Article

Discovery Medicine 2026; 38(207): 1092–1102
https://doi.org/10.24976/Discov.Med.202638207.88

Preoperative NPAR-based Nomogram Models for Predicting Lymph Node Metastasis and Postoperative Gastrointestinal Function Recovery in Colorectal Cancer

Chaoqian Wang[1], Zhiang Li[1], Zhang Du[1,*]

[1]Department of Anorectal Surgery, Dongyang People's Hospital, 322100 Dongyang, Zhejiang, China
*Correspondence: dzhang0131@163.com (Zhang Du)
Submitted: 31 January 2026 Revised: 20 March 2026 Accepted: 7 April 2026 Published: 20 April 2026

Background: Colorectal cancer (CRC) is a leading cause of cancer-related mortality, and the occurrence of lymph node metastasis (LNM) and postoperative gastrointestinal dysfunction (POGD) significantly dictates long-term survival and quality of life. Accurate preoperative risk assessment is crucial for optimizing surgical planning and perioperative management. This study aimed to evaluate the predictive value of preoperative inflammation-nutrition indicators for LNM and POGD in CRC, and to construct nomogram prediction models.

Methods: A retrospective analysis was conducted on the data from 200 CRC patients who underwent radical surgery. Multiple preoperative inflammation-nutrition indicators were collected. Logistic regression was used to screen for independent predictors of LNM and POGD, and nomogram models were constructed accordingly. Multicollinearity was assessed using variance inflation factors (VIFs), and the linearity-in-the-logit assumption for continuous predictors was evaluated using the Box-Tidwell test. Discrimination was evaluated using receiver operating characteristic (ROC) curves and the area under the curve (AUC). Model calibration, internal validation via Bootstrap resampling (1000 iterations), and clinical net benefit were assessed using calibration curves and decision curve analysis (DCA).

Results: The incidence rates of LNM and POGD were 39.0% and 32.0%, respectively. The independent predictors for LNM were neutrophil percentage-to-albumin ratio (NPAR) (per 1-unit increase; OR = 1.24, 95% CI 1.08–1.42), cT3–4 stage (OR = 3.20, 95% CI 1.62–6.33), history of smoking (OR = 3.11, 95% CI 1.50–6.46), and fibrinogen-to-albumin ratio (FAR) (per 1-unit increase; OR = 1.22, 95% CI 1.03–1.45). The independent predictors for POGD were NPAR (per 1-unit increase; OR = 1.21, 95% CI 1.08–1.35), open surgery (OR = 2.60, 95% CI 1.14–5.93), advanced age (per 1-year increase; OR = 1.09, 95% CI 1.04–1.13), and prolonged operative time (per 1-min increase; OR = 1.04, 95% CI 1.02–1.06). The AUC of the LNM predictive model was 0.80 (95% CI 0.74–0.87), and the adjusted AUC after internal validation using Bootstrap was 0.78 (95% CI 0.69–0.87); The AUC of the POGD prediction model was 0.80 (95% CI 0.73–0.87), and the adjusted AUC was 0.77 (95% CI 0.66–0.87). DCA indicated that it has a certain clinical net benefit.

Conclusion: The NPAR-based nomogram model shows promising predictive performance, and preoperative NPAR may serve as a key indicator for predicting LNM and POGD in CRC patients.

Keywords: colorectal cancer; lymph node metastasis; postoperative gastrointestinal function recovery; neutrophil percentage-to-albumin ratio; nomogram

Introduction

Colorectal cancer (CRC) ranks among the most prevalent gastrointestinal malignancies worldwide. According to GLOBOCAN 2022 statistics, approximately 1.92 million new CRC cases and 903,859 deaths were recorded globally, reflecting a significant disease burden [1]. Lymph node metastasis (LNM), as the primary metastatic pathway of CRC, is a core factor determining patient staging and long-term prognosis [2]. A previous study showed that CRC patients with lymph node metastasis have significantly worse survival outcomes than those without lymph node metastasis [3]. Therefore, precise preoperative risk assessment of lymph node metastasis is crucial for developing individualized surgical plans and perioperative management strategies.

Postoperative gastrointestinal dysfunction (POGD) is also a significant factor influencing hospital stay and perioperative outcomes [4,5]. Radical colorectal cancer surgery involves tissue dissection and bowel manipulation; the associated surgical trauma and stress response can trigger neuroinflammation, impair the intestinal barrier, and suppress gastrointestinal motility, thereby leading to delayed postoperative gastrointestinal recovery or even postoperative ileus, which in turn prolongs hospital stay and increases the risk of related complications [4,6,7]. Therefore, accu-

rately identifying patients at high risk of LNM while simultaneously predicting the risk of postoperative delayed gastrointestinal recovery is of great significance for developing and optimizing individualized enhanced recovery after surgery (ERAS) strategies.

From a pathophysiological perspective, systemic inflammatory response and nutritional imbalance are the common underlying mechanisms contributing to both the occurrence of LNM and delayed postoperative gastrointestinal recovery [8]. In this context, compared to the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR)—which only reflect inflammatory states without providing nutritional reserve information—the neutrophil percentage-to-albumin ratio (NPAR) offers a more comprehensive assessment of both immune burden and nutritional status. Furthermore, it has demonstrated strong predictive value for prognosis across various solid tumors [9,10]. Inflammation- and nutrition-related indicators were previously mainly used for long-term prognosis in CRC; NPAR, as a relatively new composite indicator, still has limited evidence for preoperative LNM stratification and postoperative prediction of gastrointestinal recovery [11,12]. Accordingly, we retrospectively evaluated the associations of preoperative NPAR and other inflammation–nutrition indices with LNM and POGD in colorectal cancer, and developed a visual prediction model for preoperative risk stratification.

Methods

Study Population

This study is a retrospective cohort study. Consecutive patients with CRC who underwent radical resection at the Dongyang People's Hospital between January 2021 and December 2021 were screened and included according to the predefined eligibility criteria: (1) Postoperative histopathological confirmation of primary colorectal adenocarcinoma; (2) Underwent radical colorectal resection with standard lymph node dissection; (3) Complete laboratory test data, including a complete blood count and serum biochemistry, obtained within one week prior to surgery; (4) Complete postoperative follow-up records and gastrointestinal function recovery records. Exclusion criteria were: (1) Received preoperative neoadjuvant chemoradiotherapy, immunotherapy, or other anti-tumor treatments; (2) Combined with other malignancies or hematological diseases; (3) Preoperative existence of acute infection, chronic inflammatory diseases, or autoimmune diseases; (4) Distant metastasis found intraoperatively or underwent palliative surgery; (5) Underwent emergency surgery (e.g., due to bowel obstruction, perforation, or hemorrhage); (6) Missing clinical pathological data or follow-up data; (7) Transferred-in patients referred from other hospitals during the index admission; (8) Preoperative length of hospital stay >7 days (from admission to surgery); (9) According to the National Comprehensive Cancer Network (NCCN) guidelines, fewer than 12 examined lymph nodes.

