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A predictive model for colorectal cancer complicated with intestinal obstruction based on specific inflammation score

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Abstract

Purpose Inflammatory factors play an important role in the onset and progression of colorectal cancer (CRC). This study aimed to develop and validate a novel scoring system that utilizes specific inflammatory factor indicators to predict intestinal obstruction in CRC patients.

Methods This study conducted a retrospective analysis of 1,470 CRC patients who underwent surgical resection between January 2013 and July 2018. These patients were randomly allocated to the training group ($n=1060$) and the validation group ($n=410$). Univariate and multivariate logistic regression analyses were performed to identify independent predictive factors for intestinal obstruction. The CRC peculiar inflammation score (CPIS), comprising lymphocyte-to-monocyte ratio (LMR), prognostic nutrition index (PNI), and alanine transaminase-to-lymphocyte ratio index (ALRI) scores, was significantly associated with the occurrence of intestinal obstruction. A nomogram combining CPIS with other clinical features was developed to predict this occurrence. Model accuracy was assessed by determining the area under the receiver operating characteristic (ROC) curve (AUC).

Results The CPIS generated by multi-factor logistic regression was as follows: $-1.576\times\mathrm{LMR}-0.067\times\mathrm{PNI}+0.018\times\mathrm{ALRI}$. Using CPIS cutoff values of 50% (−7.188) and 85% (−6.144), three predictive groups were established. Patients with a high CPIS had a significantly higher risk of intestinal obstruction than those with a low CPIS (odds ratio [OR]: 10.0, confidence interval [CI]: 5.85–17.08, $P<0.001$). The predictive nomogram demonstrated good calibration and discrimination abilities. The AUC of the ROC curve for the obstruction nomogram was 0.813 (95% CI: 0.777–0.850) in the training set and 0.806 (95% CI: 0.752–0.860) in the validation set. The calibration curve exhibited neither bias nor high credibility. Decision curve analysis indicated the utility of this predictive model.

Conclusion CRC-associated intestinal obstruction is closely linked to inflammatory markers in patients. CPIS is a CRC-specific inflammatory predictive score based on a combination of inflammatory-related indicators. A high CPIS serves as a strong indicator of intestinal obstruction. Its integration with other clinical factors and preoperative inflammatory-specific indicators significantly enhances the diagnosis and treatment of CRC patients with intestinal obstruction.

Keywords Colorectal cancer, Obstruction, Inflammation, Specific inflammation score, Prediction model

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Introduction

Colorectal cancer (CRC) is one of the most prevalent malignant tumors, ranking third in incidence but second in mortality [1]. Approximately 7%-29% of all CRC patients experience partial or complete intestinal obstruction, with nearly 70% occurring in the left colon. If not treated on time, fatal complications may occur [2–4]. Intestinal obstruction represents an acute clinical emergency. Due to the compromised condition of patients with intestinal obstruction and inadequate intestinal preparation, the risks associated with surgery, postoperative complications, and mortality, when compared with the risk associated with elective surgery, are exceptionally high. Relevant studies have indicated a postoperative morbidity rate as high as 51% and a 30-day mortality rate ranging from 8% to 13% [5–8]. The World Emergency Surgery Guide suggests a two-step approach, where obstruction caused by CRC can be pre-drained, followed by radical tumor resection. Non-obstructive CRC, on the other hand, can be treated through direct radical resection [9]. Therefore, early detection of intestinal obstruction plays a pivotal role in patient treatment. Studies have also emphasized that a timely and effective surgical intervention for CRC intestinal obstruction yields favorable outcomes [10]. Currently, the cause of obstruction due to tumor growth remains unclear, and the long-term prognosis for obstruction in CRC patients remains pessimistic. A reasonable and effective predictive model is urgently needed to screen and evaluate intestinal obstruction patients.

