 months, quartiles: 33–133). Recurrence was determined based on imaging and CEA indicators, confirmed by pathology.OS was calculated from the date of colorectal cancer diagnosis to death or the last follow-up (April 1, 2024). DFS was calculated from the date of colorectal cancer diagnosis to recurrence or the last follow-up (April 1, 2024). Recurrence diagnosis was based on imaging and endoscopic histopathological data.

Statistical analysis

Statistical analysis was conducted using SPSS (version 27.0) and R software (version 4.2.2.), and forest plots were created using GraphPad Prism (version 10). Measurement data were described as mean ± standard deviation ($\bar{x} \pm s$) and analyzed using the Student's t-test. Categorical data were described using frequencies (n) and percentages (%), and analyzed using the χ^2 test. ROC curve analysis was used to analyze the area under the curve (AUC), sensitivity, and specificity values for variables with significant differences. Based on the Youden index, cutoff values for NLR and PLR were obtained to evaluate their prognostic value for CRC and CAL. Logistic regression was used for univariate and multivariate analysis of risk factors affecting CAL, and forest plots were created. Kaplan–Meier curves were used to construct survival curves, and the log-rank test was used for comparison. Cox regression was performed for univariate and multivariate analysis to evaluate factors affecting OS and DFS, and forest plots were created. A nomogram was constructed using the Cox model in R, with calibration curves used to assess model accuracy, and decision curves and clinical impact curves used to evaluate the clinical value. A P values < 0.05 was considered statistically significant.

Results

General patient characteristics

Flow Fig. 1. shows the enrollment process of 1016 patients from January 2007 to December 2023. A total of 890 patients were enrolled in this study, including 102 (11.5%) and 788 (88.5%) patients with AL and NAL. The median follow-up was 96 months (interquartile range 33–133). There were 267 (30%) deaths and 178 (20%) confirmed recurrences or metastases during follow-up. The study included 532 (59.8%) males and 358 (40.2%) females, with a mean age of 68.66 ± 12.66 years and a BMI of 23.05 ± 3.18 kg/m^2. The average length of hospital stay was 22.51 ± 11.71 days. A history of smoking was

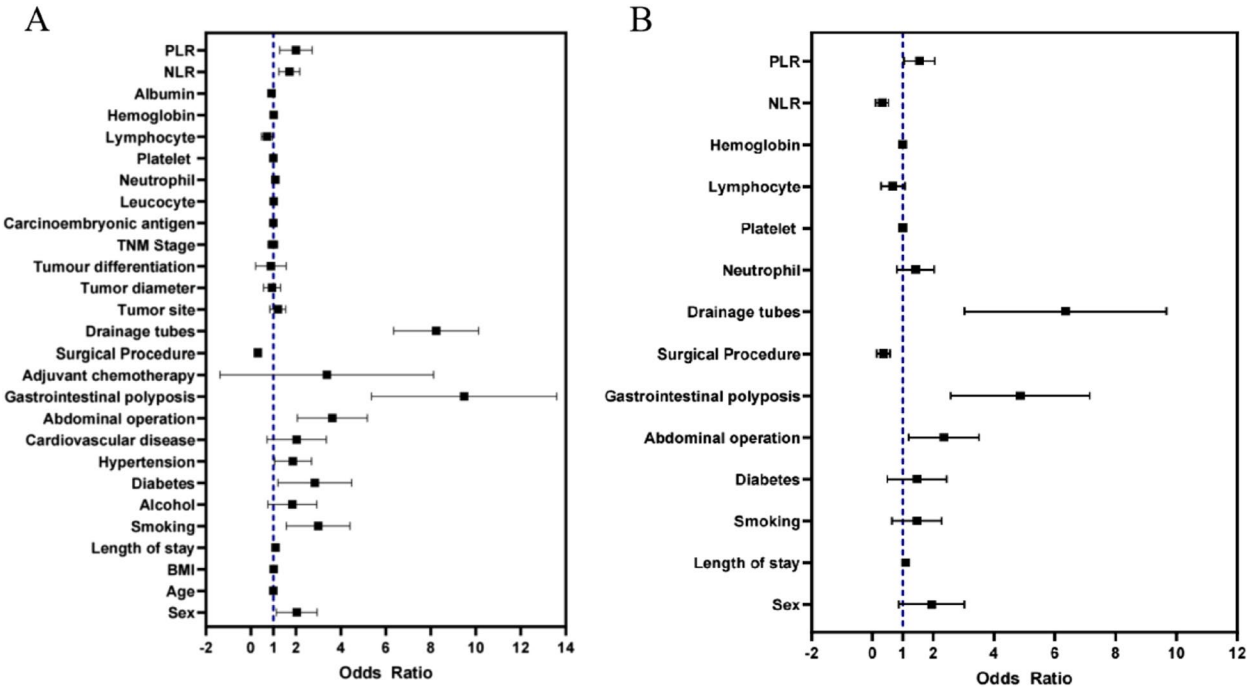

Fig. 3 Forest maps for univariate and multivariate logistic analysis of postoperative AL in patients with colorectal cancer are shown in **A** and **B**

noted in 125 cases (14%) and alcohol consumption in 84 cases (9.4%). Preoperative comorbidities included diabetes mellitus in 70 cases (7.9%), hypertension in 202 cases (22.7%), and coronary heart disease in 62 cases (7.0%). There were 171 cases (19.2%) with a history of abdominal surgery and 151 cases (17.0%) with a history of intestinal polyps. Postoperative adjuvant therapy was administered to 480 patients (53.9%), and 667 patients (74.9%) underwent laparoscopic surgery while 223 (25.1%) had open surgery. Intraoperative placement of drainage tubes occurred in 636 cases (71.5%). Tumors were located in the descending colon in 124 cases (13.9%), sigmoid colon in 274 cases (30.8%), and rectum in 492 cases (55.3%). Tumor diameter was less than 5 cm in 503 cases (56.5%) and 5 cm or greater in 387 cases (43.5%). Pathological examination revealed poorly differentiated tumors in 6 cases (0.7%), moderately differentiated tumors in 849 cases (95.5%), and highly differentiated tumors in 35 cases (3.9%). Tumor staging indicated 241 cases (27.1%) of Stage I, 340 cases (38.2%) of Stage II, 217 cases (24.4%) of Stage III, and 83 cases (9.3%) of Stage IV. Carcinoembryonic antigen levels were ≥ 5 ng/mL in

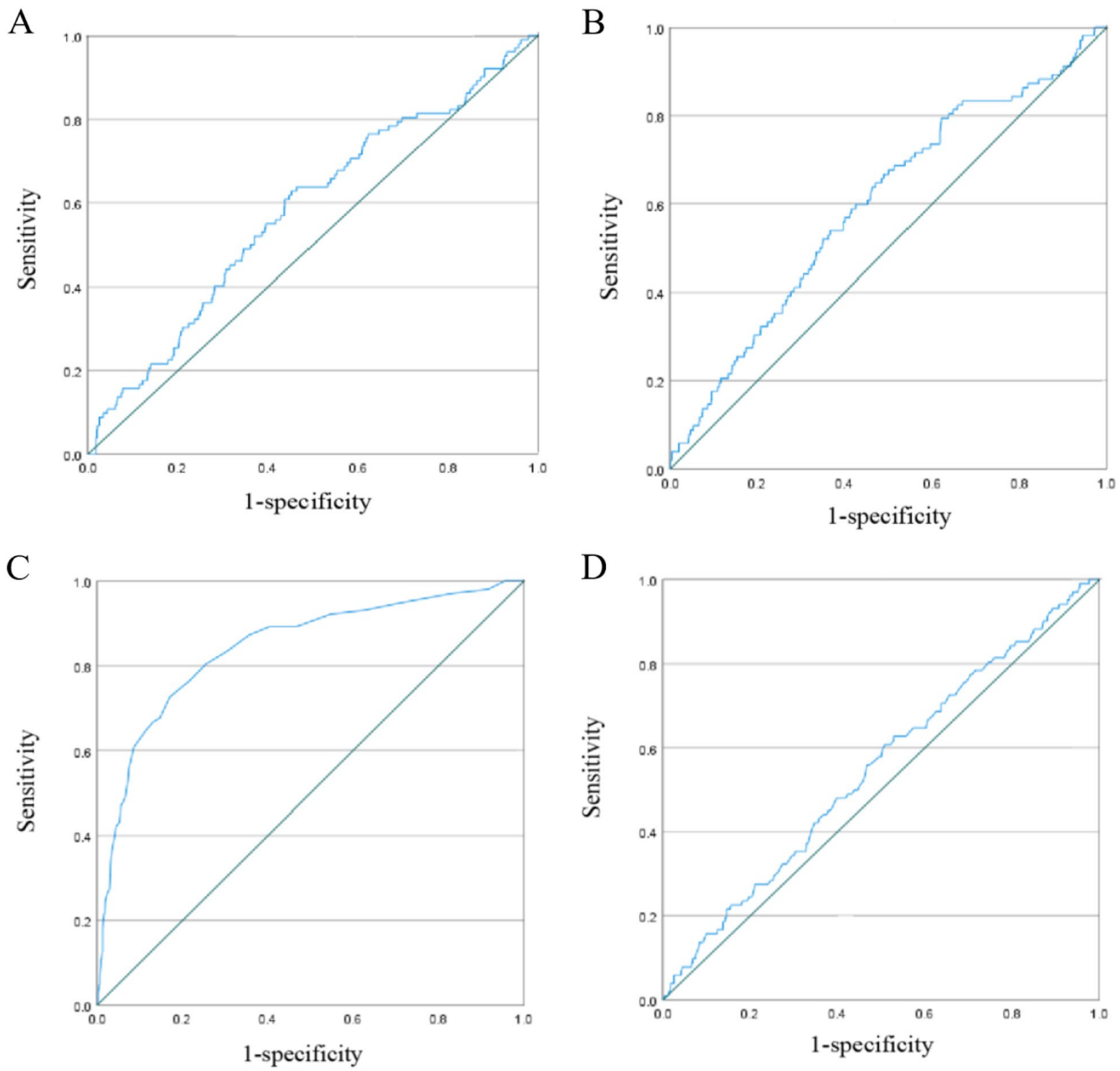

Fig. 4 Predictive ROC curve of preoperative NLR and PLR in patients with CAL are shown in **A** and **B**; Predictive ROC curve of preoperative Hospitalization and Platelet in patients with CAL are shown in **C** and **D**

402 cases (45.2%) and < 5 ng/mL in 488 cases (54.8%). Preoperative leukocyte count was $6.25 \pm 2.68 \times 10^9$/L, neutrophil count was $4.10 \pm 3.11 \times 10^9$/L, platelet count was $221.98 \pm 83.31 \times 10^9$/L, lymphocyte count was $1.62 \pm 0.67 \times 10^9$/L, hemoglobin was 117.44 ± 21.91 g/L, and albumin was 38.61 ± 4.95 g/L. Preoperative NLR was 3.05 ± 2.88, and preoperative PLR was 0.11 ± 0.06 (Table 1).