Data Collection and Definition of Variables

Patient clinical data were collected by reviewing the electronic medical record system. Demographic and clinical characteristics included age, gender, body mass index (BMI), history of smoking, history of drinking, and comorbidities (hypertension, diabetes, and coronary heart disease). Oncological characteristics included tumor location (colon/rectum), maximum tumor diameter, and clinical T stage (cT). Surgery-related indicators included surgical approach (laparoscopic/open), operative time, intraoperative blood loss, and presence of stoma. Inflammation and nutrition indicators: Results of the last fasting venous blood test before surgery were collected, including neutrophil count (NEU), neutrophil percentage (NEU%), lymphocyte count (LYM), monocyte count (MON), platelet count (PLT), albumin (ALB), C-reactive protein (CRP), and fibrinogen (FIB). Serum albumin (ALB) was reported in g/L in the laboratory information system. To ensure consistency with published definitions, ALB was converted to g/dL when calculating indices defined with ALB in g/dL (e.g., NPAR). Other composite ratios were calculated using ALB in g/L to maintain a consistent denominator unit, and all unit conversions were performed before statistical modeling. The following inflammation-nutrition-related indicators were calculated according to the literature:

(1) Neutrophil percentage-to-albumin ratio (NPAR) = NEU % $\times$ 100 / ALB (g/dL) [13]

(2) Neutrophil-to-lymphocyte ratio (NLR) = NEU / LYM

(3) Platelet-to-lymphocyte ratio (PLR) = PLT / LYM

(4) Lymphocyte-to-monocyte ratio (LMR) = LYM / MON

(5) Pan-immune-inflammation value (PIV) = [NEU $\times$ PLT $\times$ MON] / LYM

(6) Systemic inflammation response index (SIRI) = (NEU $\times$ MON) / LYM

(7) Prognostic nutritional index (PNI) = ALB (g/L) + 5 $\times$ LYM ($\times 10^9$/L) [14]

(8) Fibrinogen-to-albumin ratio (FAR) = FIB (g/L) / ALB (g/L) [15]

(9) C-reactive protein-to-albumin ratio (CAR) = CRP (mg/L) / ALB (g/L) [16].

Outcome Definitions

(1) Lymph node metastasis (LNM): Determined based on the postoperative pathology report. If at least one cancer cell metastasis was found in the dissected lymph nodes (N1 or N2 stage), it was defined as the LNM positive group; if all lymph nodes were negative (N0 stage), it was defined as the LNM negative group [17].

(2) Postoperative gastrointestinal function recovery: The GI-2 composite endpoint was used as the standard for

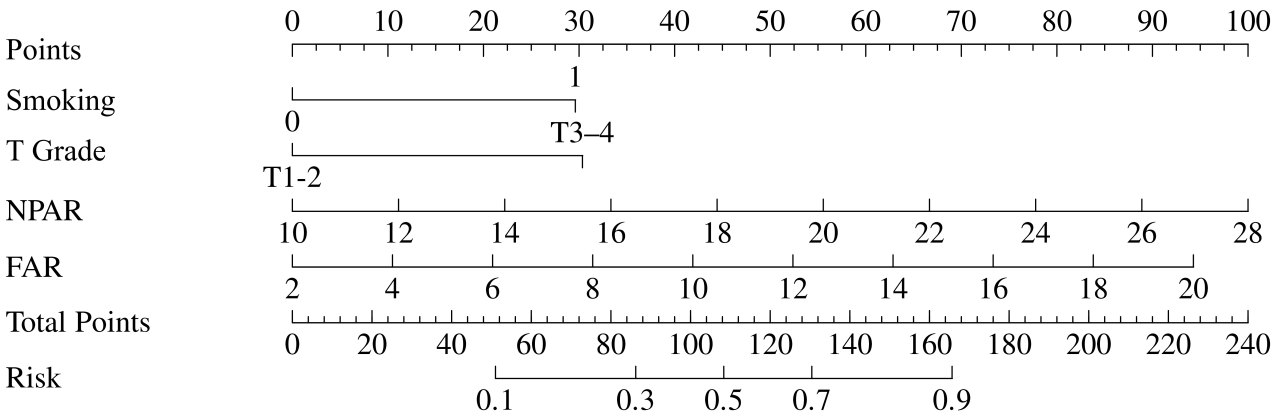

Fig. 1. Nomogram model for predicting the risk of LNM in colorectal cancer (CRC) patients.

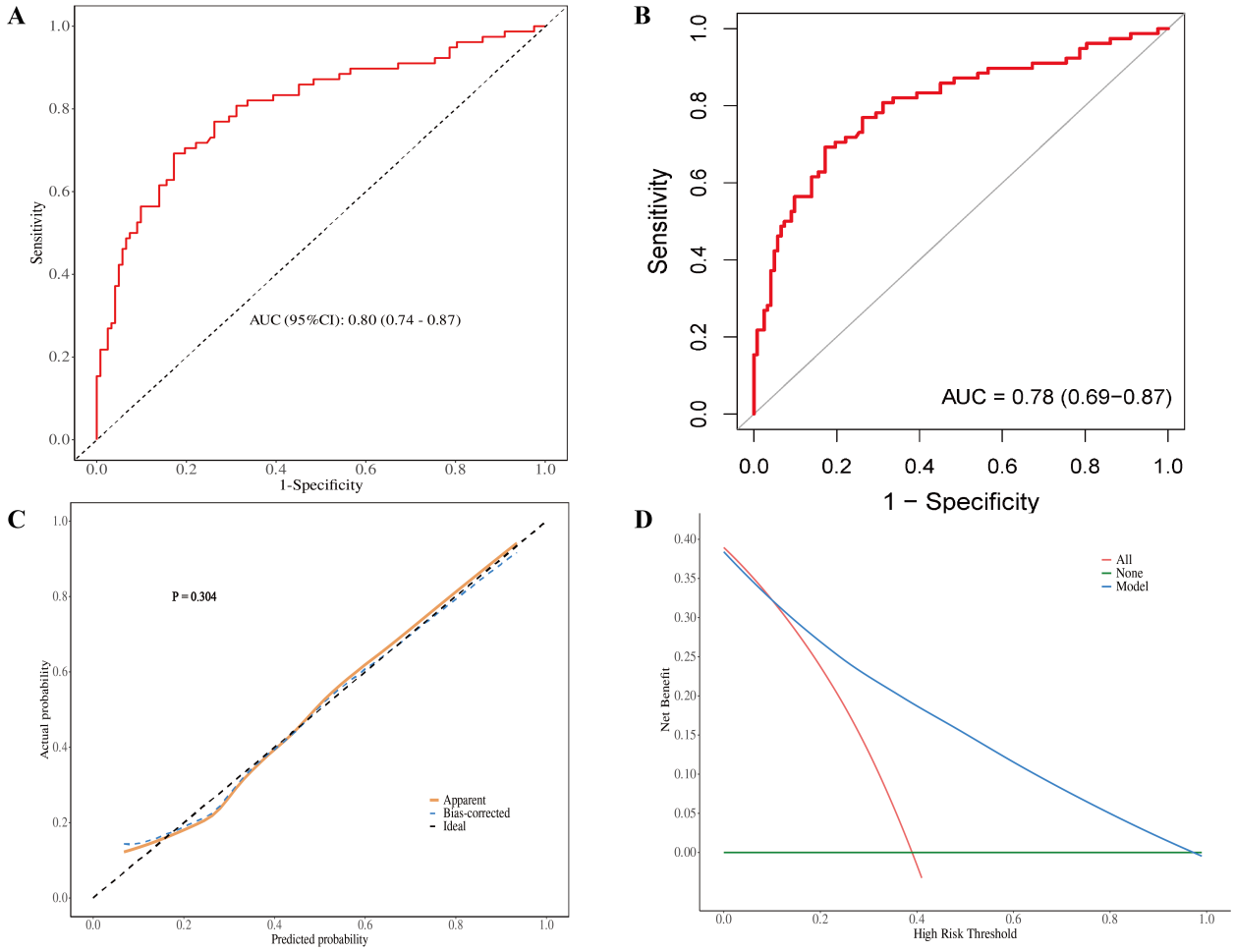

Fig. 2. Performance evaluation and validation of the LNM prediction model. (A) ROC curve. (B) Bootstrap-validated ROC curve. (C) Calibration curve. (D) DCA. ROC, receiver operating characteristic; DCA, decision curve analysis.