The integration of various information types into an accurate and personalized tool for predicting and assessing obstruction proves to be a challenging task. Currently, there is limited evaluation of the internal or external validity of prognostic models in this domain. In a preliminary study, our team utilized patient laboratory indices, including routine blood tests, biochemical assessments, and tumor markers, to formulate a simple predictive model. However, the model's accuracy was suboptimal and necessitated further refinement for improved efficacy. Other studies that used basic combination indices for predicting intestinal obstruction also reported relatively low accuracy [11, 12]. Given the multitude of factors closely linked to intestinal obstruction in CRC, it is important to design a rational, simple, accurate, and cost-effective predictive model for effectively screening high-risk patients. Many studies have confirmed the association between inflammation and both carcinogenesis and cancer progression [13, 14]. Pre-inflammatory cytokines and chemotactic factors released by tumor-infiltrating leukocytes promote tumor growth. In turn, these leukocytes are stimulated by the tumor, leading to elevated inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) in various malignancies. These markers are closely associated with the prognosis of the malignancies [15, 16]. Moreover, tumor-specific inflammatory factors are mainly associated with CRC gene mutations and play a pivotal and predictive role in the occurrence, development, and prognosis of CRC [17]. Some studies have suggested that certain plant-based foods with anti-inflammatory potential may benefit CRC patients, especially those with severe inflammation indicated by molecular markers [18]. Recent research indicates that the systemic immune inflammation index (SII) possesses robust predictive abilities for the clinical outcomes of various cancers, including pancreatic cancer, gastric cancer, and CRC, making it an increasingly scrutinized inflammatory indicator [19, 20].

Considering the key role of inflammatory factors in CRC progression, in this study, we attempted to explore the prognostic significance of CRC-specific inflammatory factors in predicting the concurrent intestinal obstruction of CRC. To the best of our knowledge, no existing predictive model addresses the concurrent occurrence of intestinal obstruction in CRC patients and its correlation with inflammatory factors. Through a thorough analysis utilizing univariate and multivariate approaches, we identified potential predictive factors for intestinal obstruction. Moreover, we developed and validated a novel CRC peculiar inflammatory score (CPIS) derived from various inflammatory indicators. This newly created inflammatory index, when combined with common clinical variables, was used to construct and validate a nomogram for predicting intestinal obstruction in CRC patients.

Material and methods

Selection of patients and research design

In this retrospective study, we selected 3,700 patients with CRC with or without intestinal obstruction admitted to Wuhan Union Hospital between January 2013 and December 2018. All patients had their CRC diagnosis at admission. We reviewed the medical records of all patients, and tumor staging was based on the American Joint Committee on Cancer (AJCC) Edition 7 staging System. The inclusion criteria were as follows: (1) CRC confirmed through pathological biopsy, (2) radical excision, and (3) complete clinicopathological data available. The exclusion criteria were as follows: (1) history of tumors, co-infections, or blood diseases, (2) prior treatment with anti-inflammatory drugs before surgical resection, (3) presence of severe cardiovascular disease or metabolic disorders, (4) lack of clinical and follow-up information; (5) received immunotherapy or medication before surgery. A total of 1,470 CRC patients were included in this study, and they were divided randomly

into a training group ($n=1,060$) and a validation group ($n=410$). A flowchart of the patient selection process is illustrated in Fig. 1. Approval for the study was obtained from the Ethics Committee of Union Hospital, affiliated with Tongji Medical College, Huazhong University of Science and Technology (No. 2018-S377). The study was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived owing to the retrospective nature of the study.

Definition and collection of data

Demographic and clinicopathological data were retrospectively collected, including age, sex, body mass index (BMI), smoking status, intestinal obstruction, tumor location, tumor history, tumor differentiation, tumor size, peripheral invasion, vascular invasion, tumor (T) stage, regional lymph node (N) stage, metastasis (M) stage, TNM stage, chemotherapy, and radiotherapy. Test indicators encompassed blood routine, blood biochemistry, and serum tumor marker (STM) information. Blood samples were collected within 1 week or up to 1 month before the formal diagnosis of intestinal obstruction in CRC patients. Routine blood and biochemical parameters included total white blood cell count, neutrophil count, lymphocyte count, monocyte count, platelet count, aspartate aminotransferase (AST), and alanine aminotransferase. All patients received at least one STM test, including carcinoembryonic antigen, carbohydrate antigen 19–9 (CA19–9), carbohydrate antigen 125 (CA125), and carbohydrate antigen 72–4 (CA72-4). Inflammation-specific indicators included preoperative neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), SII (calculated as SII = platelets × neutrophils/lymphocytes), prognostic nutritional index (PNI, calculated as PNI = serum albumin [g/L] + 5 × total number of peripheral blood lymphocytes [$\times 10^9$/L]) [21], ALRI score, and albumin bilirubin index (ALBI) grading. ALBI was calculated based on ALB and total bilirubin (TB) levels using the following formula: ALBI = 0.66 × log10 (TB [μmol/L])-0.085 × (ALB [g/L]). Classification standards were as follows: Level 1 (ALBI ≤ −2.60), Level 2 (−2.60 < ALBI score ≤ −1.39), and Level 3 (ALBI score > −1.39 [22]). The model end-stage liver disease (MELD) score was determined using the following formula: MELD = 3.78 × ln (TB [mg/dL]) + 11.2 × ln (international normalized ratio [INR]) + 9.57 × ln (Cr [mg/dL]) + 6.43. The MELD score was classified as follows: > 18 points, high risk; 15–18 points, moderate risk; and ≤ 14 points, low risk.