Factors affecting postoperative complications of CRC

As shown in Table 1, among the 890 patients who underwent surgery for CRC cancer, 102 developed AL postoperatively, while 788 did not. The study included an analysis of relevant influencing factors, and a forest plot was created using GraphPad Prism. It was found that gender, history of smoking, history of diabetes mellitus, history of hypertension, history of abdominal surgery, history of intestinal polyps, mode of surgery, intraoperative placement of drains, TNM stage, preoperative NLR, preoperative PLR, BMI, and length of stay were all statistically significant ($P < 0.05$) (Table 1 and Fig. 2).

Analysis of risk factors and preoperative predictors of AL in CRC patients and determination of preoperative NLR, PLR predictors and cutoff values for CRC patient survival prognosis

Evaluation of risk factors for postoperative AL in patients with CRC

In this study, 890 patients who underwent surgery for colorectal cancer were divided into two groups based on the occurrence of A postoperatively: the AL group and the NAL group. Logistic regression analyses were performed to compare variables associated with AL, and forest plots were created using GraphPad Prism. Univariate analysis revealed that gender, smoking history, diabetes mellitus, hypertension, history of abdominal surgery, history of intestinal polyps, mode of surgery, intraoperative placement of drains, preoperative neutrophils, preoperative lymphocytes, preoperative hemoglobin, preoperative NLR, and preoperative PLR were all statistically significant ($P < 0.005$). The multifactorial analysis indicated that a history of abdominal surgery, a history of intestinal polyps, an open surgical approach, absence of intraoperative drains, preoperative NLR ≥ 2.29, preoperative PLR ≥ 133.24, and a length of hospital stay ≥ 25.5 days were independent risk factors for the occurrence of AL in postoperative colorectal cancer patients ($P < 0.05$ for all) (Table 2 and Fig. 3).

Prediction of AL in CRC patients and determination of cut-off values

In this study, preoperative NLR, PLR, hospital stay, preoperative neutrophils, preoperative platelets, preoperative lymphocytes, and preoperative hemoglobin were calculated in 890 patients with CRC. ROC curves were constructed to evaluate the predictability of these variables. The results showed that NLR (AUC = 0.581, 95% CI: 0.521–0.641, $P = 0.008$), PLR (AUC = 0.598, 95% CI: 0.540–0.657, $P = 0.001$), length of hospital stay (AUC = 0.842, 95% CI: 0.798–0.886, $P = 0.000$), preoperative neutrophils

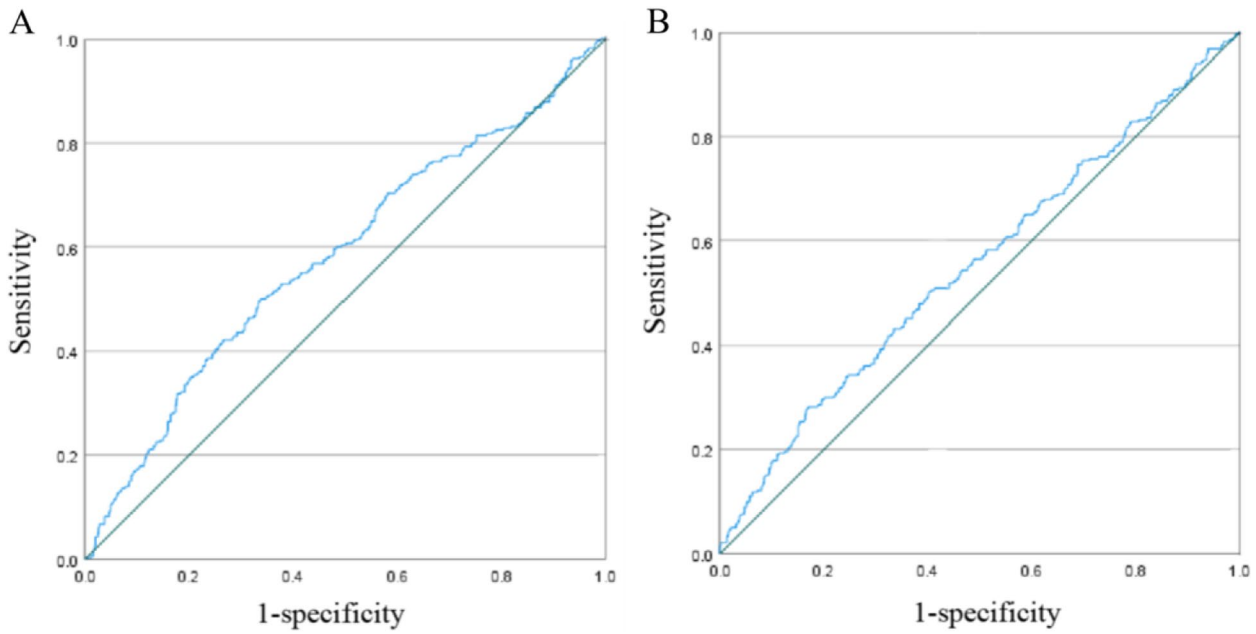

Fig. 5 ROC curve of preoperative NLR and PLR for survival prediction in CRC are shown in **A** and **B**

(AUC = 0.539, 95% CI: 0.480–0.599, $P = 0.195$), preoperative platelets (AUC = 0.549, 95% CI: 0.490–0.608, $P = 0.106$), preoperative lymphocytes (AUC = 0.426, 95% CI: 0.369–0.483, $P = 0.015$), and preoperative hemoglobin (AUC = 0.515, 95% CI: 0.453–0.577, $P = 0.621$) had varying degrees of predictive value. The optimal NLR cut-off point for predicting AL was 2.29 (sensitivity 63%, specificity 55%), and the optimal PLR cut-off point was 133.24 (sensitivity 67%, specificity 51%). The best critical value for hospital stay was 25 days (sensitivity 73%, specificity 83%), for neutrophils was 3.81 (sensitivity 53%, specificity 60%), for platelets was 206.50 (sensitivity 61%, specificity 49%), and for lymphocytes was 3.02 (sensitivity 4.9%, specificity 97%). These results indicate that NLR, PLR, hospital stay, preoperative neutrophils, preoperative platelets, and preoperative hemoglobin can all predict the probability of postoperative AL in patients with CRC. However, the AUCs for hospital stay, PLR, and NLR were higher, indicating greater predictive accuracy (Fig. 4).

Prediction of AL in CRC patients by preoperative NLR and PLR and determination of cutoff value

Among 890 CRC patients, 267 (30%) had OS and 178 (20%) had DFS based on postoperative follow-up. The survival status at postoperative follow-up was utilized as a variable to evaluate the prognostic value of NLR and PLR in predicting the postoperative outcomes of CRC patients. ROC curves were constructed to assess the predictability of NLR and PLR. The results revealed that NLR (AUC = 0.582, 95% CI: 0.541–0.623, $P = 0.000$) and PLR (AUC = 0.553, 95% CI: 0.511–0.594, $P = 0.012$) had significant predictive value. The optimal NLR critical value was 2.61 (sensitivity 50%, specificity 66%), and the best PLR critical value was 204.04 (sensitivity 28%, specificity 83%), both of which were indicative of the survival prognosis of CRC patients after surgery (Fig. 5).

Table 3 COX regression analysis of unifactorial and multifactorial OS in CRC patients ($n = 46$)

Variable		Univariate analysis		Multivariate analysis	
		OR(95%CI)	*P*	OR(95%CI)	*P*
Age(years)	(≥ 60/ < 60)	6.639 (3.132 -14.070)	< 0.001	5.015 (2.335–10.771)	< 0.001
BMI(kg/m^2)		1.026 (0.989 -1.065)	0.189		
Hospitalization (day)	(≥ 25.5/ < 25.5)	1.294 (0.998 -1.679)	0.052		
Gender	(Male/Female)	0.871 (0.680–1.116)	0.276		
Smoking	(Yes/No)	0.786 (0.559–1.105)	0.166		
Alcohol	(Yes/No)	0.775 (0.513–1.169)	0.224		
Diabetes	(Yes/No)	1.747 (1.234–2.472)	0.002	1.483 (1.021–2.156)	0.038
Hypertension	(Yes/No)	1.335 (1.035–1.721)	0.026	1.121 (0.834–1.508)	0.449
Cardiovascular disease	(Yes/No)	1.726 (1.209–2.462)	0.003	1.322 (0.894–1.955)	0.161
Abdominal operation	(Yes/No)	1.125 (0.848–1.493)	0.413		
Intestinal polyps	(Yes/No)	2.039 (1.537–2.706)	< 0.001	2.639 (1.936–3.596)	< 0.001
Chemotherapy	(Yes/No)	0.084 (0.021–0.344)	0.001	0.598 (0.142–2.523)	0.484
Surgical options	(Yes/No)	0.424 (0.310–0.580)	< 0.001	0.484 (0.313–0.614)	< 0.001
Drainage tube	(Yes/No)	0.138 (0.093–0.204)	< 0.001	0.095 (0.062–0.147)	< 0.001
Tumor location	(Descending/ Sigmoid/ Rectum)	0.583 (0.458–0.741)	< 0.001	0.834 (0.623–1.037)	0.093
Tumor diameter	(≥ 5/ < 5)	1.210 (0.952–1.538)	0.120		
Tumor differentiation	(Poor/ Medium/ High)	0.558 (0.179–1.742)	0.315		
TNM Stage	(I/II/III/IV)	1.849 (0.862–9.015)	< 0.001	3.367 (2.341–9.971)	< 0.001
CEA(ng/mL)		1.004 (1.001–1.007)	0.011	1.001 (0.998–1.004)	0.540
Leukocyte (10^9/L)		1.012 (0.971–1.055)	0.572		
Neutrophil (10^9/L)		1.047 (1.003–1.093)	0.038	1.044 (0.984–1.108)	0.155
Platelet (10^9/L)		1.001 (0.999–1.003)	0.291		
Lymphocyte (10^9/L)		0.686 (0.557–0.846)	0.182		
Hemoglobin (g/L)		0.994 (0.989–0.999)	0.024	0.998 (0.991–1.004)	0.467
Albumin (g/dL)		0.973 (0.945–1.002)	0.065	0.995 (0.967–1.024)	0.735
NLR(10^9/L)	(≥ 2.61/ < 2.61)	1.676 (1.318–2.130)	< 0.001	1.071 (0.778–1.475)	0.006
PLR(10^9/L)	(≥ 204.04/ < 204.04)	2.081 (1.592–2.719)	< 0.001	1.658 (1.192–2.307)	0.003

Univariate and multivariate COX regression analysis of survival outcomes in CRC patients

Univariate and multivariate Cox regression analyses of OS in CRC patients Using R software and Graph Prism 9, Cox regression analysis and a forest plot were utilized to identify factors influencing OS in patients with CRC. Univariate analysis indicated that age, history of diabetes, hypertension, coronary heart disease, intestinal polyps, surgical approach, intraoperative drainage, tumor location, TNM stage, preoperative neutrophil count, preoperative hemoglobin, preoperative albumin, preoperative carcinoembryonic antigen, NLR, and PLR were all significantly associated with OS ($P<0.05$). Factors showing significance ($P<0.05$) in the univariate analysis were included in the multivariate assessment. The multivariate analysis revealed that age, history of diabetes, history of intestinal polyps, open surgical procedure, intraoperative drainage, TNM stage, preoperative NLR, and preoperative PLR were independent risk factors influencing OS in CRC patients (all $P<0.05$) (Table 3 and Fig. 6).