measuring intestinal function recovery. GI-2 is defined as the time point when a patient simultaneously meets the following two conditions: (1) Tolerance of solid food for the first time (no vomiting or significant nausea within 24 hours after eating); (2) First defecation [7,18]. This study recorded the time (in days) from the end of surgery to meeting the GI-2 criteria. If the time to reach the GI-2 criteria exceeded 5 days postoperatively, or if re-insertion of a gastric tube was required due to severe abdominal distension or vomiting, it was defined as POGD [19,20].

Statistical Analysis

Missing data were excluded during the screening phase, and only complete cases were included in the analysis. Data analysis was performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA) and R software, version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were assessed for normality. Normally distributed variables are presented as mean ± standard deviation and were compared using the independent-samples *t* test. Non-normally distributed variables are presented as median (interquartile range) and were compared using the Mann–Whitney U test. Categorical variables are presented as numbers (percentages) and were compared using the Pearson chi-square test. For outcome modeling, univariable binary logistic regression was first performed to identify candidate predictors for LNM and POGD. Variables showing statistical significance in univariable analyses and/or clinical relevance were entered into multivariable binary logistic regression models, and backward stepwise selection was applied to obtain the final predictors. Odds ratios (ORs) with 95% confidence intervals (CIs) are reported. Multicollinearity among predictors was assessed using variance inflation factors (VIFs), with VIF <5 considered acceptable. The linearity assumption of the logit for continuous predictors was assessed using the Box–Tidwell test. Model discrimination was evaluated using receiver operating characteristic (ROC) curves and area under the curve (AUC). Internal validation was performed using bootstrap resampling (1000 iterations) to estimate the robustness of model performance. Calibration was assessed using calibration curves and the Hosmer–Lemeshow goodness-of-fit test. Decision curve analysis (DCA) was conducted to quantify net benefit across a range of threshold probabilities. A two-sided $p < 0.05$ was considered statistically significant.

Results

Stratification Based on LNM Status

Analysis of Baseline Characteristics Based on LNM Status in CRC Patients

A total of 200 CRC patients were included in this study, including 78 cases (39.0%) in the LNM positive group and 122 cases (61.0%) in the LNM negative group. The baseline characteristics of the two groups are detailed in Table 1. Regarding demographic and clinical characteristics, the LNM positive group showed a significantly higher proportion of smokers and later cT stage compared to the LNM negative group (All $p < 0.001$). Notably, the LNM positive group presented with a significantly high inflammatory and low nutritional status. Specifically, the systemic inflammatory response indicators (NLR, PLR, PIV, SIRI) and comprehensive inflammation-nutrition indices (NPAR, FAR, CAR) in the LNM positive group were significantly higher than those in the LNM negative group; whereas the PNI level, reflecting immuno-nutritional reserve, was significantly lower (All $p < 0.05$). Differences in other baseline characteristics between the two groups were not statistically significant.

Identification of Independent Predictors for LNM in CRC

Based on intergroup comparisons, univariate logistic regression analysis was further employed to identify potential risk factors. The results are shown in Table 2. cT stage, history of smoking, SIRI, NPAR, FAR, FIB, NLR, PLR, PIV, and PNI were significantly associated with LNM (all $p < 0.05$). These variables were further included in the multivariate logistic regression model. After screening with the backward stepwise regression method, four independent risk factors for LNM were finally identified: cT stage (T3–4) (OR = 3.20, 95% CI 1.62–6.33, $p < 0.001$), history of smoking (OR = 3.11, 95% CI 1.50–6.46, $p = 0.002$), NPAR (OR = 1.24, 95% CI 1.08–1.42, $p = 0.002$), and FAR (OR = 1.22, 95% CI 1.03–1.45, $p = 0.019$).

In addition, all included variables in the final LNM model had VIF values <5, indicating no significant multicollinearity among the predictors (**Supplementary Table 1**). The Box-Tidwell test indicated no evidence of violation of the linearity-in-the-logit assumption for the continuous predictors included in the final LNM model (all $p > 0.05$) (**Supplementary Table 2** and **Supplementary Fig. 1**).

Construction and Validation of a Nomogram for LNM Risk Prediction

Based on the four independent predictors screened by the multivariate logistic regression analysis (cT stage, history of smoking, NPAR, and FAR), this study constructed a nomogram model for predicting the risk of LNM in CRC patients (Fig. 1). In this model, each predictor is assigned a score based on its regression coefficient, and the sum of the scores corresponds to the total points axis, from which the individual predicted probability of LNM can be estimated.

Model performance evaluation showed that the nomogram exhibited good discriminatory ability in distinguishing between LNM-positive and LNM-negative patients. ROC curve analysis indicated that the AUC of the model was 0.80 (95% CI 0.74–0.87) (Fig. 2A). After Bootstrap internal validation (resampling 1000 times), the AUC was 0.78 (95% CI 0.69–0.87) (Fig. 2B), suggesting that the model has good stability and generalization. Based on the maximum Youden index, the optimal cutoff value of 0.426, at which the model achieved a prediction accuracy of 78%, with a sensitivity of 69% and a specificity of 83%. The calibration curve showed a high degree of consistency between the predicted probability of the model and the observed probability. Specifically, the model demonstrated an excellent overall performance with a Brier score of 0.168, an apparent calibration slope of 1.00, and an intercept of 0.00. The Hosmer-Lemeshow goodness-of-fit test further confirmed this high concordance ($\chi^2 = 9.472$, $p = 0.304$,

Table 1. Comparison of clinical characteristics according to LNM status in CRC patients.

