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ORIGINAL RESEARCH

# Impact of Preoperative Neutrophil Percentage-to-Albumin Ratio (NPAR) on Short-Term Complications and Long-Term Prognosis in Patients Undergoing Robot-Assisted Laparoscopic Radical Surgery for Colorectal Cancer

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**Objective:** To assess the prognostic utility of the preoperative neutrophil percentage-to-albumin ratio (NPAR) for short-term complications and long-term survival in colorectal cancer patients receiving robot-assisted laparoscopic radical surgery.

**Methods:** This retrospective study included 230 patients with stage I–III colorectal cancer who underwent Da Vinci robot-assisted laparoscopic radical resection at the Department of Gastrointestinal Surgery, Second Xiangya Hospital of Central South University, between June 2016 and December 2024. Laboratory indicators were collected within 7 days prior to surgery, and NPAR was calculated. The optimal cutoff value of NPAR (14.75) was determined using restricted cubic spline (RCS) analysis and receiver operating characteristic (ROC) curve. Based on a cutoff value of 14.75, patients were categorized into high (≥14.75) and low (<14.75) NPAR groups. Multivariate logistic regression was employed to examine the relationship between NPAR levels and postoperative complications. Additionally, Kaplan–Meier survival analysis was conducted to evaluate its influence on overall survival (OS).

**Results:** A significant non-linear positive association was observed between NPAR and the risk of postoperative complications (P for non-linearity = 0.008). The high NPAR group exhibited a markedly higher incidence of complications (OR = 138.53, 95% CI: 12.79–1500.47, P < 0.001). Kaplan–Meier analysis demonstrated significantly reduced overall survival among patients with elevated NPAR (log-rank P = $6.2 \times 10^{-7}$). Furthermore, subgroup analyses confirmed the consistent predictive performance of NPAR across diverse clinical subsets.

**Conclusion:** Elevated preoperative NPAR significantly predicts higher risks of complications and poorer survival following robotic surgery for colorectal cancer. As a straightforward and clinically applicable biomarker, it shows great promise for preoperative risk stratification and outcome evaluation, supporting its broader adoption in clinical practice.

**Keywords:** Neutrophil Percentage-to-Albumin Ratio, NPAR, colorectal cancer, robotic surgery, postoperative complications, prognosis

## Introduction

Colorectal cancer ranks as the third most prevalent malignant tumor worldwide, with both its incidence and mortality rates showing a yearly increase.[1] Owing to rapid progress in minimally invasive surgical methods, robot-assisted laparoscopic procedures have emerged as a pivotal technique for performing radical resection of colorectal cancer. In contrast to traditional laparoscopic surgery, robotic-assisted operations provide benefits including high-definition three-dimensional vision, improved dexterity of surgical instruments, and greater operative accuracy. These characteristics

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contribute to diminished blood loss during surgery, reduced hospitalization periods, and a decreased rate of postsurgical complications.[2,3] Recent evidence suggests that, compared with other approaches, robotic surgery may attenuate postoperative inflammatory stress, thereby influencing systemic inflammatory responses and patient recovery. In recent years, the utilization of robotic systems in managing colorectal cancer has expanded quickly, establishing itself as a major trend shaping the advancement of colorectal surgical care.[4,5]

Notwithstanding the ongoing advancements in robotic surgical technology, substantial interindividual variations persist with respect to the incidence of short-term postoperative complications and long-term therapeutic outcomes. Accurate prognostic assessment is of paramount importance for the formulation of personalized therapeutic regimens and the improvement of patients' quality of life. Conventional prognostic evaluation approaches primarily rely on tumor-node-metastasis (TNM) staging and pathological subtypes;[6] however, these indicators often fail to adequately capture the comprehensive physiological status of patients.

Recent studies have highlighted the role of systemic inflammation and nutritional status as important factors affecting cancer prognosis.[7] Inflammation can promote tumor progression and metastasis by stimulating angiogenesis, suppressing immune surveillance, and altering the tumor microenvironment through cytokine dysregulation.[8] Neutrophils, as central mediators of inflammatory responses, serve as indicators of systemic inflammation when elevated.[9] Meanwhile, serum albumin levels reflect the nutritional state and hepatic synthetic function; hypoalbuminemia is commonly associated with malnutrition and poor prognosis.[10]

Numerous studies have explored systemic inflammation-nutrition biomarkers in colorectal cancer, including the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR).[11] While these indices can predict outcomes, they may inadequately capture the integrated dynamics of inflammation and nutrition. The neutrophil percentage-to-albumin ratio (NPAR) is an emerging biomarker that incorporates both inflammatory and nutritional dimensions. It is cost-effective and simple to calculate and has demonstrated significant prognostic value across various malignancies.[12,13] Recent studies have shown that elevated NPAR is significantly associated with poorer outcomes in patients with bladder cancer, breast cancer, and other solid tumors.[14–16]

Related indices, such as the neutrophil-to-albumin ratio (NAR), have shown comparable prognostic utility in colorectal cancer, linking elevated levels with increased postoperative complications and reduced survival.[17] In contrast, the neutrophil percentage-albumin ratio (NPAR) integrates both neutrophil percentage and albumin concentration, thereby capturing two core signals: shifts in inflammatory cell distribution and declines in nutritional-hepatic reserve. As a comprehensive assessment metric, NPAR may reflect the systemic inflammation-nutrition coupling more sensitively and stably, which in turn effectively enhances the predictive efficacy for both the risk of short-term complications and long-term therapeutic outcomes. A recent large-scale retrospective study further confirmed that elevated NPAR levels were independently associated with poorer progression-free survival and overall survival in colorectal cancer (CRC) patients who underwent surgical resection.[18]

However, despite recent evidence supporting NPAR's prognostic value in general colorectal cancer cohorts, there is a critical lack of data focusing on patients undergoing robot-assisted laparoscopic resection—a population with distinct perioperative inflammatory and nutritional dynamics. This study specifically investigates the impact of preoperative NPAR on short- and long-term outcomes in this surgical context. Our findings aim to provide a tailored prognostic tool for this increasingly prevalent surgical approach, supporting personalized clinical management.