Univariate and multivariate Cox regression analysis of DFS in CRC patients Using R software and Graph Prism 9, Cox regression analysis and a forest plot were employed to determine the factors influencing DFS in patients with CRC. Univariate analysis indicated a close relationship between DFS and age, BMI, length of hospital stay, history of intestinal polyps, surgical approach, intraoperative drainage, tumor location, tumor diameter, tumor differentiation, TNM stage、preoperative hemoglobin、NLR and PLR (all $P<0.05$). Factors showing significance ($P<0.05$) in the univariate analysis were incorporated into the multivariate analysis. The multivariate analysis demonstrated that age, BMI, length of hospital stay, history of intestinal polyps, open surgical procedure, intraoperative drainage, tumor location, tumor differentiation, preoperative NLR, and preoperative PLR were independent risk factors influencing DFS in CRC patients (all $P<0.05$) (Table 4 and Fig. 7).

Construction and validation of nomograms for Overall Survival (OS) and Disease-Free Survival (DFS) in CRC patients In the analysis of OS, we employed R software along with a Cox proportional hazards model to forecast the 1-year, 3-year, and 5-year survival rates after CAL surgery. A nomogram was devised using prognostic factors for predicting 1-year, 3-year, and 5-year OS for patients with CRC. This nomogram encompassed eight indicators: age, history of diabetes, history of intestinal polyps, open surgical approach, intraoperative drainage, TNM stage, preoperative NLR, and PLR. The outcomes revealed that age ≥ 60, history of diabetes, history of intestinal polyps, open surgical approach, intraoperative drainage, low/moderate tumor differentiation, stage III/

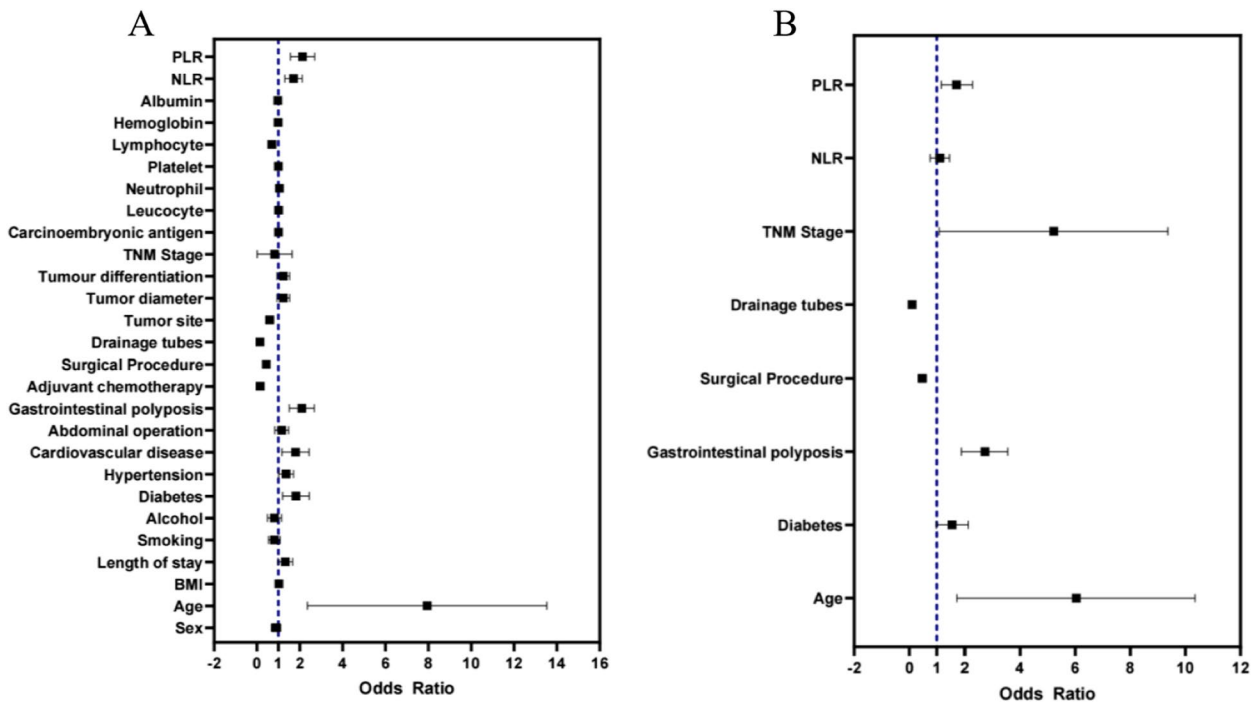

Fig. 6 Forest plot of univariate and multivariate Cox regression analysis of OS in CRC patients are shown in **A** and **B**

Table 4 COX regression analysis of unifactorial and multifactorial DFS in CRCpatients ($n=16$)

Variable		Univariate analysis		Multivariate analysis	
		OR(95%CI)	*P*	OR(95%CI)	*P*
Age(years)	(≥ 60/ < 60)	0.448 (0.296 -0.680)	0.000	0.521 (0.354–0.847)	0.003
BMI(kg/m^2)		1.052 (1.006 -1.099)	0.027	1.061 (1.014–1.112)	0.015
Hospitalization (day)	(≥ 25.5/ < 25.5)	1.549 (1.146 -2.095)	0.004	1.524 (1.166–2.176)	0.008
Gender	(Male/Female)	0.916 (0.677 -1.239)	0.568		
Smoking	(Yes/No)	1.214 (0.859–1.714)	0.272		
Alcohol	(Yes/No)	1.210 (0.807–1.814)	0.356		
Diabetes	(Yes/No)	1.074 (0.610–1.892)	0.804		
Hypertension	(Yes/No)	0.930 (0.668–1.295)	0.667		
Cardiovascular disease	(Yes/No)	0.828 (0.470–1.458)	0.513		
Abdominal operation	(Yes/No)	0.998 (0.703–1.418)	0.993		
Intestinal polyps	(Yes/No)	2.047 (1.416–2.959)	< 0.001	2.123 (1.593–3.476)	< 0.001
Chemotherapy	(Yes/No)	2.755 (1.064–3.325)	0.995		
Surgical options	(Yes/No)	0.653 (0.473–0.901)	0.009	0.641 (0.461–0.910)	0.010
Drainage tube	(Yes/No)	0.523 (0.265–1.029)	0.061		
Tumor location	(Descending/ Sigmoid/ Rectum)	2.407 (1.685–3.437)	< 0.001	2.542 (1.846–3.926)	< 0.001
Tumor diameter	(≥ 5/ < 5)	0.692 (0.504–0.951)	0.023	0.911 (0.652–1.273)	0.594
Tumor differentiation	(Poor/ Medium/ High)	4.887 (2.450–9.749)	< 0.001	3.546 (1.637–6.938)	< 0.001
TNM Stage	(I/II/III/IV)	0.705 (0.517–0.962)	0.028	0.836 (0.603–6.938)	0.283
CEA(ng/mL)		0.997 (0.989–1.005)	0.474		
Leukocyte (10^9/L)		1.020 (0.970–1.073)	0.430		
Neutrophil (10^9/L)		0.983 (0.924–1.045)	0.573		
Platelet (10^9/L)		1.001 (0.999–1.003)	0.291		
Lymphocyte (10^9/L)		1.082 (0.878–1.332)	0.457		
Hemoglobin (g/L)		1.009 (1.001–1.016)	0.019	1.003 (0.603–6.938)	0.484
Albumin (g/dL)		1.037 (0.999–1.076)	0.053		
NLR (10^9/L)	(≥ 2.61/ < 2.61)	0.904 (0.318–1.130)	0.012	0.797 (0.564–1.124)	< 0.001
PLR (10^9/L)	(≥ 204.04/ < 204.04)	1.202 (0.128–2.582)	0.009	1.980 (1.260–3.112)	0.003

IV, NLR ≥ 2.61, and PLR ≥ 204.04 increased the risk of poor prognosis. The C-index for OS was 0.871 (95% CI: 0.853–0.888). The calibration curves for 5-year OS and DFS demonstrated a high level of consistency between predicted and observed survival rates. Furthermore, the decision curve analysis (DCA) and clinical impact curve for the 5-year OS nomogram provided additional confirmation of its clinical applicability. These results suggest that the nomogram is highly accurate in foreseeing the prognosis after CAL surgery.For the assessment of DF, R software and a Cox model were used to forecast the 1-year, 3-year, and 5-year survival rates following CAL surgery. A nomogram was developed to forecast the 1-year, 3-year, and 5-year DFS for CRC patients, including nine indicators: age, length of hospital stay, history of intestinal polyps, open surgical approach, intraoperative drainage, tumor location, tumor differentiation, preoperative NLR, and preoperative PLR. The findings indicated that age ≥ 60, hospital stay ≥ 25 days, history of intestinal polyps, open surgical approach, intraoperative drainage, low/moderate tumor differentiation, stage III/IV, NLR ≥ 2.61, and PLR ≥ 204.04 were associated with an increased risk of poor prognosis. The C-index for DFS was 0.671 (95% CI: 0.608–0.722). Similar to the results for OS, the calibration curves for 5-year OS and DFS exhibited a high level of conformity between predicted and observed survival rates. Moreover, clinical impact curve for the 5-year DFS nomogram further endorsed its clinical relevance. These results indicate that the nomogram is highly precise in predicting the prognosis after CAL surgery (Fig. 8).