Variables	Total (n = 200)	LNM (–) (n = 122)	LNM (+) (n = 78)	$Z/\chi^2/t$	*p*
Demographics and Comorbidities					
Age (years)	67.00 (59.00, 74.00)	68.50 (61.00, 75.00)	66.00 (58.00, 73.00)	–1.63	0.103
Male, n (%)	117 (58.50)	69 (56.56)	48 (61.54)	0.49	0.486
BMI (kg/m²)	22.86 (21.51, 25.14)	22.77 (21.49, 24.61)	23.02 (21.62, 25.33)	–0.35	0.724
Smoking, n (%)	68 (34.00)	30 (24.59)	38 (48.72)	12.34	<0.001
Drinking, n (%)	36 (18.00)	18 (14.75)	18 (23.08)	2.23	0.135
Hypertension, n (%)	53 (26.50)	31 (25.41)	22 (28.21)	0.19	0.662
Diabetes, n (%)	49 (24.50)	29 (23.77)	20 (25.64)	0.09	0.764
Coronary heart disease, n (%)	30 (15.00)	17 (13.93)	13 (16.67)	0.28	0.598
Oncological Characteristics					
Tumor Location, n (%)				2.15	0.142
Colon	82 (41.00)	55 (45.08)	27 (34.62)		
Rectum	118 (59.00)	67 (54.92)	51 (65.38)		
cT Stage, n (%)				20.07	<0.001
cT1–2	96 (48.00)	74 (60.66)	22 (28.21)		
cT3–4	104 (52.00)	48 (39.34)	56 (71.79)		
Max Tumor Diameter (cm)	4.50 (3.20, 5.50)	4.50 (3.02, 5.50)	4.50 (3.40, 5.50)	–0.14	0.891
Inflammation and Nutrition Indicators					
NLR	2.35 (1.93, 2.99)	2.26 (1.89, 2.71)	2.63 (1.98, 3.51)	–2.79	0.005
PLR	150.79 (121.89, 186.69)	143.28 (117.99, 184.23)	164.99 (130.52, 193.85)	–2.56	0.011
LMR	4.20 (2.99, 5.74)	4.41 (3.11, 6.01)	3.62 (2.84, 5.24)	–1.86	0.063
PIV	184.54 (106.42, 314.83)	156.72 (101.76, 260.70)	241.75 (149.45, 377.15)	–3.44	<0.001
SIRI	0.82 (0.56, 1.34)	0.76 (0.53, 1.12)	1.03 (0.62, 1.58)	–2.71	0.007
PNI	47.95 ± 5.53	49.52 ± 4.98	45.50 ± 5.48	5.35	<0.001
NPAR	15.33 (13.65, 17.51)	14.37 (13.07, 16.11)	16.41 (14.91, 19.49)	–5.27	<0.001
FAR	8.68 (7.30, 10.53)	8.25 (6.81, 9.87)	9.63 (8.39, 12.09)	–4.45	<0.001
CAR	11.88 (7.90, 20.56)	10.31 (7.50, 17.32)	14.58 (9.65, 23.25)	–2.38	0.017
Surgical Indicators					
Surgical Approach, n (%)				3.07	0.080
Laparoscopic	161 (80.50)	103 (84.43)	58 (74.36)		
Open	39 (19.50)	19 (15.57)	20 (25.64)		
Operative Time (min)	167.00 (152.75, 179.00)	165.00 (151.50, 178.00)	169.00 (154.00, 180.00)	–1.20	0.229
Blood Loss (mL)	58.50 (44.00, 77.00)	57.50 (44.00, 73.00)	61.00 (44.00, 81.50)	–1.26	0.209
Stoma, n (%)	60 (30.00)	34 (27.87)	26 (33.33)	0.68	0.411

LNM, lymph node metastasis; CRC, colorectal cancer; BMI, body mass index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PIV, pan-immune-inflammation value; SIRI, systemic inflammation response index; PNI, prognostic nutritional index; NPAR, neutrophil percentage-to-albumin ratio; FAR, fibrinogen-to-albumin ratio; CAR, C-reactive protein-to-albumin ratio.

df = 8) (Fig. 2C). Furthermore, DCA confirmed that using this nomogram model for clinical decision-making provides significant net benefit for patients compared to "treat all" or "treat none" strategies across a wide range of threshold probabilities (Fig. 2D).

Stratification Based on Postoperative GI Recovery

Comparison of Baseline Data Between POGD and Non-POGD Groups

Patients were divided into the delayed recovery group (POGD, n = 64) and the normal recovery group (Non-POGD, n = 136) based on postoperative gastrointestinal function recovery. The incidence of POGD was 32.0%. The comparison of baseline data between the two groups is shown in Table 3. Univariate analysis showed that patients in the POGD group were older, more likely to undergo open surgery, and had longer operative times (All $p < 0.05$). Regarding inflammation and nutrition indicators, the POGD group presented a more significant state of inflammatory activation and nutritional consumption, characterized by significantly elevated preoperative NPAR, NLR, PLR, and PIV levels, along with a significantly lower PNI,

Table 2. Univariate and multivariate logistic regression analyses of predictors for LNM in CRC.

Variables	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	*p*	OR (95% CI)	*p*
cT Stage				
T1–2	1.00 (Reference)		1.00 (Reference)	
T3–4	3.92 (2.13~7.24)	<0.001	3.20 (1.62~6.33)	<0.001
Smoking	2.91 (1.59~5.34)	<0.001	3.11 (1.50~6.46)	0.002
SIRI	2.00 (1.28~3.14)	0.002		
NPAR	1.34 (1.20~1.50)	<0.001	1.24 (1.08~1.42)	0.002
FAR	1.35 (1.18~1.55)	<0.001	1.22 (1.03~1.45)	0.019
FIB	1.58 (1.11~2.26)	0.011		
NLR	1.56 (1.20~2.04)	<0.001		
PLR	1.01 (1.01~1.01)	0.004		
PIV	1.01 (1.01~1.01)	<0.001		
PNI	0.87 (0.82~0.92)	<0.001		

The blank spaces indicate that these variables were excluded from the stepwise regression screening process because they lacked independent statistical significance.

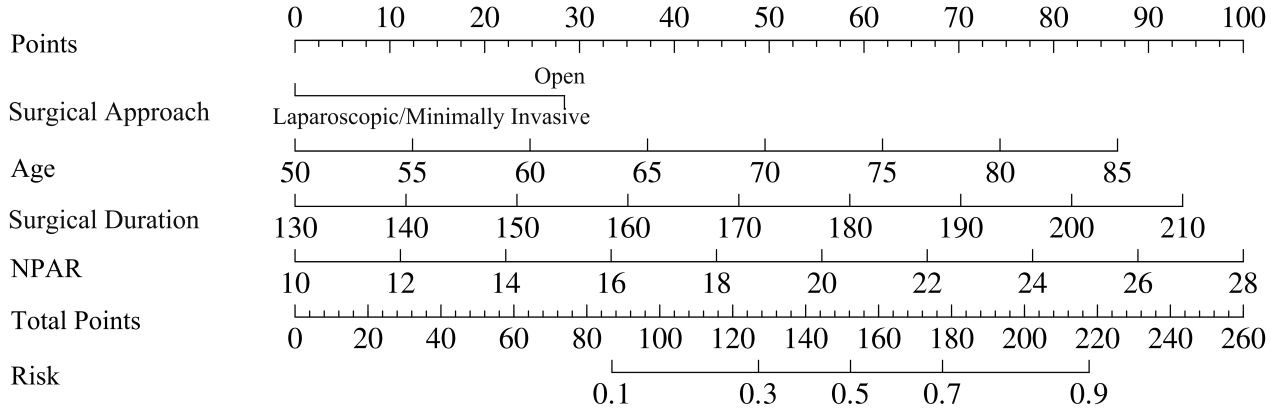

Fig. 3. Nomogram model for predicting the risk of postoperative gastrointestinal dysfunction (POGD) in CRC patients.

which reflects immuno-nutritional status (All $p < 0.05$). In addition, there were no statistically significant differences between the two groups in terms of gender, BMI, smoking and drinking history, comorbidities, tumor location, and pathological characteristics (All $p > 0.05$).