# Materials and Methods

## Study Population

This retrospective analysis included patients who underwent robotic-assisted laparoscopic radical surgery for colorectal cancer using the Da Vinci platform in the Gastrointestinal Surgery Unit of the Second Xiangya Hospital, Central South University, between June 2016 and December 2024. All operations were conducted by an experienced colorectal surgical team skilled in robotic techniques. A total of 230 patients meeting the inclusion criteria were included in the final analysis. Data were retrieved from the hospital's electronic medical record system and independently verified by two investigators. This retrospective study utilized anonymized data from existing medical records and, in accordance with national regulations and institutional policies

for retrospective studies involving de-identified data. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Second Xiangya Hospital of Central South University.

### Inclusion Criteria

Patients were eligible for inclusion if they met the following criteria: 1) Age ≥18 years; 2) Postoperative pathological diagnosis confirmed primary colorectal adenocarcinoma; 3) Underwent elective robot-assisted laparoscopic radical resection (R0); 4) Stage I–III disease (according to TNM staging) without distant metastasis (M0) confirmed by preoperative imaging; 5) Availability of preoperative laboratory data (within 7 days) including neutrophil percentage and serum albumin levels; 6) Complete clinical, perioperative, pathological, and follow-up data; 7) Minimum follow-up duration of 6 months or until death.

### Exclusion Criteria

Patients were excluded if they met any of the following criteria: 1) Emergency surgery, palliative resection, or non-robotic surgical approach; 2) Presence of distant metastasis (stage IV) or other synchronous/metachronous malignancies; 3) Coexisting severe infections, autoimmune diseases, or hepatic dysfunction that may affect inflammatory or nutritional markers; 4) Received neoadjuvant chemoradiotherapy before surgery; 5) Diagnosis of hereditary colorectal cancer syndromes (eg, familial adenomatous polyposis or Lynch syndrome); 6) Missing critical variables (eg, neutrophil percentage, albumin, follow-up data); 7) Lost to follow-up or incomplete survival data.

## Data Collection and Variable Definitions

### Data Source and Collection

All relevant data were obtained from the Hospital Information System (HIS) of the Second Xiangya Hospital. Two trained researchers independently extracted and cross-verified information from inpatient medical records, laboratory reports, surgical notes, pathology findings, and follow-up documents. Patients with missing critical data were excluded to maintain data integrity and accuracy. The datasets used and analyzed during the present study are available from the corresponding author on reasonable request.

### Preoperative Laboratory Parameters and NPAR Calculation

Preoperative laboratory values were collected within 7 days prior to surgery to reflect baseline physiological and inflammatory status. Parameters included neutrophil percentage, white blood cell count, carbohydrate antigen 19–9 (CA19-9, U/mL), serum albumin (g/dL), and carcinoembryonic antigen (CEA, ng/mL). These biomarkers were measured according to standard clinical laboratory protocols (eg, CEA and CA19-9 per ASCO guidelines[19]). The neutrophil percentage-to-albumin ratio (NPAR) was computed as:

NPAR = Neutrophil Percentage /Serum Albumin (g/dL)

To establish the optimal predictive threshold for postoperative complications and long-term outcomes, restricted cubic spline (RCS) regression and the Youden index derived from receiver operating characteristic (ROC) analysis were employed. This method identified an optimal cutoff value of 14.75. Based on this threshold, patients were stratified into a high NPAR group (≥14.75) and a low NPAR group (<14.75).

### Demographic and Clinical Variables

Baseline demographic and clinical variables comprised age, sex, and body mass index (BMI, $kg/m^2$). Lifestyle factors including smoking and alcohol consumption were documented. Socioeconomic status was evaluated via educational attainment (high vs low) and marital status (married vs unmarried). The American Society of Anesthesiologists (ASA) classification (grades I–III) was applied to evaluate perioperative risk. Other comorbidities, including previous abdominal surgery, hypertension, diabetes, coronary artery disease, cerebral infarction, and other chronic diseases, were also recorded.All variables were incorporated as covariates in multivariate logistic regression models.

### Surgical and Pathological Characteristics

Surgical data were obtained from intraoperative and postoperative records. Surgical variables included tumor location (right colon, left colon, rectum), operative time (minutes), and estimated blood loss (mL). Perioperative recovery

indicators such as time to first flatus (days), time to resume normal diet (days), and postoperative hospital stay (days) were also documented. Pathological variables included tumor size ($cm^2$), histological differentiation (G1: well-differentiated, G2: moderately differentiated, G3: poorly differentiated), and TNM stage (based on the 8th edition AJCC guidelines[6]). The number of harvested lymph nodes and positive nodes were recorded to assess lymphatic involvement. T stage (T1–T4) and N stage (N0–N2) were included in the multivariate models as prognostic factors.

### Postoperative Recovery and Complication Assessment

Postoperative recovery data were obtained from daily progress notes and nursing records. Recovery indicators included time to first flatus, time to normal diet, and length of hospital stay. Pain severity was assessed using the visual analog scale (VAS) and analgesic usage and classified into mild (1–3 scores) and moderate pain levels (4–6 scores).[20]

Postoperative complications were defined and graded using the Clavien–Dindo classification system, with complications grade II or higher considered clinically significant.[21] Data was obtained from postoperative physician notes, hospitalization records, discharge summaries, and 30-day readmission records. Common complications included surgical site infection, bowel obstruction, anastomotic leakage, postoperative hemorrhage, urinary retention, pulmonary infection, and cardiovascular events. The primary short-term outcome of interest was the occurrence of grade II or higher postoperative complications.