Determination of survival prediction and cut-off values of preoperative NLR and PLR in patients with CAL and subgroup studies of NLR and PLR

Preoperative NLR, PLR for survival prediction and determination of cut-off values in CAL patients

To evaluate the prognostic significance of preoperative NLR and PLR in patients with CAL, we conducted an

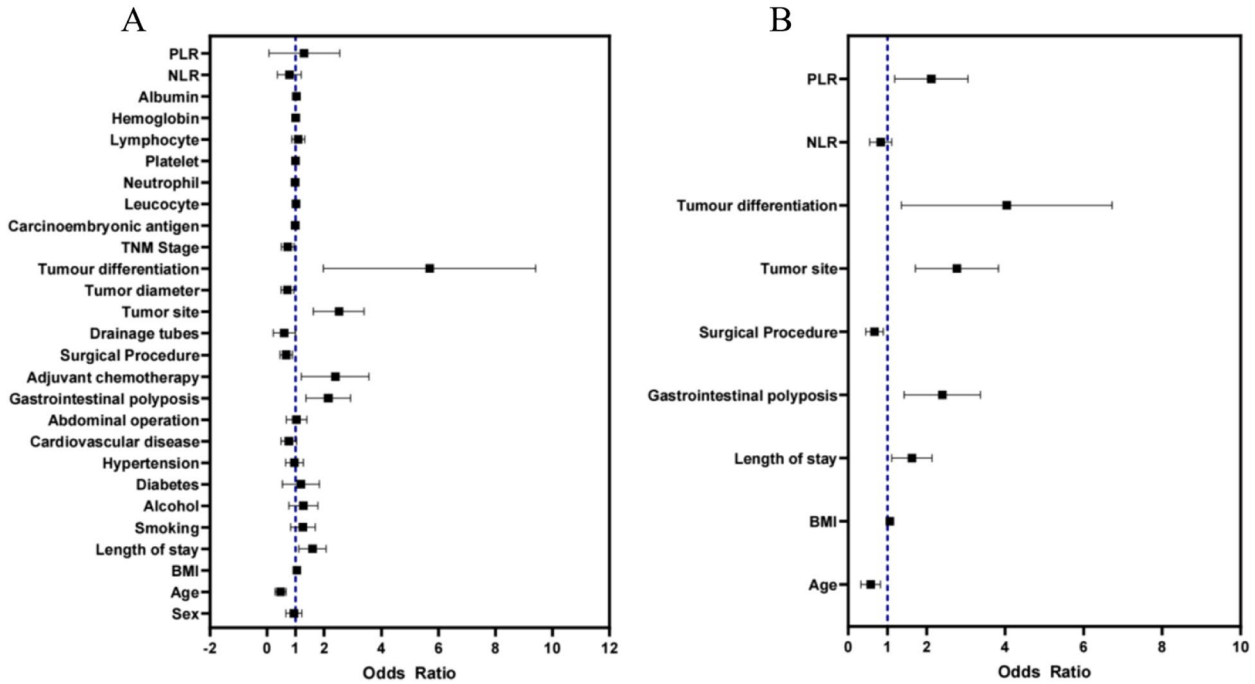

Fig. 7 Forest plot of univariate and multivariate Cox regression analysis of DFS in CRC patients are shown in **A** and **B**

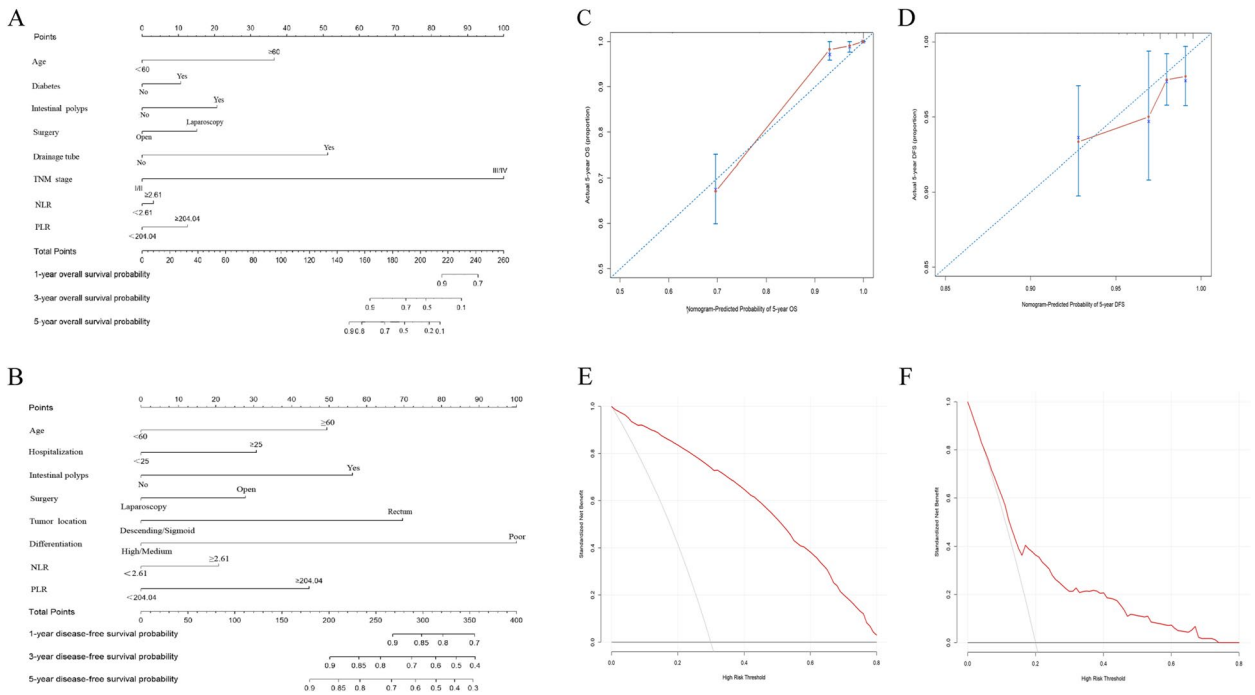

Fig. 8 Nomogram to predict the probability of OS (**A**) and DFS (**B**) after radical resection of colorectal cancer. This nomogram model was used to predict the calibration curves of OS (**C**) and DFS (**D**) at 5 years after radical resection of colorectal cancer. nomogram model for prediction of OS (**E**) and DFS (**F**) decision curves 5 years after radical resection of colorectal cancer

analysis of the NLR and PLR indices of 102 CAL patients and generated ROC curves. These curves indicated that the optimal NLR (AUC = 0.924, 95% CI: 0.870–0.978, $P = 0.000$) and PLR (AUC = 0.875, 95% CI: 0.803–0.947, $P = 0.000$) values were achieved. The best NLR cutoff for predicting CAL was 2.89 (sensitivity 83%, specificity 93%), while the best PLR cutoff was 157.62 (sensitivity 87%, specificity 79%). Both NLR and PLR exhibited AUCs exceeding 70%, signifying higher prediction accuracy and effectiveness in forecasting the prognosis of CAL patients (Fig. 9).

Preoperative NLR and PLR cut-off values classify CAL patients into high and low NLR and PLR groups

The NLR and PLR cut-off points of 2.89 and 157.62, respectively, were derived from the results of the ROC curve. Subsequently, the study cohort was classified into high NLR (NLR ≥ 2.89), low NLR (NLR < 2.89), high PLR (PLR ≥ 157.62), and low PLR (PLR < 157.62) groups for clinical characterization. Significant differences between high and low NLR groups were observed in surgical methods, tumor site, preoperative leukocytes, preoperative neutrophils, preoperative platelets, preoperative lymphocytes, and preoperative NAR ($P < 0.05$). Similarly, the high and low PLR groups exhibited differences in age, surgical method, intraoperative placement of drains, tumor differentiation, preoperative leukocytes, preoperative platelets, preoperative lymphocytes, and preoperative hemoglobin ($P < 0.05$). Please refer to Table 5 for details.

Clinical characteristics and risk factors affecting OS and DFS in patients with CAL.

Comparative analysis of clinical characteristics of OS and DFS in patients with CAL

Based on the follow-up results, it was determined that out of the 102 (11.46%) patients with CAL, 46 (45.10%) were classified as OS patients, 16 (15.69%) as DFS patients, and 40 (39.22%) as survivors. A comprehensive analysis was conducted to compare the subgroups of variables that could potentially influence the association of OS and DFS. The results of the analysis revealed significant differences ($P < 0.05$) between OS and DFS in terms of age, history of smoking, history of alcohol consumption, diabetes mellitus, hypertension, history of abdominal surgery, history of intestinal polyps, tumor diameter, TNM stage, preoperative hemoglobin, and hospitalization duration.(Table 6).

Univariate and multivariate Cox regression analyses of OS in patients with CAL

COX regression analysis was conducted to identify factors impacting OS in patients with CAL. The R software was used for analysis, and Graph Prism9 was utilized to generate forest plots. Univariate analysis demonstrated

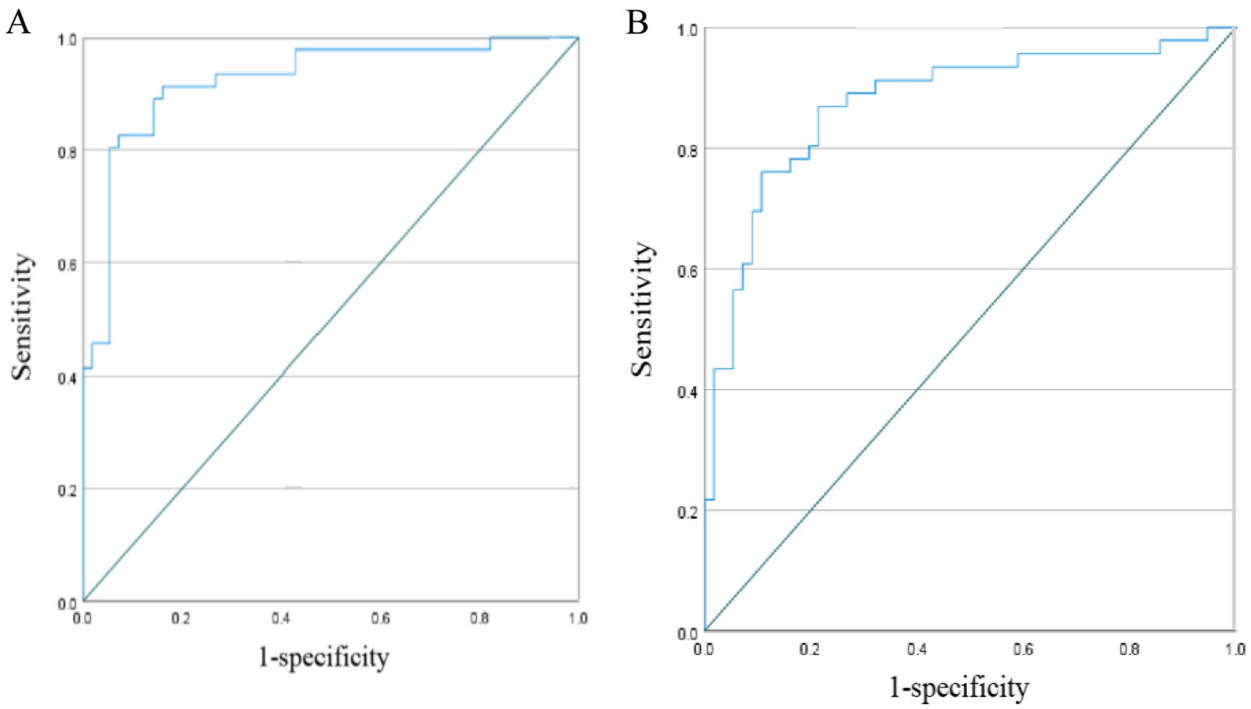

Fig. 9 ROC curves for survival prediction of CAL patients by preoperative NLR and PLR are shown in **A** and **B**