Screening of Independent Predictors for POGD in CRC Patients

Further analysis using univariate logistic regression revealed that surgical approach (open), age, operative time, and multiple inflammation-nutrition indicators (NLR, PLR, PNI, NPAR) were significantly associated with POGD (All $p < 0.05$, Table 4). Through backward stepwise multivariate Logistic regression analysis, four independent predictors were finally determined: surgical approach (open) (OR = 2.60, 95% CI 1.14–5.93, $p = 0.024$), age (OR = 1.09, 95% CI 1.04–1.13, $p < 0.001$), operative time (OR = 1.04, 95% CI 1.02–1.06, $p < 0.001$), and preoperative NPAR (OR = 1.21, 95% CI 1.08–1.35, $p < 0.001$).

In addition, all included variables in the final POGD model had VIF values <5 (**Supplementary Table 3**). Similarly, in the final POGD model, the Box–Tidwell test showed that operative time and NPAR satisfied the linearity-in-the-logit assumption (all $p > 0.05$), whereas age showed a borderline deviation from linearity ($p = 0.038$) (**Supplementary Table 4** and **Supplementary Fig. 2**).

Construction and Performance Evaluation of a Nomogram for POGD Risk

Based on the above independent predictors (surgical approach, age, operative time, and NPAR), this study constructed a nomogram model for predicting the risk of POGD in CRC patients (Fig. 3). The model demonstrated good discrimination (AUC = 0.80, 95% CI 0.73–0.87) (Fig. 4A), and after internal validation using the Bootstrap method (1000 times), the corrected AUC was 0.77 (95% CI 0.66–0.87), indicating the robustness of the model (Fig. 4B). The optimal cutoff value was determined based on the maximum

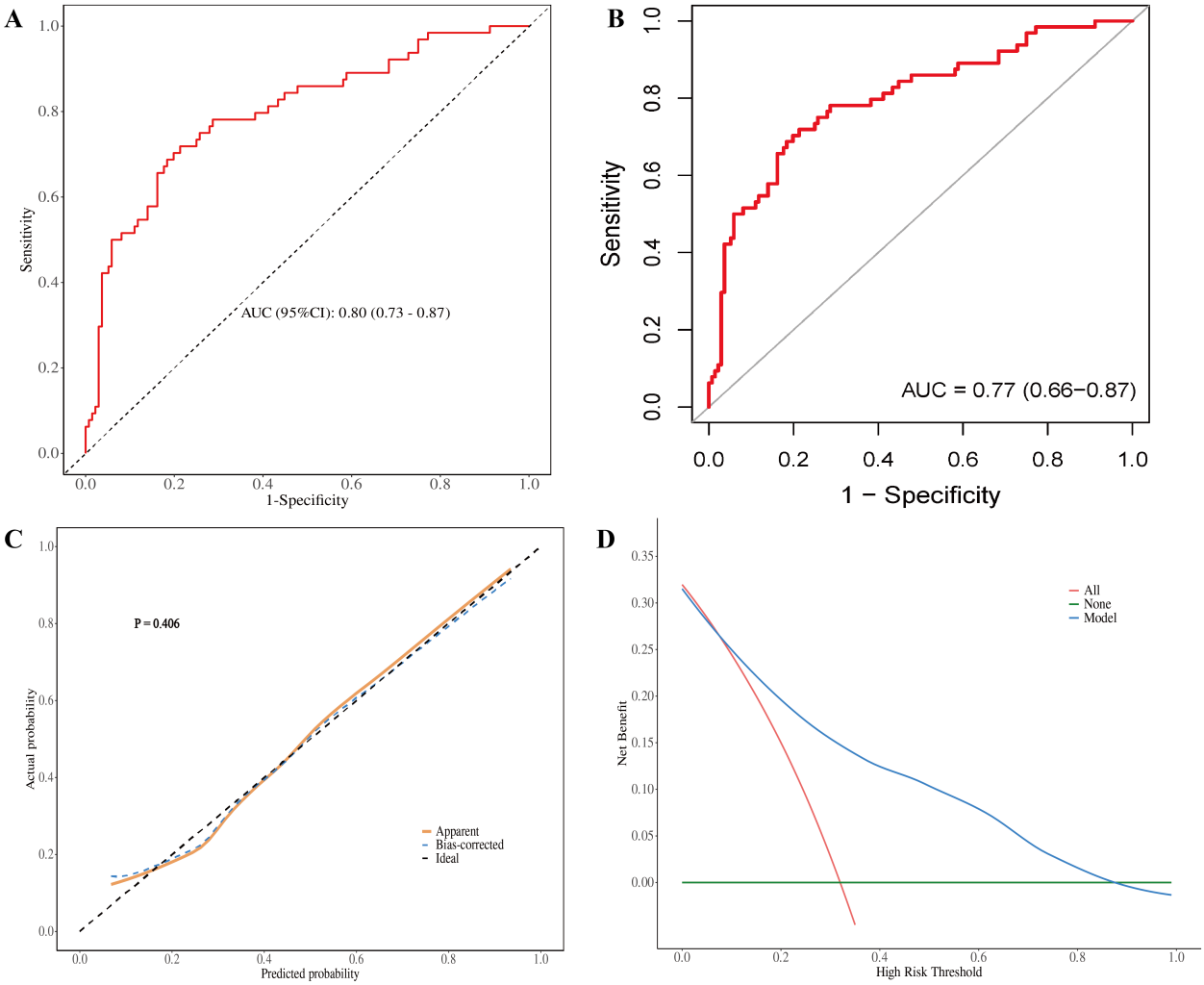

Fig. 4. Performance evaluation and validation of the POGD prediction model. (A) ROC curve. (B) Bootstrap-validated ROC curve. (C) Calibration curve. (D) DCA.

Youden index. At the optimal cutoff value of 0.347, the prediction accuracy of the model was 77%, with a sensitivity of 72% and a specificity of 79%. In addition, the calibration curve showed good consistency between the predicted probability and the observed probability (Hosmer-Lemeshow χ^2 = 8.291, p = 0.406, df = 8), with no significant calibration bias (Fig. 4C). DCA results indicated that, within a risk threshold range of approximately 10% to 90%, using this model to guide clinical decision-making provided a greater net benefit than the "treat all" or "treat none" strategies, suggesting high clinical utility (Fig. 4D).

Discussion

This study retrospectively analyzed the clinicopathological data from 200 CRC patients and innovatively explored the dual value of preoperative NPAR, a comprehensive inflammation-nutrition indicator, in LNM risk stratification and POGD prediction in CRC patients. The results showed that elevated preoperative NPAR levels were not only an independent risk factor for LNM in CRC patients but also an important predictor for the occurrence of postoperative POGD. Based on this, we constructed two targeted nomogram models, both of which demonstrated excellent discrimination and calibration.

It is noteworthy that this study also included various novel inflammation and nutrition-related indicators, including NLR, PLR, LMR, PIV, SIRI, PNI, FAR, and CAR, for comparative analysis. However, the multivariate regression model showed that only NPAR maintained an independent association with the outcomes after adjusting for potential confounding factors. This advantage may be attributed to the uniqueness of its composition: First, compared to indicators mainly based on peripheral blood cell counts, such as NLR, SIRI, or PIV, NPAR organically combines neutrophils and albumin levels, capable of simultane-

Table 3. Comparison of clinical data between non-POGD and POGD groups.