### Survival Outcomes and Follow-up

Survival data were collected via standardized follow-up procedures. Follow-up began on the date of surgery and ended at the time of death or study endpoint (December 31, 2024). The primary long-term outcome was overall survival (OS), defined as the time from surgery to death from any cause (in months). Patients who remained alive were censored at the time of last follow-up. Follow-up methods included outpatient visits, hospital records review, and telephone interviews. All survival statuses were cross verified by two investigators.

In the survival analysis, survival time was used as the time variable and survival status (1 = death, 0 = censored) as the event variable. Kaplan–Meier survival curves were plotted, and Cox proportional hazards models were used for multivariate analysis. Based on the NPAR cutoff value (14.75), patients were grouped and compared to assess the prognostic value of preoperative inflammation and nutritional status. All data was managed using standardized Excel spreadsheets and analyzed with R software to ensure reproducibility and consistency.

## Statistical Analysis

All statistical analyses were conducted using SPSS software (version 26.0; IBM Corp., Armonk, NY) and the online platform Sangerbox (http://vip.sangerbox.com). Normally distributed continuous data are presented as mean ± standard deviation and compared with the independent-sample *t*-test, whereas non-normally distributed data are reported as median (interquartile range, IQR) and compared with the Mann–Whitney *U*-test. Categorical variables are expressed as number (percentage) and analyzed using the chi-square or Fisher's exact test, as appropriate. The Youden index derived from receiver operating characteristic (ROC) curve analysis, complemented by restricted cubic spline (RCS) modeling, was utilized to determine the optimal NPAR cutoff value for predicting clinical outcomes. Subsequently, multivariate logistic regression analysis was conducted to identify independent risk factors for postoperative complications, with findings reported as odds ratios (ORs) and corresponding 95% confidence intervals (CIs). Survival probabilities were estimated using the Kaplan–Meier method and compared with the Log rank test. For all analyses, a two-sided p-value below 0.05 indicated statistical significance.

# Results

## Baseline Characteristics

A total of 230 patients were included in this study and were divided into two groups based on the median preoperative neutrophil-to-albumin ratio (NPAR): the low NPAR group (n=115) and the high NPAR group (n=115). Statistically significant differences (P<0.05) were observed between the two groups in the following variables: age, gender, smoking history, alcohol use history, enhanced recovery after surgery (ERAS) application, surgery year, history of abdominal surgery, body mass index (BMI), and postoperative complications. No significant differences (P>0.05) were found

between the groups in preoperative carcinoembryonic antigen (CEA), preoperative carbohydrate antigen 199 (CA199), number of lymph nodes dissected, tumor size, American Society of Anesthesiologists (ASA) grade, tumor location, coronary heart disease, hypertension, diabetes, cerebral infarction, T stage, and N stage. (Table 1).

**Table 1** Baseline Characteristics

| Variables | Total (n = 230) | Low (n = 115) | High (n = 115) | Statistic | *P* |
|---|---|---|---|---|---|
| Age, n (%) | | | | $\chi^2$=8.50 | 0.004 |
| <65 | 164 (71.30) | 92 (80.00) | 72 (62.61) | | |
| ≥65 | 66 (28.70) | 23 (20.00) | 43 (37.39) | | |
| Gender, n (%) | | | | $\chi^2$=5.91 | 0.015 |
| Female | 90 (39.13) | 54 (46.96) | 36 (31.30) | | |
| Male | 140 (60.87) | 61 (53.04) | 79 (68.70) | | |
| Smoking History, n (%) | | | | $\chi^2$=23.33 | <.001 |
| No | 196 (85.22) | 111 (96.52) | 85 (73.91) | | |
| Yes | 34 (14.78) | 4 (3.48) | 30 (26.09) | | |
| Alcohol Use History, n (%) | | | | $\chi^2$=12.11 | <.001 |
| No | 190 (82.61) | 105 (91.30) | 85 (73.91) | | |
| Yes | 40 (17.39) | 10 (8.70) | 30 (26.09) | | |
| ERAS, n (%) | | | | $\chi^2$=8.50 | 0.004 |
| No | 66 (28.70) | 23 (20.00) | 43 (37.39) | | |
| Yes | 164 (71.30) | 92 (80.00) | 72 (62.61) | | |
| Surgery Year, n (%) | | | | $\chi^2$=163.34 | <.001 |
| 2016 | 24 (10.43) | 24 (20.87) | 0 (0.00) | | |
| 2017 | 22 (9.57) | 22 (19.13) | 0 (0.00) | | |
| 2018 | 34 (14.78) | 27 (23.48) | 7 (6.09) | | |
| 2019 | 34 (14.78) | 7 (6.09) | 27 (23.48) | | |
| 2020 | 20 (8.70) | 1 (0.87) | 19 (16.52) | | |
| 2021 | 31 (13.48) | 0 (0.00) | 31 (26.96) | | |
| 2022 | 31 (13.48) | 29 (25.22) | 2 (1.74) | | |
| 2023 | 23 (10.00) | 0 (0.00) | 23 (20.00) | | |
| 2024 | 11 (4.78) | 5 (4.35) | 6 (5.22) | | |
| ASA grade, n (%) | | | | $\chi^2$=2.05 | 0.359 |
| I | 58 (25.22) | 28 (24.35) | 30 (26.09) | | |
| II | 157 (68.26) | 82 (71.30) | 75 (65.22) | | |
| III | 15 (6.52) | 5 (4.35) | 10 (8.70) | | |
| History of Abdominal Surgery, n (%) | | | | $\chi^2$=5.71 | 0.017 |
| No | 188 (81.74) | 87 (75.65) | 101 (87.83) | | |
| Yes | 42 (18.26) | 28 (24.35) | 14 (12.17) | | |
| Location, n (%) | | | | $\chi^2$=5.55 | 0.062 |
| left colon | 72 (31.30) | 38 (33.04) | 34 (29.57) | | |
| Rectum | 132 (57.39) | 59 (51.30) | 73 (63.48) | | |
| Right colon | 26 (11.30) | 18 (15.65) | 8 (6.96) | | |