Table 5 Preoperative NLR and PLR cutoffs group CAL patients together

Variables	NLR ≥ 2.89×10^{-9} ($n=42$)	NLR < 2.89×10^{-9} ($n=60$)	$t/Z/\chi^2$	P	PLR ≥ 157.62×10^{-9} ($n=52$)	PLR < 157.62×10^{-9} ($n=50$)	$t/Z/\chi^2$	*P*
Age(years)	68.71 ± 13.96	69.00 ± 12.15	-0.133	0.895	68.88 ± 12.86	72.04 ± 12.17	-3.466	0.001
BMI(kg/m^2)	22.86 ± 2.58	23.15 ± 4.49	-0.722	0.474	22.75 ± 2.35	23.32 ± 4.90	-1.758	0.085
Hospitalization (day)	40.07 ± 18.55	35.22 ± 14.17	1.695	0.098	35.77 ± 16.44	38.72 ± 15.98	-1.294	0.201
Gender								
Male	30(71.43)	44(73.33)	0.045	0.832	38(73.08)	36(72.00)	2.125	0.145
Female	12(28.57)	16(26.67)			14(26.92)	24(48.00)		
Smoking								
Yes	11(26.19)	17(28.33)	0.811	0.057	16(30.77)	12(24.00)	0.586	0.444
No	31(73.81)	43(71.67)			36(69.23)	38(76.00)		
Alcohol								
Yes	4(9.52)	10(1.67)	1.064	0.302	10(19.23)	4(8,00)	2.715	0.099
No	38(90.48)	50(83.33)			42(80.77)	46(12.00)		
Diabetes								
Yes	8(19.05)	8(13.33)	0.610	0.435	7(13.46)	9(18.00)	0.397	0.529
No	34(80.95)	52(86.67)			45(86.54)	41(82.00)		
Hypertension								
Yes	14(33.33)	19(31.67)	0.031	0.859	18(34.62)	15(3.00)	0.248	0.618
No	28(4.76)	41(68.33)			34(65.38)	35(7.00)		
Cardiovascular disease								
Yes	5(11.90)	6(10.00)	0.093	0.760	5(9.62)	6(12.00)	0.151	0.698
No	37(88.10)	54(90.00)			47(90.38)	44(88.00)		
Abdominal operation								
Yes	19(45.24)	22(36.67)	0.755	0.385	24(46.15)	17(34.00)	1.566	0.211
No	23(54.76)	38(63.33)			28(53.85)	33(66.00)		
Intestinal polyps								
Yes	26(61.90)	30(50.00)	1.414	0.234	33(63.46)	23(46.00)	3.139	0.076
No	16(38.10)	30(50.00)			19(36.54)	27(54.00)		
Chemotherapy								
Yes	24(57.14)	25(41.67)	2.371	0.124	28(53.85)	21(42.00)	1.433	0.231
No	18(42.86)	35(58.33)			24(3.85)	29(58.00)		
Surgical options								
laparoscopy	32(76.19)	59(98.33)	12.590	< 0.001	40(76.92)	46(92.00)	4.381	0.036
open	10(23.81)	1(1.67)			12(23.08)	4(8.00)		
Drainage tube								
Yes	40(95.24)	59(98.33)	0.829	0.363	40(76.92)	49(98.00)	10.183	0.001
No	2(4.76)	1(1.67)			12(23.08)	1(2.00)		
Tumor location								
Descending	13(30.95)	2(3.33)	15.052	< 0.001	12(23.08)	3(6.00)	6.004	0.050
Sigmoid	8(19.05)	15(25.00)			10(19.23)	13(26.00)		
Rectum	21(50.00)	43(71.67)			30(57.69)	34(68.00)		
Tumor diameter								
< 5 cm	21(50.00)	39(65.00)	2.295	0.130	28(53.85)	32(64.00)	1.085	0.298
≥ 5 cm	21(50.00)	21(35.00)			24(46.15)	18(36.00)		
Tumor differentiation								
Poor	1(2.38)	1(1.67)	0.068	0.967	1(1.92)	3(6.00)	8.400	0.015
Medium	39(92.86)	56(93.33)			48(92.31)	35(70.00)		
High	2(4.76)	3(5.00)			3(5.77)	12(24.00)		

Table 5 (continued)

Variables	NLR ≥ 2.89 × 10^{-9} (*n* = 42)	NLR < 2.89 × 10^{-9} (*n* = 60)	*t*/*Z*/χ^2	P	PLR ≥ 157.62 × 10^{-9} (*n* = 52)	PLR < 157.62 × 10^{-9} (*n* = 50)	*t*/*Z*/χ^2	*P*
TNM Stage								
I	9(21.43)	11(18.33)	3.339	0.342	9(17.31)	11(22.00)	72.047	0.424
II	19(45.24)	34(56.67)			28(53.85)	25(50.00)		
III	13(30.95)	11(18.33)			14(26.92)	10(20.00)		
IV	1(2.38)	4(6.67)			1(1.92)	4(8.00)		
CEA(ng/mL)								
CEA(ng/mL)	4.04(1.99, 17.07)	5.39(2.08, 32.79)	-0.673	0.501	5.70(2.07, 27.88)	3.55(1.83, 29.27)	-1.285	0.199
Leukocyte (10^9/L)	7.41 ± 3.23	5.57 ± 1.52	3.686	< 0.001	6.85 ± 3.18	5.57 ± 1.44	2.912	0.005
Neutrophil (10^9/L)	6.38 ± 4.77	3.20 ± 1.05	4.321	< 0.001	4.87 ± 2.97	4.13 ± 4.00	1.788	0.080
Platelet (10^9/L)	240.40 ± 76.27	231.92 ± 94.77	0.729	0.470	236.75 ± 87.97	191.14 ± 56.82	6.903	< 0.001
Lymphocyte(I10^9/L)	1.14 ± 0.52	1.72 ± 0.55	-7.249	< 0.001	1.48 ± 0.60	1.77 ± 0.59	-8.356	< 0.001
Hemoglobin (g/L)	119.50 ± 23.07	117.15 ± 22.96	0.660	0.513	112.88 ± 24.442	123.56 ± 20.04	-3.149	0.003
Albumin (g/dL)	37.59 ± 4.61	38.49 ± 3.54	-1.261	0.214	38.32 ± 4.30	37.92 ± 3.73	0.663	0.510

significant associations between OS and age, smoking, alcohol, diabetes, abdominal surgery,intestinal polyps, degree of tumor differentiation, and TNM stage (all $P < 0.05$).The multifactorial analysis indicated that a history of alcohol consumption, a history of intestinal polyps, degree of tumor differentiation, TNM stage, NLR, and PLR were independent risk factors influencing OS in patients with CRC (all $P < 0.05$) (Table 7 and Fig. 10).

Univariate and multivariate Cox regression analysis of DFS in CAL patients

COX regression analysis was conducted to study the factors influencing DFS in CAL patients. The R software was used for the analysis, and Graph Prism9 was utilized to create forest plots. The univariate analysis indicated that patients' age, smoking,alcohol,diabetes, abdominal surgery, history of intestinal polyps, degree of tumor differentiation, and TNM stage were significantly associated with DFS (all $P < 0.05$). The multifactorial analysis revealed that a history of alcohol consumption, a history of intestinal polyps, degree of tumor differentiation, TNM stage, NLR, and PLR were independent risk factors impacting the DFS of CAL patients (all $P < 0.05$) (Table 8 and Fig. 11).

Relationship between NLR and PLR levels in high and low groups and patients' OS and DFS

The patients with OS and DFS were stratified into high and low NLR groups and high and low PLR groups based on the optimal cut-off points for NLR and PLR. In the high NLR group, 18 cases (42.86%) had OS, 18 cases (42.86%) had overall survival, and 6 cases (14.29%) had DFS; in the low NLR group, 22 cases (36.67%) had OS, 28 cases (46.67%) had overall survival, and 10 cases (16.67%) had DFS. For the high PLR group, 23 cases (44.23%) had OS, 20 cases (38.46%) had overall survival, and 9 cases (17.31%) had DFS; While in the low PLR group, 17 cases (34.00%) had OS, 26 cases (52.00%) had overall survival, and 7 cases (14.00%) had DFS. The statistical analysis revealed that the Kaplan–Meier curves for OS demonstrated a significantly higher OS in CAL patients in the low NLR group compared with the high NLR group, with a statistically significant difference ($\chi 2 = 16.397$, $P < 0.001$). Similarly, OS was significantly higher in CAL patients in the low PLR group ($\chi 2 = 6.601$, $P = 0.010$). Moreover, the Kaplan–Meier curves for DFS showed significantly higher DFS in CRC patients in the low NLR group compared to the high NLR group, with a statistically significant difference ($\chi 2 = 4.446$, $P = 0.035$), and in the low PLR group, with a statistically significant difference ($\chi 2 = 4.338$, $P = 0.037$) (Figs. 12 and 13).

Construction and validation of OS and DFS nomograms for CAL patients

In OS and DFS survival analyses, a Cox model was applied using R software to predict 1, 3, and 5-year survival after CAL. A nomogram was constructed from these prognostic factors to predict the OS of CRC patients at 1, 3, and 5 years after surgery.The nomogram included four indicators: history of alcohol consumption, history of intestinal polyps, degree of tumour differentiation, tumour stage, NLR, and PLR.From the results, it can be seen that a history of alcohol consumption, a history of intestinal polyps, low/moderately-differentiated tumour, stage III/IV, NLR ≥ 2.89 × 10–2, PLR ≥ 157.62 × 10–2, and PLR ≥ 157.62 × 10–2 were found to be significant. 10–2, and PLR ≥ 157.62 × 10–2, the risk of poor prognosis was increased. The C-indices for OS and DFS were 0.782

Table 6 Clinical characterization of OS and DFS in CAL patients

Variables	OS ($n=46$)	DFS ($n=16$)	$t/Z/\chi^2$	P
Age(years)	76.54 ± 9.35	59.81 ± 14.86	12.133	< 0.001
BMI(kg/m^2)	23.31 ± 3.73	23.24 ± 2.73	0.133	0.895
Hospitalization (day)	39.83 ± 15.31	32.88 ± 13.54	3.076	0.004
Gender				
Male	35(76.09)	11(68.75)	0.334	0.563
Female	11(23.91)	5(31.25)		
Smoking				
Yes	34(73.91)	4(25.00)	11.971	< 0.001
No	12(26.09)	12(75.00)		
Alcohol				
Yes	42(91.30)	2(12.5)	35.780	< 0.001
No	4(8.70)	14(87.50)		
Diabetes				
Yes	39(84.78)	1(6.25)	31.981	< 0.001
No	7(15.22)	15(93.75)		
Hypertension				
Yes	15(32.61)	2(12.5)	2.412	0.013
No	31(67.39)	14(87.50)		
Cardiovascular disease				
Yes	7(15.22)	1(6.25)	2.591	0.120
No	39(84.78)	15(93.75)		
Abdominal operation				
Yes	31(67.39)	3(18.75)	11.341	< 0.001
No	15(32.61)	13(81.25)		
Intestinal polyps				
Yes	29(63.04)	3(18.75)	23.525	< 0.001
No	17(36.96)	13(81.25)		
Chemotherapy				
Yes	22(47.83)	11(68.75)	2.088	0.149
No	24(52.17)	5(31.25)		
Surgical options				
laparoscopy	39(92.86)	14(87.50)	0.071	0.790
open	7(15.22)	2(12.5)		
Drainage tube				
Yes	45(97.83)	15(93.75)	0.632	0.427
No	1(2.17)	1(6.25)		
Tumor location				
descending colon	5(10.87)	1(6.25)	0.570	0.752
sigmoid colon	11(23.91)	3(18.75)		
rectum	30(65.22)	12(75.00)		
Tumor diameter				
< 5 cm	21(45.65)	14(87.50)	8.456	0.004
≥ 5 cm	25(54.35)	2(12.5)		
Tumor differentiation grade				
Poor	5(10.87)	1(6.25)	1.307	0.520
Medium	44(95.65)	14(87.50)		
High	1(2.17)	1(6.25)		
TNM Stage				
I	5(10.87)	6(37.5)	7.934	0.047
II	12(26.09)	5(31.25)		
III	24(52.17)	3(18.75)		
IV	5(10.87)	2(12.5)		
CEA(ng/mL)				
≥ 5	28(17.39)	11(68.75)	0.316	0.574
< 5	18(39.13)	5(31.25)		
Leukocyte (10^9/L)	5.97 ± 1.65	6.44 ± 2.95	-1.948	0.058
Neutrophil (10^9/L)	4.47 ± 4.17	5.15 ± 4.32	-1.107	0.274
Platelet (10^9/L)	219.43 ± 71.43	239.50 ± 126.28	-1.905	0.063
Lymphocyte (l10^9/L)	1.53 ± 0.59	1.53 ± 0.65	0.013	0.990
Hemoglobin (g/L)	116.46 ± 23.11	125.38 ± 21.96	-2.619	0.012
Albumin (g/dL)	37.92 ± 4.08	38.48 ± 3.81	-0.923	0.361
NLR(10^9/L)	3.40 ± 3.11	3.86 ± 1.22	-1.014	0.316
PLR(10^9/L)	169.37 ± 110.08	162.61 ± 66.50	0.417	0.679