Variables	Total (n = 200)	Non-POGD (n = 136)	POGD (n = 64)	$Z/\chi^2/t$	*p*
Demographics and Comorbidities					
Age (years)	67.00 (59.00, 74.00)	65.00 (58.00, 71.25)	71.50 (64.75, 78.00)	–3.99	<0.001
Male, n (%)	117 (58.50)	75 (55.15)	42 (65.62)	1.97	0.161
BMI (kg/m^2)	22.86 (21.51, 25.14)	22.95 (21.41, 24.61)	22.69 (21.82, 25.44)	–0.46	0.642
Smoking, n (%)	68 (34.00)	44 (32.35)	24 (37.50)	0.51	0.474
Drinking, n (%)	36 (18.00)	28 (20.59)	8 (12.50)	1.93	0.165
Hypertension, n (%)	53 (26.50)	36 (26.47)	17 (26.56)	0.00	0.989
Diabetes, n (%)	49 (24.50)	36 (26.47)	13 (20.31)	0.89	0.345
Coronary heart disease, n (%)	30 (15.00)	21 (15.44)	9 (14.06)	0.06	0.799
Oncological Characteristics					
Tumor Location, n (%)				2.15	0.142
Colon	82 (41.00)	51 (37.50)	31 (48.44)		
Rectum	118 (59.00)	85 (62.50)	33 (51.56)		
cT Stage, n (%)				2.05	0.152
cT1–2	96 (48.00)	70 (51.47)	26 (40.63)		
cT3–4	104 (52.00)	66 (48.53)	38 (59.38)		
Max Tumor Diameter (cm)	4.50 (3.20, 5.50)	4.40 (3.18, 5.50)	4.60 (3.38, 5.50)	–0.63	0.526
Inflammation and Nutrition Indicators					
NLR	2.35 (1.93, 2.99)	2.29 (1.87, 2.80)	2.63 (2.18, 3.46)	–2.86	0.004
PLR	150.79 (121.89, 186.69)	142.07 (119.33, 180.27)	168.50 (134.93, 203.75)	–2.77	0.006
LMR	4.20 (2.99, 5.74)	4.20 (3.04, 5.92)	4.20 (2.83, 5.22)	–0.88	0.377
PIV	184.54 (106.42, 314.83)	163.04 (101.87, 300.26)	230.97 (152.06, 354.24)	–2.45	0.014
SIRI	0.82 (0.56, 1.34)	0.79 (0.51, 1.28)	0.90 (0.69, 1.40)	–1.94	0.052
PNI	47.95 ± 5.53	48.59 ± 5.32	46.59 ± 5.75	2.41	0.017
NPAR	15.33 (13.65, 17.51)	14.67 (13.37, 16.36)	16.33 (14.13, 18.84)	–3.35	<0.001
FAR (%)	8.68 (7.30, 10.53)	8.57 (7.33, 10.27)	8.90 (7.28, 10.97)	–0.64	0.520
CAR (%)	11.88 (7.90, 20.56)	12.03 (7.75, 19.91)	11.64 (8.33, 22.51)	–0.30	0.766
Surgical Indicators					
Surgical Approach, n (%)				8.28	0.004
Laparoscopic	161 (80.50)	117 (86.03)	44 (68.75)		
Open	39 (19.50)	19 (13.97)	20 (31.25)		
Operative Time (min)	167.00 (152.75, 179.00)	163.00 (150.00, 175.00)	173.00 (166.75, 188.25)	–4.36	<0.001
Blood Loss (mL)	58.50 (44.00, 77.00)	59.00 (44.00, 77.25)	57.00 (39.75, 76.25)	–0.59	0.556
Stoma, n (%)	60 (30.00)	43 (31.62)	17 (26.56)	0.53	0.467

POGD, postoperative gastrointestinal dysfunction.

ous assessment of systemic inflammatory response and nutritional metabolic reserve, which theoretically aligns more closely with the pathophysiological characteristics of high metabolic consumption and inflammation-related malnutrition commonly observed in colorectal cancer patients [21,22]. Second, compared to indicators that also include the albumin dimension, such as FAR, NPAR demonstrates superior comprehensive predictive efficacy. FAR primarily reflects the association between acute-phase reactive proteins and nutritional status, focusing more on coagulation-related inflammatory phenotypes [23]; whereas neutrophils in NPAR, as inflammatory effectors, can more directly reflect the inflammatory burden and damage at the tissue level. Although Wen *et al.* [2] and Wu *et al.* [8] have confirmed the effectiveness of indicators such as FAR and NLR in LNM prediction, respectively, the results of this study suggest that NPAR has higher sensitivity in capturing the complex impact of inflammation-nutrition interaction on the tumor microenvironment [24]. Furthermore, unlike PNI, which reflects the host's immuno-nutritional defense capability, NPAR more intuitively quantifies the relative imbalance between pro-inflammatory burden and nutritional reserve, potentially offering better discriminatory ability for perioperative risk stratification [25–27].

From the perspective of pathophysiological mechanisms, the association between elevated NPAR and LNM has clear biological plausibility. The study by Quan *et al.* [17] provided strong corroborative evidence for this conclu-

Table 4. Logistic regression analysis of independent predictors for POGD in CRC.

Variables	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Surgical Approach				
Laparoscopic	1.00 (Reference)		1.00 (Reference)	
Open	2.80 (1.37~5.73)	0.005	2.60 (1.14~5.93)	0.024
Age	1.07 (1.04~1.11)	<0.001	1.09 (1.04~1.13)	<0.001
Operative Time	1.04 (1.02~1.06)	<0.001	1.04 (1.02~1.06)	<0.001
NLR	1.47 (1.14~1.90)	0.003		
PLR	1.01 (1.01~1.01)	0.009		
PNI	0.94 (0.89~0.99)	0.019		
NPAR	1.18 (1.07~1.30)	0.001	1.21 (1.08~1.35)	<0.001

The blank spaces indicate that these variables were excluded from the stepwise regression screening process because they lacked independent statistical significance.

sion. Using the LASSO regression model, they found that neutrophil count was a significant risk factor for LNM (OR = 8.113), supporting the core driving role of the numerator of NPAR (i.e., neutrophils) in the tumor metastasis cascade. Mechanistically, tumor-associated neutrophils can remodel the extracellular matrix by secreting vascular endothelial growth factor and matrix metalloproteinases, thereby facilitating tumor cell invasion into lymphatic vessels; meanwhile, a decreased albumin level, as the denominator, often indicates compromised anti-tumor immune defense and diminished nutritional reserves [28–30]. In addition, the other independent predictors identified in this study also hold important clinical significance: T3–4 stage indicates an deeper tumor invasion, significantly increasing the probability of contact with the submucosal lymphatic network; smoking, as an inducer of chronic systemic inflammation, may further worsen the tumor microenvironment through persistent inflammatory stimulation; and the inclusion of FAR reaffirms the synergistic effect of coagulation-inflammation system dysregulation in CRC metastasis [31,32].