(*Continued*)


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**Table 1** (Continued).

| Variables | Total (n = 230) | Low (n = 115) | High (n = 115) | Statistic | *P* |
|---|---|---|---|---|---|
| Coronary Heart Disease, n (%) | | | | $\chi^2$=0.28 | 0.598 |
| No | 191 (83.04) | 94 (81.74) | 97 (84.35) | | |
| Yes | 39 (16.96) | 21 (18.26) | 18 (15.65) | | |
| Hypertension, n (%) | | | | $\chi^2$=1.31 | 0.252 |
| No | 160 (69.57) | 84 (73.04) | 76 (66.09) | | |
| Yes | 70 (30.43) | 31 (26.96) | 39 (33.91) | | |
| Diabetes, n (%) | | | | $\chi^2$=1.93 | 0.164 |
| No | 201 (87.39) | 104 (90.43) | 97 (84.35) | | |
| Yes | 29 (12.61) | 11 (9.57) | 18 (15.65) | | |
| Cerebral Infarction, n (%) | | | | $\chi^2$=0.16 | 0.687 |
| No | 202 (87.83) | 102 (88.70) | 100 (86.96) | | |
| Yes | 28 (12.17) | 13 (11.30) | 15 (13.04) | | |
| BMI, n (%) | | | | $\chi^2$=8.33 | 0.040 |
| Normal(18.5-24.9 kg/m²) | 151 (65.65) | 78 (67.83) | 73 (63.48) | | |
| Obese(≥30 kg/m²) | 11 (4.78) | 5 (4.35) | 6 (5.22) | | |
| Overweight(25-29.9 kg/m²) | 51 (22.17) | 29 (25.22) | 22 (19.13) | | |
| Underweight(<18.5 kg/m²) | 17 (7.39) | 3 (2.61) | 14 (12.17) | | |
| T Stage, n (%) | | | | $\chi^2$=1.64 | 0.651 |
| T 1 | 45 (19.57) | 23 (20.00) | 22 (19.13) | | |
| T 2 | 107 (46.52) | 54 (46.96) | 53 (46.09) | | |
| T 3 | 50 (21.74) | 27 (23.48) | 23 (20.00) | | |
| T 4 | 28 (12.17) | 11 (9.57) | 17 (14.78) | | |
| N Stage, n (%) | | | | $\chi^2$=1.99 | 0.369 |
| N 0 | 129 (56.09) | 61 (53.04) | 68 (59.13) | | |
| N1 | 53 (23.04) | 31 (26.96) | 22 (19.13) | | |
| N2 | 48 (20.87) | 23 (20.00) | 25 (21.74) | | |
| Complications, n (%) | | | | $\chi^2$=49.65 | <.001 |
| No | 177 (76.96) | 111 (96.52) | 66 (57.39) | | |
| Yes | 53 (23.04) | 4 (3.48) | 49 (42.61) | | |
| Preoperative CEA, Mean ± SD | 5.27 ± 12.29 | 4.82 ± 13.38 | 5.73 ± 11.15 | t=-0.56 | 0.577 |
| Preoperative CA199, Mean ± SD | 17.08 ± 25.98 | 15.46 ± 27.76 | 18.70 ± 24.07 | t=-0.95 | 0.345 |
| Number of Lymph Nodes Dissected, Mean ± SD | 15.87 ± 5.62 | 16.10 ± 6.21 | 15.63 ± 4.98 | t=0.64 | 0.520 |
| Tumor Size (cm²), Mean ± SD | 7.65 ± 21.78 | 9.95 ± 29.37 | 5.35 ± 8.93 | t=1.61 | 0.109 |

**Notes**: t: t-test; $\chi^2$: Chi-square test; -: Fisher's exact test; SD: standard deviation

## Nonlinear Relationship and Discriminative Performance of NPAR for Postoperative Complications

To further examine the relationship between NPAR and postoperative complications, a Restricted Cubic Spline (RCS) regression model was applied. As illustrated in Figure 1A, a significant nonlinear correlation was identified between NPAR and complication risk (P for nonlinearity = 0.008), with an overall statistically significant association (P for overall < 0.001). The spline curve indicated that complication risk began to rise progressively once NPAR exceeded