(95% CI: 0.723–0.841) and 0.844 (95% CI: 0.769–0.920), respectively.The calibration curves for 5-year OS and DFS showed that the predicted survival was highly consistent with the observed results. In addition, DCA and clinical impact curve of the nomogram model for 5-year OS and DFS further confirmed the value of the nomogram for clinical application. These results demonstrate the high accuracy of nomogram in predicting CAL prognosis (Fig. 14).

Discussion

In the past few years, there has been a growing focus on inflammation as a susceptibility factor for tumor development [34, 35]. Both infectious and non-infectious (idiopathic) inflammation can contribute to tumorigenesis In numerous instances, detecting micrometastases of cancer is challenging, and using more sensitive inflammation markers may aid in achieving an accurate diagnosis [36]. The immune reaction is a pivotal factor in tumor progression and a significant determinant of the prognosis of cancer patients.Combinations of these systemic inflammatory markers, such as the systemic immune-inflammatory index (SII), NLR, and PLR, serve as markers of tumor inflammatory activity and play a vital role in promoting tumor progression [37]. In recent years, several indicators of the inflammatory response, including the C-reactive protein to albumin ratio (CAR), NLR, and PLR, have proven to be highly useful in predicting postoperative complications and prognosis in patients with CRC [38–40]. Previous studies have confirmed the

Table 7 Univariate and multivariate COX regression analysis of OS in patients with CAL

Variable		Univariate analysis		Multivariate analysis	
		OR(95%CI)	*P*	OR(95%CI)	*P*
Age(years)	(≥ 60/ < 60)	5.880 (1.420–10.350)	0.015	4.883 (1.151–10.710)	0.032
BMI(kg/m^2)		0.966 (0.921–1.081)	0.961		
Hospitalization (day)	(≥ 25.5/ < 25.5)	2.093 (0.929–4.709)	0.074	4.192 (2.638–6.350)	0.002
Gender	(Male/Female)	0.883 (0.445 -1.751)	0.721		
Smoking	(Yes/No)	3.641 (1.421–9.326)	0.007	0.036 (0.001–1.720)	0.092
Alcohol	(Yes/No)	8.478 (2.046–10.130)	0.003	4.859 (3.907–9.430)	0.007
Diabetes	(Yes/No)	1.865 (0.938–3.709)	0.075	2.043 (1.988–6.674)	0.003
Hypertension	(Yes/No)	1.314 (0.696–2.483)	0.400		
Cardiovascular disease	(Yes/No)	4.214 (1.817–9.769)	0.000	7.351 (1.395–8.727)	0.019
Abdominal operation	(Yes/No)	2.377 (1.104–5.114)	0.002	1.078 (0.160–7.262)	0.938
Intestinal polyps	(Yes/No)	1.922 (1.025–3.605)	0.042	0.008 (0.002–0.178)	0.002
Chemotherapy	(Yes/No)	2.920 (1.400–6.089)	0.004	1.002 (0.010–1.178)	0.002
Surgical options	(Yes/No)	1.243 (0.576–2.683)	0.579		
Drainage tube	(Yes/No)	1.867 (0.444–7.852)	0.394		
Tumor location	(Descending/ Sigmoid/ Rectum)	2.025 (0.819–5.009)	0.127		
Tumor diameter	(≥ 5/ < 5)	2.318 (1.195–4.496)	0.012	1.541 (0.677–3.510)	0.303
Tumor differentiation	(Poor/ Medium/ High)	3.569 (1.098 -11.600)	0.034	3.762 (1.102–10.845)	0.035
TNM Stage	(I/II/III/IV)	4.501 (1.063–9.066)	0.041	4.860 (2.341–9.331)	0.004
CEA(ng/mL)		0.989 (0.954–1.026)	0.547		
Leukocyte (10^9/L)		0.904 (0.784–1.041)	0.162		
Neutrophil (10^9/L)		0.970 (0.891–1.055)	0.477		
Platelet (10^9/L)		1.001 (1.002–1.017)	0.013	0.999 (0.996–1.003)	0.622
Lymphocyte (10^9/L)		0.908 (0.558–1.478)	0.698		
Hemoglobin (g/L)		0.972 (0.947–0.998)	0.034	0.995 (0.983–1.007)	0.425
Albumin (g/dL)		0.995 (0.925–1.070)	0.893		
NLR(10^9/L)	(≥ 2.61/ < 2.61)	2.002 (1.433–3.882)	0.040	5.571 (1.736–7.878)	0.004
PLR(10^9/L)	(≥ 204.04/ < 204.04)	0.481 (0.248–0.934)	0.031	0.477 (0.243–0.839)	0.032

impact of a high peripheral blood NLR on postoperative CRC complications, tumor prognosis, and patient survival [41, 42].

Hung H C et al. [43] demonstrated that NLR and PLR indices have a positive predictive power for prognosis in patients who combine cell reduction surgery with intraperitoneal thermochemotherapy (CRS-HIPEC) for peritoneal surface malignancies (PSM).Takeda Y et al. indicated that high preoperative NLR levels affected the median cancer-specific survival (CSS) and overall survival of patients with renal cell carcinoma (RCC) and inferior vena cava cancer thrombus (IVCTT) who underwent radical nephrectomy and thrombectomy Independent adverse prognostic factors (OS). Another study showed that [44] Preoperative NLR, PLR, LAR and advanced tumor stage may help to determine the survival rate of patients with gastric cancer, and is a good method to predict the prognosis of patients with gastric cancer. Shoichi et al. [45] found that a high preoperative NLR level was an independent poor prognostic factor influencing cancer-specific survival and overall survival of patients with renal cell carcinoma and inferior vena cava tumor thrombus who underwent radical nephrectomy and thrombectomy. NLR and PLR are better predictors of anastomotic leak compared with other proinflammatory and nutritional confounders.

[46]. Earlier research has primarily emphasized the prognostic significance of traditional clinical indicators for CRC, with fewer investigations dedicated to the outlook for patients with AL, which is the most serious complication of CRC. Moreover, there has been scarce examination of the combined prognostic value of these factors [47]. Our study involved the analysis of preoperative NLR and PLR indexes to predict the incidence of AL and the survival status of CRC patients by ROC curves. We also assessed the predictive significance of these markers in CAL patients. While prior studies predominantly focused on predicting short-term

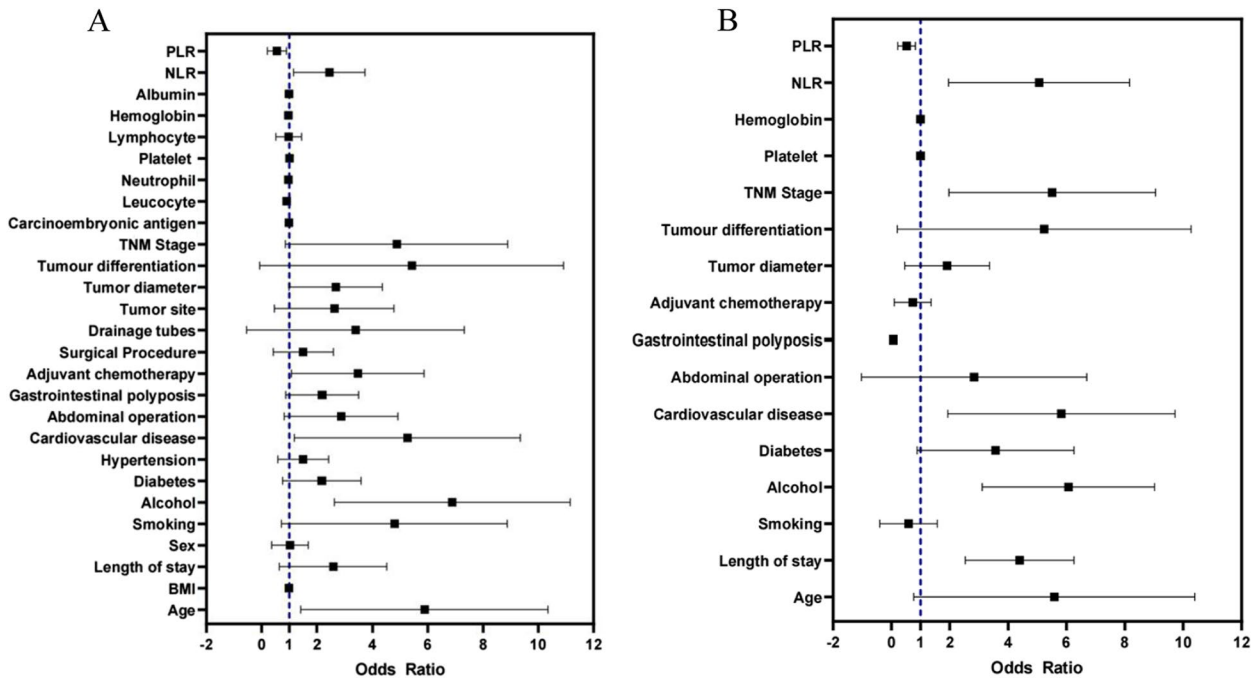

Fig. 10 Forest plot of univariate and multivariate Cox regression analysis of OS in CAL patients are shown in **A** and **B**

complications, literature significantly lacks reports on survival prediction at 1, 3, and 5 years postoperatively. In contrast, our prognostic study assessed the performance of two biomarkers (NLR and PLR) in predicting long-term outcomes in CAL patients, offering a departure from previous single biomarker or combination studies. Studies have indicated that elevated NLR and PLR are correlated with an unfavorable prognosis in patients with tumors [48], NLR and PLR can act as predictive markers for patients with colorectal cancer [49, 50]. A meta-analysis of 100 studies has confirmed the established prognostic significance of NLR in various solid tumors. Additionally, it revealed that elevated pre-treatment NLR is linked to unfavorable treatment response, pathological outcomes, and survival [51]. Xie et al. [52] found NAR to be a good predictor of postoperative prognosis in CRC patients. In addition, Chao-Yang Wang et al. [53] Studies have shown that high NLR in elderly patients undergoing colorectal cancer surgery is associated with the development of postoperative symptomatic AL. Hui Eun Ju et al. [54] indicated that patients undergoing neoadjuvant chemoradiotherapy for rectal cancer surgery, the incidence of late AL is higher than that of early AL, and the incidence of stoma reconstruction is also higher than that of early AL.