Regarding postoperative rehabilitation assessment, the occurrence of POGD essentially reflects the imbalance between surgical stress and the body's compensatory reserve. This study used the GI-2 composite endpoint as the evaluation standard, a choice with key methodological significance. Van Bree *et al*. [7] confirmed using radionuclide imaging that GI-2 more accurately reflects substantial recovery of colonic transit function than simple flatus time and has the best predictive efficacy for hospital stay duration. Gosavi *et al*. [18] also emphasized that GI-2, as a validated objective indicator, effectively avoids the defect that simple flatus time is easily interfered with by patients' subjective perception, possessing higher clinical relevance and reliability. In contrast, although Yang *et al*. [19] constructed a machine learning model based on flatus and defecation times, its assessment of the full picture of functional gastrointestinal recovery may be limited due to the lack of a composite endpoint. Regarding predictors, in addition to NPAR, open surgery was confirmed to be the strongest independent risk factor for POGD (OR = 2.60). Compared to minimally invasive surgery, the extensive tissue damage and direct traction on the bowel accompanying the open approach induce more severe local inflammatory cascades and neural inhibition in the abdominal cavity [33]. Furthermore, advanced age and prolonged operative time represent the decline of physiological functional reserve and cumulative surgical trauma, respectively. These factors act synergistically to constitute the pathological basis leading to delayed recovery of gastrointestinal motility.

At the clinical application level, the nomogram models constructed in this study demonstrated robust predictive performance in internal validation, and DCA further confirmed their superior clinical net benefit. Clinicians may integrate preoperative NPAR with routinely available clinical characteristics to identify patients at higher risk of LNM, which may facilitate preoperative counseling, meticulous pathological evaluation, and postoperative treatment planning while maintaining adherence to guideline-based oncologic resection. Similarly, the POGD model may aid in identifying patients at increased risk of delayed gastrointestinal recovery, allowing earlier implementation of targeted perioperative interventions within ERAS pathways.

However, this study has several limitations. This study employed a single-center retrospective design with a relatively small sample size (n = 200), potentially introducing inherent selection bias. Although patients transferred during admission and those with excessively prolonged preoperative hospitalization were excluded, residual unmeasured confounders may still exist. Despite rigorous internal validation of the model using Bootstrap methods, external validation in independent cohorts remains lacking, highlighting the need to further assess its generalizability. Furthermore, GI-2 is inherently a continuous variable, and its dichotomization using literature-based cutoff values may result in information loss and potential misclassification. Finally, this study analyzed only preoperative baseline NPAR levels, without capturing perioperative dynamic changes. Future prospective studies could further explore

the prognostic value of longitudinal NPAR trajectories to provide a more comprehensive assessment.

Conclusion

Elevated preoperative NPAR levels are an independent risk factor for the occurrence of LNM and POGD in CRC patients. Multivariate analysis shows that NPAR, cT stage, history of smoking, and FAR can effectively predict LNM; whereas NPAR, surgical approach, advanced age, and operative duration can effectively predict POGD. The two nomogram models constructed based on the above factors both demonstrate good discrimination and calibration. As an easy-to-use quantitative tool, the proposed model may support preoperative risk stratification and perioperative planning. However, given the single-center design and modest sample size, external multicenter validation and prospective evaluation are required before it can be considered for routine clinical implementation.

Availability of Data and Materials

The datasets used and/or analyzed in this study are not currently publicly available because they contain sensitive patient information from electronic medical records and are subject to institutional restrictions. However, they may be obtained from the corresponding author upon reasonable request and require approval from an ethics committee.

Author Contributions

CQW, ZAL and ZD provided the conceptual framework for this study. CQW and ZAL collected the data. CQW and ZD performed the statistical analyses and interpreted the results. CQW drafted the manuscript. CQW, ZAL, and ZD critically revised the manuscript. All authors read and approved the final manuscript and agreed to take responsibility for all aspects of the work.

Ethics Approval and Consent to Participate

The study protocol was reviewed and approved by the Ethics Committee of Dongyang People's Hospital (Approval No.: Dong Ren Yi 2026-YX-047). This study was conducted in strict accordance with the medical ethical principles outlined in the Declaration of Helsinki and its later amendments. Given the retrospective observational nature of this study and the fact that all patient clinical data were anonymized and kept strictly confidential, the requirement for written informed consent was waived by the Ethics Committee.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.24976/Discov.Med.202638207.88.

References

[1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, *et al*. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a Cancer Journal for Clinicians. 2024; 74: 229–263. https://doi.org/10.3322/caac.21834.

[2] Wen X, Sun H, Du S, Xia J, Zhang W, Zhang F. A nomogram of inflammatory indexes for preoperatively predicting the risk of lymph node metastasis in colorectal cancer. Techniques in Coloproctology. 2024; 28: 148. https://doi.org/10.1007/s10151-024-03010-5.

[3] Hu S, Li S, Teng D, Yan Y, Lin H, Liu B, *et al*. Analysis of risk factors and prognosis of 253 lymph node metastasis in colorectal cancer patients. BMC Surgery. 2021; 21: 280. https://doi.org/10.1186/s12893-021-01276-2.

[4] Gustafsson UO, Rockall TA, Wexner S, How KY, Emile S, Marchuk A, *et al*. Guidelines for perioperative care in elective colorectal surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations 2025. Surgery. 2025; 184: 109397. https://doi.org/10.1016/j.surg.2025.109397.

[5] Gustafsson UO, Scott MJ, Hubner M, Nygren J, Demartines N, Francis N, *et al*. Guidelines for Perioperative Care in Elective Colorectal Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations: 2018. World Journal of Surgery. 2019; 43: 659–695. https://doi.org/10.1007/s00268-018-4844-y.

[6] Chapman SJ, Thorpe G, Vallance AE, Harji DP, Lee MJ, Fearnhead NS, *et al*. Systematic review of definitions and outcome measures for return of bowel function after gastrointestinal surgery. BJS Open. 2019; 3: 1–10. https://doi.org/10.1002/bjs5.102.

[7] van Bree SHW, Bemelman WA, Hollmann MW, Zwinderman AH, Matteoli G, El Temna S, *et al*. Identification of clinical outcome measures for recovery of gastrointestinal motility in postoperative ileus. Annals of Surgery. 2014; 259: 708–714. https://doi.org/10.1097/SLA.0b013e318293ee55.

[8] Wu H, Wang Y, Deng M, Zhai Z, Xue D, Luo F, *et al*. Preoperative inflammatory markers and tumor markers in predicting lymphatic metastasis and postoperative complications in colorectal cancer: a retrospective study. BMC Surgery. 2025; 25: 71. https://doi.org/10.1186/s12893-025-02795-y.

[9] Li X, Wu M, Chen M, Liu R, Tao Q, Hu Y, *et al*. The Association Between Neutrophil-Percentage-to-Albumin Ratio (NPAR) and Mortality Among Individuals With Cancer: Insights From National Health and Nutrition Examination Survey. Cancer Medicine. 2025; 14: e70527. https://doi.org/10.1002/cam4.70527.

[10] Wang M, Wang S, Hu J, Wang X, Pang Y, Sun X. Associations between neutrophil percentage-to-albumin ratio with all-cause

and cause-specific mortality among US cancer survivors: evidence from NHANES 2005-2018. Frontiers in Nutrition. 2025; 12: 1541609. https://doi.org/10.3389/fnut.2025.1541609.

[11] Li MX, Liu XM, Zhang XF, Zhang JF, Wang WL, Zhu Y, *et al*. Prognostic role of neutrophil-to-lymphocyte ratio in colorectal cancer: a systematic review and meta-analysis. International Journal of Cancer. 2014; 134: 2403–2413. https://doi.org/10.1002/ijc.28536.