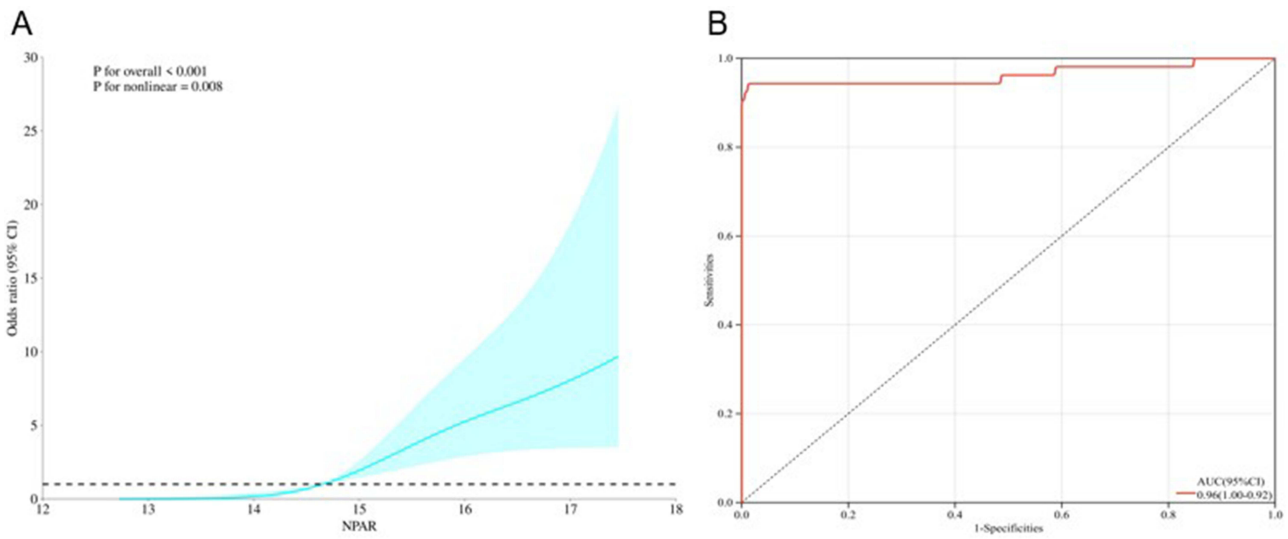


**Figure 1** (**A**) Restricted cubic spline (RCS) regression curve illustrating the nonlinear association between the neutrophil percentage-to-albumin ratio (NPAR) and the risk of postoperative complications; (**B**) Receiver operating characteristic (ROC) curve for NPAR predicting postoperative complications.

14.75, with the rate of increase accelerating at higher NPAR values. This supports the potential role of NPAR as a sensitive predictor for postoperative complications and confirms the clinical relevance of the optimal threshold (14.75) for risk stratification, as further supported by ROC analysis (Figure 1B; AUC = 0.9634, sensitivity = 92%, specificity = 99% at the cutoff of 14.75).

## Multivariate Logistic Regression Analysis of NPAR Stratification and Risk of Postoperative Complications

Using the optimal cutoff value of 14.75 derived from the RCS curve, patients were categorized into high- and low-NPAR groups. To examine the association between NPAR and complications, four multivariate logistic regression models were constructed (Table 2). In the unadjusted Model 1, the high-NPAR group exhibited a significantly elevated risk of complications (OR = 12.42, 95% CI: 5.65–27.31, P < 0.001). After adjusting for baseline factors—including sex, smoking, alcohol use, pathological type, T and N stage, age, BMI, preoperative CEA, CA19-9, and tumor size—Model 2 continued to show a significant association (OR = 9.56, 95% CI: 3.76–24.28, P < 0.001). Model 3 incorporated additional clinical covariates such as ASA score, history of abdominal surgery, tumor location, coronary artery disease, hypertension, diabetes, cerebral infarction, and other comorbidities. High NPAR remained significantly associated with complication risk (OR = 23.75, 95% CI: 6.60–85.51, P < 0.001). In the fully adjusted Model 4, which further included perioperative variables—preoperative

**Table 2** Multivariate Logistic Regression Analysis of the Association Between NPAR Stratification (Cutoff Value: 14.75) and Risk of Postoperative Complications

| Variables | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | *P* | OR (95% CI) | *P* | OR (95% CI) | *P* | OR (95% CI) | *P* |
| Low NPAR | 1.00 (Reference) | | 1.00 (Reference) | | 1.00 (Reference) | | 1.00 (Reference) | |
| High NPAR | 12.42 (5.65–27.31) | <0.001 | 9.56 (3.76–24.28) | <0.001 | 23.75 (6.60–85.51) | <0.001 | 138.53 (12.79–1500.47) | <0.001 |

**Notes**: Model 1: Crude. Model 2: Adjust: Gender, Smoking History, Alcohol Use History, Pathological Type, T Stage, N Stage, Age, BMI, Preoperative CEA, Preoperative CA199, Tumor Size. Model 3: Adjust: Gender, Smoking History, Alcohol Use History, ASA grade, History of Abdominal Surgery, Tumor Location, Coronary Heart Disease, Hypertension, Diabetes, Cerebral Infarction, Other Comorbidities, Pathological Type, T Stage, N Stage, Age, BMI, Preoperative CEA, Preoperative CA199, Tumor Size. Model 4: Adjust: Gender, Smoking History, Alcohol Use History, ASA grade, History of Abdominal Surgery, Tumor Location, Coronary Heart Disease, Hypertension, Diabetes, Cerebral Infarction, Other Comorbidities, Preoperative Chemoradiotherapy, Pathological Type, Postoperative Pain Status, Postoperative Pain Medication, T Stage, N Stage, Age, BMI, Preoperative CEA, Preoperative CA199, Number of Lymph Nodes Dissected, Positive Lymph Nodes, Surgery Duration, Intraoperative Blood Loss, First Normal Meal, Tumor Size.
**Abbreviations**: OR: Odds Ratio, CI: Confidence Interval.


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chemoradiotherapy, postoperative pain status, analgesic use, lymph node status, operative duration, intraoperative blood loss, and time to oral intake—high NPAR persisted as a strong independent risk factor (OR = 138.53, 95% CI: 12.79–1500.47, P < 0.001). These results indicate that preoperative NPAR is a robust and independent predictor of postoperative complications, supporting its utility in preoperative risk assessment and clinical decision-making.