In this study, most of the included research subjects were male patients and patients with low rectal conditions. According to the univariate analysis, the majority of CAL patients were male, and they had a poorer prognosis. Aliyev V et al. [55] Studies have shown that patients under the age of 65 and male patients have a positive impact on the postoperative functional outcomes of rectal cancer. All CAL patients were male patients who underwent intersphincteric resection for low rectal cancer, with 1-year and 5-year survival rates without colostomy being 96% and 89%, respectively. Furthermore, our study only included two surgical methods: open surgery and laparoscopy; cases involving robotic surgery were not provided.Another study indicates that compared to the laparoscopic patient group, robotic surgery performed by experienced surgeons has a better overall survival rate for male patients with mid-to-low rectal cancer [56]. Gender (male/female) and surgical method (laparoscopic/robotic) are of significant importance in the prognosis of survival and functional outcomes in patients with rectal cancer [57, 58]. Robotic surgery can improve specimen quality, tumor outcomes, and functional prognosis in male rectal cancer patients, due to the high flexibility advantages of robotic surgery in narrow pelvis and mesocolon in male patients [59, 60].

This study aimed to assess the risk factors and survival status of patients with CAL. Among the 890 patients, 102 (11.46%) developed anastomotic leakage. Logistic regression analysis identified several independent risk factors for CAL, including a history of abdominal surgery,

Table 8 Univariate and multivariate COX regression analysis of DFS in patients with CAL

Variable		Univariate analysis		Multivariate analysis	
		OR(95%CI)	*P*	OR(95%CI)	*P*
Age(years)	(≥ 60/ < 60)	0.071 (0.016–0.318)	0.001	5.500 (1.094–7.654)	0.039
BMI(kg/m^2)		1.046 (0.936–1.170)	0.427		
Hospitalization (day)	(≥ 25.5/ < 25.5)	2.683 (0.947–7.602)	0.063		
Gender	(Male/Female)	2.752 (1.027–7.374)	0.044	1.061 (0.302–3.720)	0.927
Smoking	(Yes/No)	2.001 (1.873–6.158)	0.004	3.882 (0.517–7.052)	0.117
Alcohol	(Yes/No)	0.051 (0.007–0.388)	0.004	4.394 (1.288–10.991)	0.018
Diabetes	(Yes/No)	2.286 (1.294–6.092)	< 0.001	0.188 (0.054–0.661)	0.009
Hypertension	(Yes/No)	0.726 (0.300–1.756)	0.477		
Cardiovascular disease	(Yes/No)	2.310 (0.645–8.273)	0.198		
Abdominal operation	(Yes/No)	0.277 (0.017–4.628)	0.371		
Intestinal polyps	(Yes/No)	0.065 (0.020–0.215)	< 0.001	0.004 (0.001–0.249)	0.011
Chemotherapy	(Yes/No)	1.375 (0.583–3.240)	0.467		
Surgical options	(Yes/No)	1.256 (0.365–4.320)	0.717		
Drainage tube	(Yes/No)	2.368 (0.207–7.145)	0.681		
Tumor location	(Descending/ Sigmoid/ Rectum)	1.469 (0.832–2.594)	0.185		
Tumor diameter	(≥ 5/ < 5)	1.611 (0.686–3.784)	0.274		
Tumor differentiation	(Poor/ Medium/ High)	0.186 (0.053–0.654)	0.009	0.264 (0.073–0.956)	0.042
TNM Stage	(I/II/III/IV)	0.266 (0.086 -0.828)	0.022	4.467 (1.021 -9.541)	0.047
CEA(ng/mL)		0.994 (0.971–1.016)	0.576		
Leukocyte (10^9/L)		0.881 (0.730–1.063)	0.187		
Neutrophil (10^9/L)		0.809 (0.893–1.156)	0.921		
Platelet (10^9/L)		0.996 (0.991–1.001)	0.100		
Lymphocyte (10^9/L)		1.420 (0.681–2.958)	0.350		
Hemoglobin (g/L)		0.995 (0.989–1.000)	0.060		
Albumin (g/dL)		0.983 (0.885–1.091)	0.744		
NLR(10^9/L)	(≥ 2.61/ < 2.61)	0.232 (0.066–0.617)	0.023	9.282 (0.908–10.222)	0.031
PLR(10^9/L)	(≥ 204.04/ < 204.04)	0.358 (0.148–0.762)	0.022	8.305 (1.079–9.862)	0.042

a history of intestinal polyps, open surgery, absence of drainage tube placement during surgery, preoperative NLR ≥ 2.29, preoperative PLR ≥ 133.24, and hospital stay ≥ 25.5. The ROC curve analysis based on these factors demonstrated that preoperative NLR (AUC = 0.924, 95%CI: 0.870–0.978, $P = 0.000$) and preoperative PLR (AUC = 0.875, 95%CI: 0.803–0.947, $P = 0.000$) were more effective predictors of postoperative anastomotic leakage, with the optimal NLR cutoff value at 2.89 (sensitivity 83%, specificity 93%) and the optimal PLR cutoff value at 157.62 (sensitivity 87%, specificity 79%). Patients were categorized into high NLR (NLR ≥ 2.89), low NLR (NLR < 2.89), high PLR (PLR ≥ 157.62), and low PLR (PLR < 157.62) groups. Based on survival status, patients were divided into OS and DFS groups to evaluate the prognostic value of NLR and PLR. Cox regression analysis revealed that a history of alcohol consumption, a history of intestinal polyps, tumor differentiation, tumor TNM staging, preoperative NLR, and preoperative PLR were independent risk factors for OS and DFS in CAL patients (all $P < 0.05$). Furthermore, a nomogram was constructed using the Cox proportional hazards model to visualize the impact of various factors on the prognosis of CAL patients and to predict 1-, 3-, and 5-year survival rates post-surgery. The nomogram indicated that a history of alcohol consumption, a history of intestinal polyps, low/medium tumor differentiation, stage III/IV, NLR ≥ 2.89, and PLR ≥ 157.62 increased the adverse risk for OS and DFS in CAL patients. The 5-year OS DCA and clinical impact curve of the nomogram further validated its clinical utility, demonstrating high accuracy in predicting CRC prognosis.

Additionally, the study assessed the predictive value of preoperative NLR and PLR on the survival of postoperative CRC patients. ROC curve analysis revealed that preoperative NLR (AUC = 0.582, 95%CI: 0.541–0.623, $P = 0.000$)

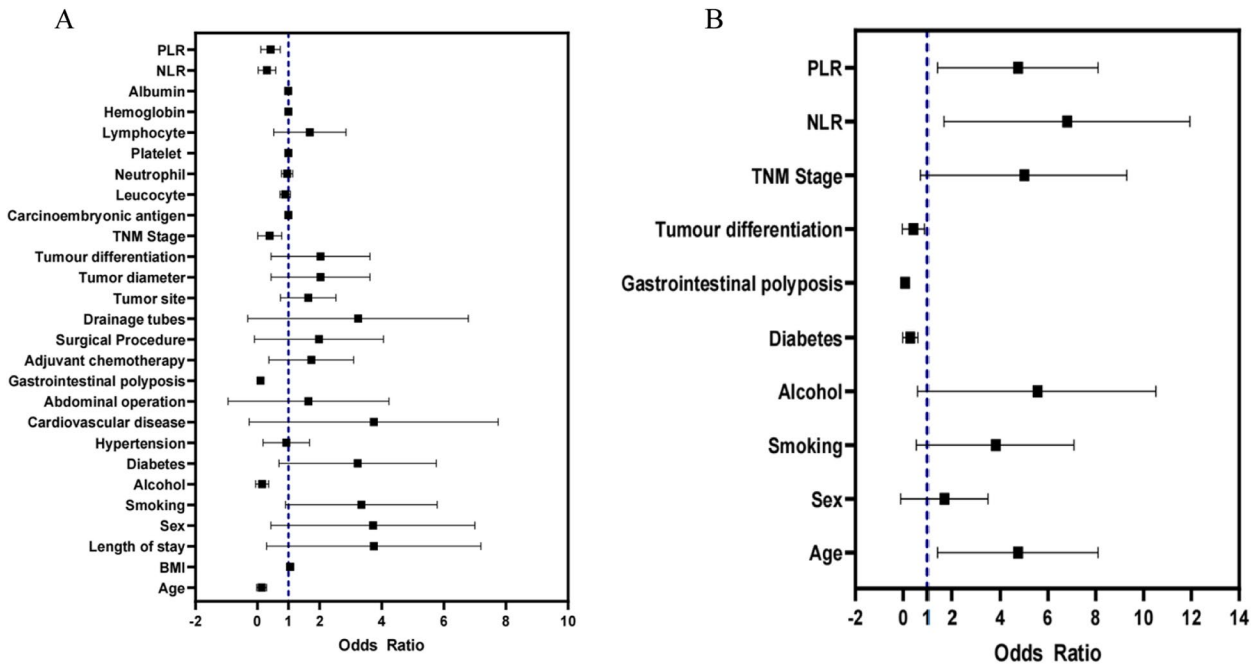

Fig. 11 Forest plot of univariate and multivariate Cox regression analysis of DFS in CAL patients are shown in **A** and **B**