[12] Pouwels KB, Bozdemir SE, Yegenoglu S, Celebi S, McIntosh ED, Unal S, *et al*. Potential Cost-Effectiveness of RSV Vaccination of Infants and Pregnant Women in Turkey: An Illustration Based on Bursa Data. PloS One. 2016; 11: e0163567. https://doi.org/10.1371/journal.pone.0163567.

[13] Liu CF, Chien LW. Predictive Role of Neutrophil-Percentage-to-Albumin Ratio (NPAR) in Nonalcoholic Fatty Liver Disease and Advanced Liver Fibrosis in Nondiabetic US Adults: Evidence from NHANES 2017-2018. Nutrients. 2023; 15: 1892. https://doi.org/10.3390/nu15081892.

[14] Li Y, Tang J, Zhou Y, Bai L. Association of prognostic nutritional index and severe abdominal aortic calcification in middle-aged adults: a cross-sectional study. BMC Cardiovascular Disorders. 2025; 25: 608. https://doi.org/10.1186/s12872-025-05083-y.

[15] Huang X, Wang H, Yuan W. Fibrinogen-to-Albumin Ratio Predicts Acute Kidney Injury in Very Elderly Acute Myocardial Infarction Patients. Biomedicines. 2025; 13: 1909. https://doi.org/10.3390/biomedicines13081909.

[16] Liu X, Pan LX, Pei JX, Pu T, Wen HT, Zhao Y. Role of serological biomarkers in evaluating and predicting endoscopic activity in inflammatory bowel disease. World Journal of Gastroenterology. 2025; 31: 104206. https://doi.org/10.3748/wjg.v31.i18.104206.

[17] Quan X, Deng Y, Liu Z, Gao Z, Yi H, Li M. LASSO-derived nomogram prediction model for lymph node metastasis in colorectal cancer: a retrospective analysis. PeerJ. 2025; 13: e19148. https://doi.org/10.7717/peerj.19148.

[18] Gosavi R, Dudi-Venkata NN, Xu S, Asghari-Jafarabadi M, Wilkins S, Nguyen TC, *et al*. Safety and efficacy of gastrointestinal motility agents following elective colorectal surgery: a systematic review and meta-analysis of randomised controlled trials. International Journal of Colorectal Disease. 2025; 40: 131. https://doi.org/10.1007/s00384-025-04924-8.

[19] Yang S, Zhao H, An Y, Guo F, Zhang H, Gao Z, *et al*. Machine learning-based prediction models affecting the recovery of postoperative bowel function for patients undergoing colorectal surgeries. BMC Surgery. 2024; 24: 143. https://doi.org/10.1186/s12893-024-02437-9.

[20] Paterson H, Vadiveloo T, Innes K, Balfour A, Atter M, Stoddart A, *et al*. Intravenous Lidocaine for Gut Function Recovery in Colonic Surgery: A Randomized Clinical Trial. JAMA. 2025; 333: 39–48. https://doi.org/10.1001/jama.2024.23898.

[21] Nakamura Y, Imada A, Fukugaki A, Kanto S, Yamaura T, Kinjo Y, *et al*. Association of nutritional risk and systemic inflammation with survival in patients with colorectal cancer who underwent curative surgery. Clinical Nutrition ESPEN. 2022; 49: 417–424. https://doi.org/10.1016/j.clnesp.2022.03.011.

[22] Javed A, Khan A, Asif R, Salim A, Bano S, Aziz I, *et al*. Diagnostic and Prognostic Role of Neutrophil Percentage to Albumin Ratio (NPAR) in Systemic Inflammatory and Neoplastic Disorders: A Pathological Insight. Pakistan Journal of Medicine and Dentistry. 2025; 14. https://doi.org/10.36283/ziun-pjmd14-4/043.

[23] Ma S, Wang L. Fibrinogen-to-albumin ratio (FAR) is the best biomarker for the overall survival of patients with non-small-cell lung cancer. Frontiers in Oncology. 2024; 14: 1396843. https://doi.org/10.3389/fonc.2024.1396843.

[24] Tan X, Zhang H, Yang C, Chen J. Association between the neutrophil percentage-to-albumin ratio and pelvic adhesion severity in endometriosis: A retrospective cross-sectional study. PloS One. 2025; 20: e0337077. https://doi.org/10.1371/journal.pone.0337077.

[25] Kitahara H, Shoji F, Akamine T, Kinoshita F, Haratake N, Takenaka T, *et al*. Preoperative prognostic nutritional index level is associated with tumour-infiltrating lymphocyte status in patients with surgically resected lung squamous cell carcinoma. European Journal of Cardio-thoracic Surgery: Official Journal of the European Association for Cardio-thoracic Surgery. 2021; 60: 393–401. https://doi.org/10.1093/ejcts/ezab046.

[26] Lei L, Liang Y, Chen J, Cui T, Fang J, Fei L, *et al*. Preoperative neutrophil percentage-to-albumin ratio as a postoperative AKI predictor in non-cardiac surgery: a retrospective cohort secondary analysis. Scientific Reports. 2025; 15: 27994. https://doi.org/10.1038/s41598-025-12949-w.

[27] Mohri Y, Inoue Y, Tanaka K, Hiro J, Uchida K, Kusunoki M. Prognostic nutritional index predicts postoperative outcome in colorectal cancer. World Journal of Surgery. 2013; 37: 2688–2692. https://doi.org/10.1007/s00268-013-2156-9.

[28] Mizuno R, Kawada K, Itatani Y, Ogawa R, Kiyasu Y, Sakai Y. The Role of Tumor-Associated Neutrophils in Colorectal Cancer. International Journal of Molecular Sciences. 2019; 20: 529. https://doi.org/10.3390/ijms20030529.

[29] Jaillon S, Ponzetta A, Di Mitri D, Santoni A, Bonecchi R, Mantovani A. Neutrophil diversity and plasticity in tumour progression and therapy. Nature Reviews. Cancer. 2020; 20: 485–503. https://doi.org/10.1038/s41568-020-0281-y.

[30] Huang X, Nepovimova E, Adam V, Sivak L, Heger Z, Valko M, *et al*. Neutrophils in Cancer immunotherapy: friends or foes? Molecular Cancer. 2024; 23: 107. https://doi.org/10.1186/s12943-024-02004-z.

[31] Zhu L, Wang L, Gao Z, Zeng Y, Tao K, Wang Q, *et al*. Examined lymph node numbers influence prognosis in rectal cancer treated with neoadjuvant therapy. Cancer Pathogenesis and Therapy. 2023; 1: 168–176. https://doi.org/10.1016/j.cpt.2023.01.001.

[32] Elisia I, Lam V, Cho B, Hay M, Li MY, Yeung M, *et al*. The effect of smoking on chronic inflammation, immune function and blood cell composition. Scientific Reports. 2020; 10: 19480. https://doi.org/10.1038/s41598-020-76556-7.

[33] Nguyen JD, Chen AJ, Snee I, Khong J, Poisler MA, Elhelali A, *et al*. Peripheral Nerve Injuries in Laparoscopic and Open Thoracoabdominal Surgeries: A Systematic Review and Meta-Analysis. Journal of Reconstructive Microsurgery. 2025. https://doi.org/10.1055/a-2751-8638. (online ahead of print)