## Subgroup Analysis of NPAR Stratification and Postoperative Complication Risk

To evaluate the consistency of NPAR's predictive value across clinical subgroups, a subgroup analysis was performed (Table 3). Overall, patients in the high-NPAR group had a significantly higher risk of complications than those in the

**Table 3** Presents the Results of the Subgroup Analysis Based on NPAR Levels and Postoperative Complication Risk

| Variables | n (%) | Low | High | OR (95% CI) | *P* | *P* for Interaction |
|---|---|---|---|---|---|---|
| All patients | 230 (100.00) | 9/136 | 44/94 | 12.42 (5.65–27.31) | <0.001 | |
| Age | | | | | | 0.248 |
| <65 | 164 (71.30) | 6/109 | 27/55 | 16.55 (6.22–44.03) | <0.001 | |
| ≥65 | 66 (28.70) | 3/27 | 17/39 | 6.18 (1.59–24.01) | 0.009 | |
| Gender | | | | | | 0.255 |
| Female | 90 (39.13) | 1/60 | 11/30 | 34.16 (4.14–282.03) | 0.001 | |
| Male | 140 (60.87) | 8/76 | 33/64 | 9.05 (3.75–21.85) | <0.001 | |
| Smoking History | | | | | | 0.514 |
| No | 196 (85.22) | 7/130 | 24/66 | 10.04 (4.03–24.99) | <0.001 | |
| Yes | 34 (14.78) | 2/6 | 20/28 | 5.00 (0.76–32.93) | 0.094 | |
| Alcohol Use History | | | | | | 0.872 |
| No | 190 (82.61) | 6/121 | 25/69 | 10.89 (4.19–28.34) | <0.001 | |
| Yes | 40 (17.39) | 3/15 | 19/25 | 12.67 (2.65–60.46) | 0.001 | |
| ASA grade | | | | | | 0.588 |
| I | 58 (25.22) | 1/32 | 13/26 | 31.00 (3.67–262.05) | 0.002 | |
| II | 157 (68.26) | 4/97 | 24/60 | 15.50 (5.03–47.79) | <0.001 | |
| III | 15 (6.52) | 4/7 | 7/8 | 5.25 (0.40–68.95) | 0.207 | |
| Tumor Location | | | | | | 0.826 |
| Left Colon | 72 (31.30) | 3/48 | 10/24 | 10.71 (2.58–44.45) | 0.001 | |
| Rectum | 132 (57.39) | 4/70 | 28/62 | 13.59 (4.41–41.91) | <0.001 | |
| Right colon | 26 (11.30) | 2/18 | 6/8 | 24.00 (2.73–210.82) | 0.004 | |
| Hypertension | | | | | | 0.020 |
| No | 160 (69.57) | 3/101 | 28/59 | 29.51 (8.39–103.74) | <0.001 | |
| Yes | 70 (30.43) | 6/35 | 16/35 | 4.07 (1.35–12.25) | 0.013 | |
| Diabetes | | | | | | 0.139 |
| No | 201 (87.39) | 4/122 | 33/79 | 21.16 (7.10–63.08) | <0.001 | |
| Yes | 29 (12.61) | 5/14 | 11/15 | 4.95 (1.02–24.10) | 0.048 | |
| Cerebral Infarction | | | | | | 0.442 |
| No | 202 (87.83) | 7/123 | 36/79 | 13.87 (5.74–33.52) | <0.001 | |
| Yes | 28 (12.17) | 2/13 | 8/15 | 6.29 (1.02–38.65) | 0.047 | |
| Other Comorbidities | | | | | | 0.402 |
| No | 197 (85.65) | 6/113 | 39/84 | 15.46 (6.11–39.07) | <0.001 | |
| Yes | 33 (14.35) | 3/23 | 5/10 | 6.67 (1.18–37.78) | 0.032 | |
| Preoperative Chemoradiotherapy | | | | | | 0.322 |
| No | 213 (92.61) | 8/126 | 38/87 | 11.44 (4.98–26.29) | <0.001 | |
| Yes | 17 (7.39) | 1/10 | 6/7 | 54.00 (2.80–1039.92) | 0.008 | |
| Pathological Type | | | | | | 0.071 |
| G1 | 28 (12.17) | 2/17 | 5/11 | 6.25 (0.94–41.52) | 0.058 | |
| G2 | 163 (70.87) | 7/96 | 29/67 | 9.70 (3.91–24.07) | <0.001 | |
| G3 | 39 (16.96) | 0/23 | 10/16 | 14.54 (2.00–7.89) | 0.995 | |

**Abbreviations**: OR, Odds Ratio; CI, Confidence Interval.

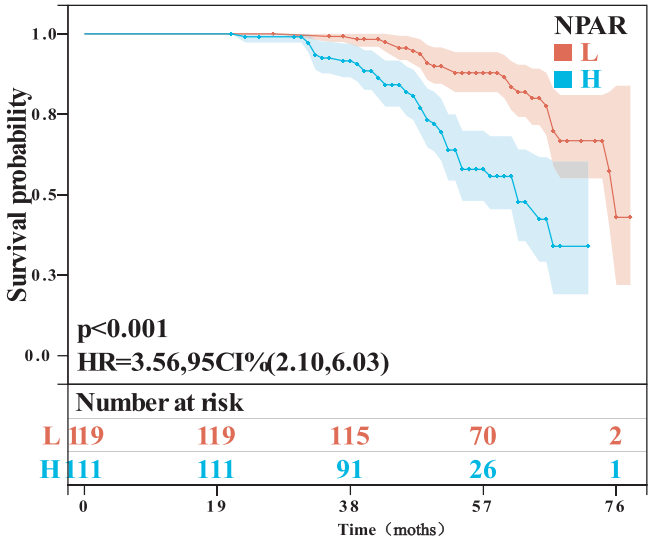


**Figure 2** Kaplan-Meier survival curves stratified by high and low NPAR groups.

low-NPAR group (OR = 12.42, 95% CI: 5.65–27.31, P < 0.001). Stratified analyses revealed that elevated NPAR was associated with significantly increased complication risk in most subgroups, with no significant interactions observed (P for interaction > 0.05), supporting the stability of this association across populations.