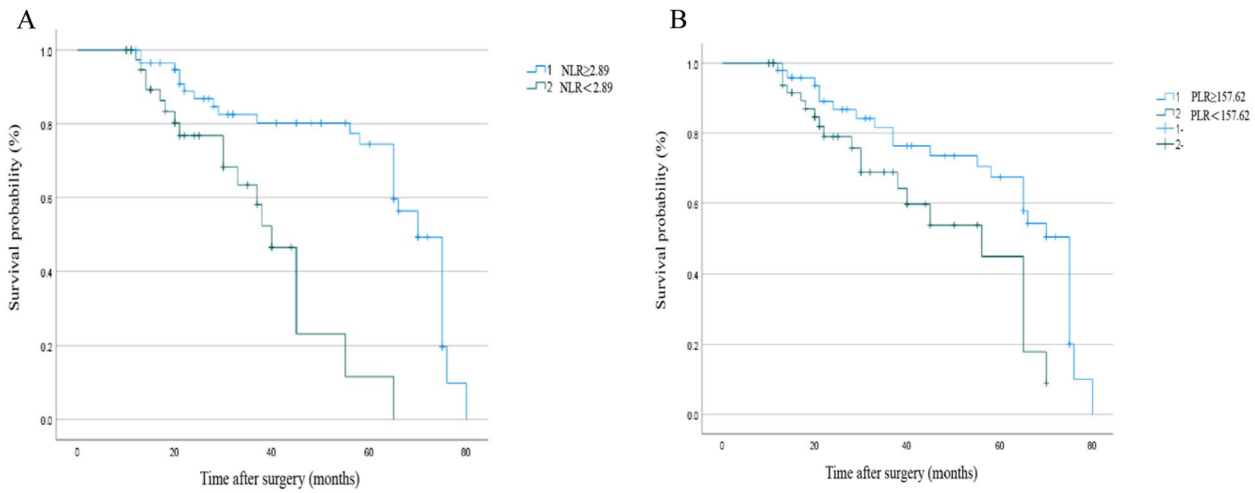

Fig. 12 Kaplan–Meier curves of preoperative NLR and PLR for OS in patients with CAL are shown in **A** and **B**

and preoperative PLR (AUC = 0.553, 95%CI: 0.511–0.594, $P = 0.012$) could predict CRC survival prognosis, with the optimal NLR cutoff value at 2.61 (sensitivity 50%, specificity 66%) and the optimal PLR cutoff value at 204.04 (sensitivity 28%, specificity 83%). Furthermore, CRC patients were categorized into two groups: OS with 267 cases (30%) and DFS with 178 cases (20%). They were also divided into high NLR (NLR ≥ 2.61), low NLR (NLR < 2.61), high PLR (PLR ≥ 204.04), and low PLR (PLR < 204.04) groups to evaluate the impact of these indicators on survival prognosis. Kaplan–Meier curves illustrated that OS and DFS were significantly higher in the low NLR and PLR groups compared to the high NLR and PLR groups, with statistical significance. Additionally, Cox regression analysis identified several independent risk factors for OS and DFS in CRC patients, including age ≥ 60, a history of diabetes, a history of intestinal polyps, open surgery, drainage tube placement during surgery, TNM stage, preoperative NLR, preoperative PLR, BMI, and length of hospital stay. A nomogram based on the Cox proportional hazards model was developed

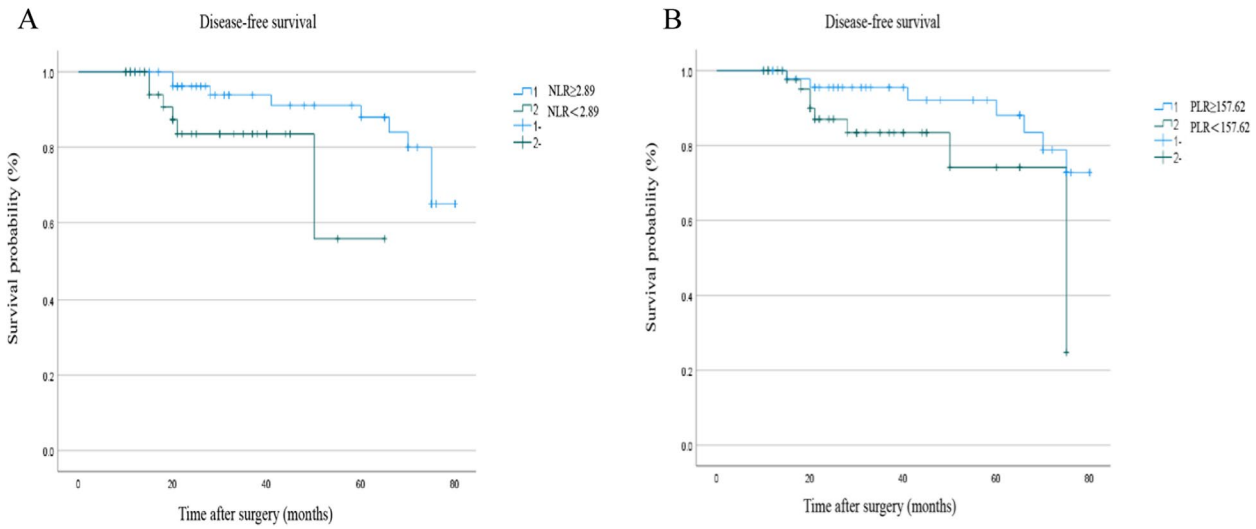

Fig. 13 Kaplan–Meier curves of preoperative NLR and PLR for DFS in patients with CAL are shown in **A** and **B**

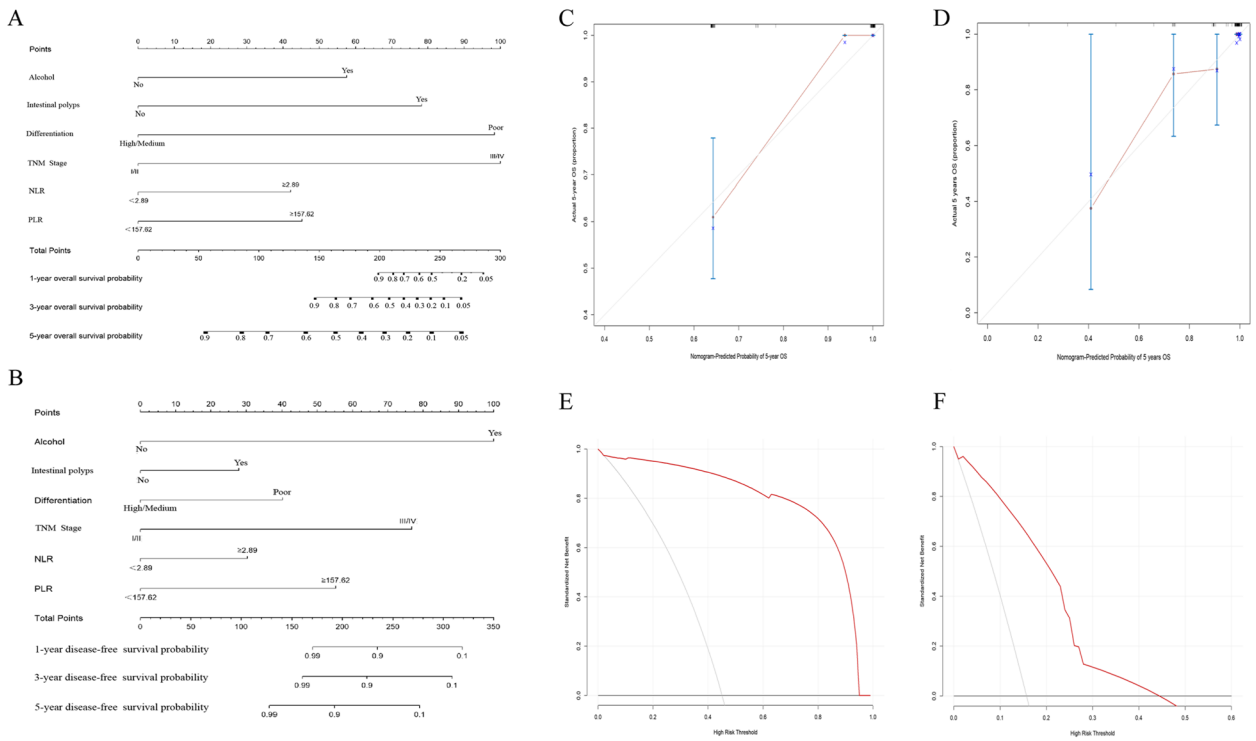

Fig. 14 Nomogram to predict the probability of OS (**A**) and DFS (**B**) after radical resection of CAL. This nomogram model was used to predict the calibration curves of OS (**C**) and DFS (**D**) at 5 years after radical resection of CAL. nomogram model for prediction of OS (**E**) and DFS (**F**) decision curves 5 years after radical resection of CAL

to visualize the impact of various factors on OS and DFS in CRC patients and to predict 1-, 3-, and 5-year survival rates post-surgery. The study demonstrated that preoperative NLR ≥ 2.61 and PLR ≥ 204.04 increased the risk of poor prognosis. Furthermore, the 5-year OS DCA and clinical impact curve of the nomogram confirmed its clinical utility, demonstrating high accuracy in predicting CRC prognosis.

This study has several limitations. Firstly, due to its retrospective nature, not all covariates that might have influenced the analyses were assessed, potentially resulting in unavoidable selection bias. Secondly, being a single-centre

study with a limited number of patients, missing information, and limited generalizability, the findings may lack broader applicability. Thirdly, the predictive role of preoperative NLR and PLR should be confirmed in larger clinical studies. Additionally, for a more effective prediction of AL patients' prognosis, preventive approaches should be investigated through interventional prospective studies, stratifying risks based on preoperative NLR and PLR values. Fourthly, further analysis of OS and DFS of CRC patients in the present study is warranted to understand differences in survival prognosis between CRC and CAL patients. Moreover, Further research is needed to confirm the correlation between preoperative NLR、PLR and other postoperative symptomatic AL. Lastly, the exclusion of key inflammatory markers such as CRP, IL-6, and calcitoninogen in our study requires further investigations to explore additional haematological markers or alternatives.

Conclusion

In summary, our study demonstrated that preoperative NLR and PLR can serve as prognostic indicators for long-term outcomes in CAL. NLR $\geq$ 2.89 and PLR $\geq$ 157.62 were significantly linked to a favorable long-term prognosis in patients with CAL.Furthermore, NLR and PLR also proved to be valuable in predicting A and survival prognosis after CRC. Preoperative NLR and PLR are cost-effective, convenient to obtain, and have high predictive value, which can accurately evaluate the risk and prognosis of AL after CRC operation, so as to guide clinicians to prevent high-risk patients, prolong survival time, and improve survival rate.

Clinical trial number

Not applicable.

Authors' contributions

All authors listed on the submission made significant contributions to the scientific work and, therefore, share responsibility for the results. Nuo Xu was responsible for data analysis, and paper writing; Jian-Xin Zhang was responsible for polishing the research content of the article and guiding the typesetting. Zhuo Huang , Lianchun Mao and Jia-Jie Zhang were responsible for data collection.Zhi-Yong Zhang and Weidong Jin were responsible for the conception and design.

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Data availability

The datasets generated and/or analyzed during the current study are not publicly available due to the closed management of patient information in military hospitals and at the same time, the data are not publically available as they are pseudonymised medical records. But are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The Authors reporting experiments on humans and/or the use of human tissue samples must confirm that all experiments were performed in accordance with relevant guidelines and regulations.The authors are responsible for all aspects of the work and ensure that any questions regarding the accuracy or integrity of any part are thoroughly investigated and addressed. As a retrospective study, the patients included complied with the requirements set by the Ethics Committee, and informed consent for the treatment was obtained from the patients, which was approved by the Ethics Committee of the General Hospital of the Central Theatre of War [(2023) Lun Audit Zi (092–01) No.]

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Wuhan University of Science and Technology, School of Medicine, Wuhan, Hubei 430081, China. [2]Chinese People's Liberation Army Central Theater General Hospital General Surgery Department, Wuhan, Hubei 4300770, China. [3]Department of Statistics and Applied Probability, University of California, Santa Barbara, CA 93106, USA.

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