In gender-based subgroups, both females (OR = 34.16, P = 0.001) and males (OR = 9.05, P < 0.001) showed significant associations. In age subgroups, the OR was 16.55 for patients under 65 years and 6.18 for those 65 or older, with no significant interaction (P interaction = 0.248). Notably, a significant interaction was observed based on hypertension status (P interaction = 0.020), with a more pronounced risk increase in non-hypertensive patients (OR = 29.51) compared to hypertensive patients (OR = 4.07). In other subgroups—including smoking, alcohol use, diabetes, cerebral infarction, tumor location, pathological type, and ASA classification—the high-NPAR group consistently showed higher complication risk (all P < 0.05), with no significant interactions, further supporting NPAR as a broadly applicable predictor.

## Survival Analysis of Patients Stratified by NPAR

Based on Kaplan-Meier analysis, the high-NPAR group exhibited significantly reduced overall survival relative to the low-NPAR group (Figure 2). The Log rank test revealed a statistically significant disparity ($P = 6.2 \times 10^{-7}$). Cox regression analysis revealed that the high-NPAR group had a 3.56-fold increased risk of death compared to the low-NPAR group (HR = 3.56, 95% CI: 2.10–6.03). Throughout the follow-up period, survival probability declined more rapidly in the high-NPAR group, suggesting that elevated NPAR is an independent risk factor for poor postoperative prognosis.

# Discussion

With the rapid advancement of surgical techniques, robot-assisted laparoscopic surgery (RALC) has become increasingly prevalent in the treatment of colorectal cancer. Compared to traditional open surgery and standard laparoscopic techniques, robotic surgery offers high-definition three-dimensional visualization, precise manipulation with robotic arms, and more flexible control of the operative field. These advantages have been shown to reduce intraoperative trauma, postoperative pain, and accelerate recovery.[5] However, despite continuous technological improvements, the incidence of postoperative complications remains high, significantly affecting patient prognosis and the allocation of medical resources. Against this backdrop, the importance of preoperative risk assessment tools has become increasingly prominent. Traditional risk assessments mainly rely on clinical history, imaging examinations, and basic laboratory


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indicators, but their predictive value for short-term postoperative complications and long-term survival outcomes is limited.[22] In recent years, researchers have begun to focus on the potential of systemic inflammatory and nutritional markers in tumor prognosis, especially single inflammatory indicators such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR).[23]

Amid this trend, the neutrophil percentage-to-albumin ratio (NPAR)—a composite index integrating both inflammation and nutritional status—has drawn growing interest owing to its simplicity and low cost. Previous studies have shown that NPAR holds predictive value for postoperative infections, recurrence, and survival in several solid tumors.[15] Emerging findings have further extended this observation to a broader spectrum of solid malignancies: elevated NPAR remains a notable indicator of a worse survival prognosis.[14–16] However, a critical research gap remains studies on NPAR specifically in patients undergoing robot-assisted laparoscopic resection are extremely limited. It is well established that the minimally invasive nature of this surgical approach modulates perioperative inflammatory responses (eg, reducing the peak of inflammatory reactions and accelerating inflammatory resolution), and this characteristic may alter the predictive efficacy of inflammation-nutrition indices such as NPAR. Therefore, by investigating the prognostic value of NPAR in this specific surgical context, the present study further extends previous research insights.

This retrospective analysis included 230 patients receiving robot-assisted radical laparoscopic resection for colorectal cancer, representing the first systematic evaluation of the association between preoperative NPAR, postoperative complications, and long-term survival. The results revealed a significant nonlinear relationship between NPAR and complication risk, with a threshold value of 14.75 identified through RCS and confirmed by ROC analysis (AUC = 0.9634; sensitivity = 92%, specificity = 99%). Beyond this threshold, complication rates rose sharply. Multivariate logistic regression further established NPAR as an independent risk factor for postoperative morbidity. Additionally, survival analyses demonstrated that patients with elevated NPAR had significantly worse overall survival, with a 3.56-fold increase in mortality risk compared to those with lower NPAR.

As a composite marker integrating inflammatory and nutritional dimensions, NPAR has been increasingly studied across multiple cancer types. Elevated neutrophil levels indicate a chronic pro-tumor inflammatory state, promoting angiogenesis, tumor invasion, and an immunosuppressive microenvironment.[24–26] Unlike absolute neutrophil counts, neutrophil percentage reflects relative inflammatory burden, minimizing the influence of total leukocyte variability. Serum albumin, by contrast, reflects both nutritional status and systemic inflammatory load; hypoalbuminemia is associated with impaired immunity, delayed recovery, and increased risk of complications.[15] By combining these elements, NPAR offers a more comprehensive view of baseline patient status. Our analysis confirmed that even after extensive adjustment for confounders, NPAR remained a robust and independent predictor of complications and survival, underscoring its clinical reliability.

Mechanistically, NPAR reflects the synergistic amplification of systemic inflammation and malnutrition. Neutrophils release inflammatory mediators, promote coagulation and vascular permeability, and generate neutrophil extracellular traps (NETs) that exacerbate tissue injury and immune evasion.[27,28] Hypoalbuminemia further impairs collagen synthesis, drug and cytokine transport, and antioxidant buffering, weakening tissue repair and barrier function.[29] Multi-omics studies increasingly link systemic inflammation and malnutrition to tumor–immune microenvironment imbalance, characterized by altered cytokine profiles, T-cell exhaustion, and metabolic reprogramming of tumor and immune cells.[30,31] Transcriptomic and single-cell analyses have begun to implicate states of high inflammation and low nutrition in poor long-term patient outcomes; however, the underlying molecular mechanisms remain elusive. Burgeoning research in epigenetics and tumor immunology now reveals that systemic inflammatory and nutritional status can critically influence tumor progression by modulating miRNA networks, dysregulating key signaling pathways such as NF-κB and STAT3, and altering immune cell functions, including macrophage polarization.[32–34] Additionally, inflammation and malnutrition may weaken mucosal barrier function, predisposing to enteric infections that amplify inflammatory cascades via antimicrobial peptide release, macrophage activation.[35] Therefore, the NPAR can serve as a surrogate marker of preoperative immune-inflammatory and nutritional status in colorectal cancer patients. An elevated NPAR may signify a dysregulated tumor immune microenvironment, ultimately impacting both short-term postoperative complications and long-term survival following robot-assisted laparoscopic radical resection. Utilizing multi-omics technologies to

delineate the key targets and pathways governing the colorectal cancer immune microenvironment and nutrient metabolism will provide a foundation for clinical prognosis assessment and the development of targeted interventions.[36–38]

In comparison to previously established inflammatory markers such as Neutrophil to lymphocyte ratio (NLR), Prognostic Nutritional Index (PNI),[39,40] NPAR demonstrated superior predictive accuracy in our cohort. Compared with NLR (focused on inflammation) or PNI (emphasizing nutrition), NPAR integrates both dimensions and in recent study has shown higher AUC values for predicting colorectal cancer survival.[18] In the robotic surgery context, however, head-to-head comparative studies remain warranted. Our findings extend the applicability of NPAR to robotic colorectal surgery, supporting its broader relevance. Moreover, relative to other composite indices such as the C-reactive protein-to-albumin ratio (CAR) or PNI, NPAR requires fewer parameters, is easier to calculate, and shows strong potential for routine clinical use.[41,42]

Robotic surgery is increasingly employed in radical resections for colorectal cancer owing to its precision, minimally invasive nature, and superior visualization.[43] Despite these technical advantages, postoperative complications remain a key factor that hinders patient recovery and impacts long-term survival. Notably, patients with elevated baseline NPAR exhibit increased perioperative risk, a phenomenon that may stem from the synergistic effects of preoperatively existing inflammation and malnutrition. Our study findings further confirm that NPAR retains effective predictive value for both postoperative complications and mortality risk, even in the context of robotic surgery. This underscores the important role of preoperative NPAR assessment in such patient cohorts, as it holds significant implications for clinical decision-making amid the continuous advancement of surgical techniques. An elevated NPAR can inform both preoperative interventions and perioperative monitoring. Risk stratification based on NPAR thresholds could aid in formulating risk-adapted care plans. When integrated with dynamic network biomarker approaches,[44] it holds the potential to identify critical transition points for timely intervention, ultimately paving the way for personalized management of patients undergoing robotic colorectal cancer surgery.

Subgroup analysis indicated that NPAR was an independent risk factor for complications across most clinical strata, with its predictive ability particularly pronounced in females and patients without hypertension. Although some subgroups showed interactions, such as hypertension interfering with the predictive effect of NPAR, the overall trend remained consistent, supporting its broad applicability as a preoperative risk assessment tool. This finding has important implications for precise preoperative evaluation and the development of individualized treatment strategies. Furthermore, our study demonstrated that high-NPAR patients experienced significantly shorter overall survival, underscoring that preoperative inflammation and malnutrition not only affect short-term recovery but also have profound effects on long-term tumor control and survival, consistent with prior studies.[15,18]

Given its simplicity, affordability, and ease of implementation, NPAR represents a practical adjunct to standard preoperative evaluation. It may assist clinicians in identifying high-risk individuals, optimizing prehabilitation strategies, and tailoring perioperative care. For patients with elevated NPAR, interventions such as nutritional supplementation, anti-inflammatory measures, and intensified monitoring should be considered. In selected cases, surgical timing or approach may be adapted to reduce risks, and dynamic perioperative monitoring of NPAR may identify actionable inflection points for intervention.

This single-center retrospective design may introduce selection bias and limit generalizability; future multicenter prospective studies are recommended. With 230 patients and 53 complications, power for subgroup analyses is limited, post-hoc power analysis (using G Power) indicates 80% power for detecting OR>2 at $\alpha$=0.05, but larger samples could enhance reliability for rare subgroups. Expanded samples could refine cutoff values or interactions. Although multivariate adjustments were applied, unmeasured confounders may persist. The follow-up duration was relatively short, and some patients had not reached final survival endpoints. Additionally, NPAR was assessed only preoperatively; dynamic monitoring of postoperative changes in NPAR may provide further prognostic insight. Integrating NPAR with other biomarkers such as circulating tumor DNA (ctDNA) or imaging markers may further enhance prognostic accuracy and should be explored in future research.

## Conclusion

In summary, preoperative NPAR is a stable predictor of short-term postoperative complications and long-term survival outcomes following robot-assisted laparoscopic radical resection for colorectal cancer. It demonstrates a significant nonlinear relationship with complications and maintains good predictive performance after multivariable adjustment and in subgroup analyses. NPAR can be incorporated into routine preoperative assessment to assist in perioperative

management and individualized treatment optimization. Future multicenter, prospective studies are needed to validate these findings and explore the prognostic significance of dynamic changes in NPAR.

## Data Sharing Statement

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

## Author Contributions

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

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## Disclosure

The authors declare that there are no competing interests.

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