Construction of a CRC-specific inflammation system and decision curve analysis

Blood routine and biochemical tests were conducted for each CRC patient from the first day of admission. The tumor-specific inflammatory indicators investigated in our study included NLR, PLR, LMR, SII, ALRI, ALBI, MELD, and PNI, calculated based on patients' blood examination results using specific formulas [23].

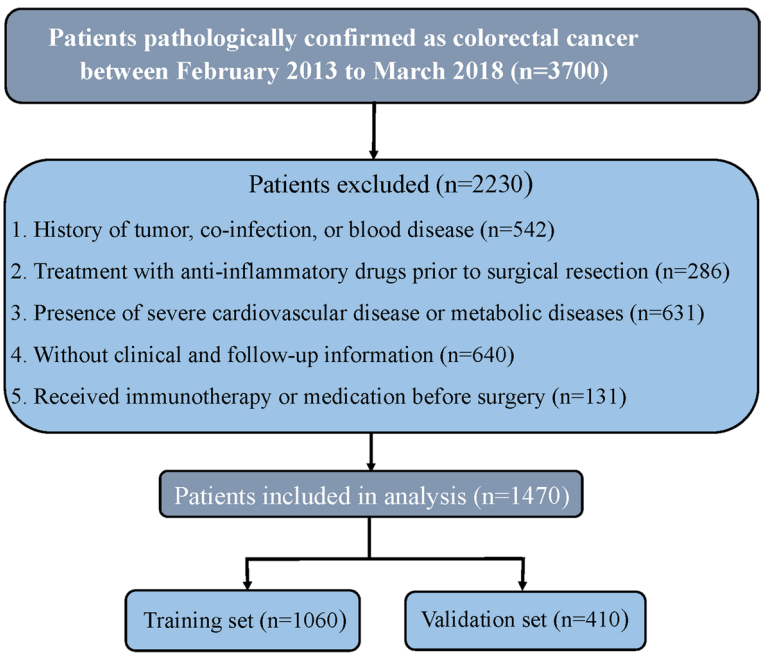

Fig. 1 Strategies for selecting patients to be included in the study

Table 1 Clinicopathological characteristics of all patients

Characteristics	Training set ($n=1060$)	Validation set ($n=410$)	*P* value
Age (years), n (%)			0.836
≥ 60	564 (53.2)	215 (52.4)	
< 60	496 (46.8)	195 (47.6)	
Gender, n (%)			0.567
Male	637 (60.1)	239 (58.3)	
Female	423 (39.9)	171 (41.7)	
BMI, Kg/m^2 (Q1,Q3)	22.7 (20.8, 24.5)	22.7 (20.9, 24.2)	0.908
Smoker, n (%)	246 (23.2)	90 (22)	0.656
Primary.site, n (%)			0.702
Left colon	259 (24.4)	100 (24.4)	
Right colon	256 (24.2)	91 (22.2)	
Rectum	545 (51.4)	219 (53.4)	
Family history of cancer, n (%)	106 (10)	34 (8.3)	0.368
Histological grade, n (%)			0.816
Well differentiated	210 (19.8)	78 (19)	
Moderately differentiated	743 (70.1)	294 (71.7)	
Poorly differentiated	107 (10.1)	38 (9.3)	
Tumor size, n (%)			0.350
< 2 cm	30 (2.8)	12 (2.9)	
2-5 cm	625 (59)	258 (62.9)	
≥ 5 cm	405 (38.2)	140 (34.1)	
T stage, n (%)			0.359
T1	61 (5.8)	34 (8.3)	
T2	161 (15.2)	62 (15.1)	
T3	617 (58.2)	233 (56.8)	
T4	221 (20.8)	81 (19.8)	
N stage, n (%)			0.514
N0	594 (56)	231 (56.3)	
N1	279 (26.3)	116 (28.3)	
N2	187 (17.6)	63 (15.4)	
M stage, n (%)			0.374
M0	957 (90.3)	377 (92)	
M1	103 (9.7)	33 (8)	
TNM stage, n (%)			0.941
Stage I	162 (15.3)	66 (16.1)	
Stage II	381 (35.9)	148 (36.1)	
Stage III	406 (38.3)	157 (38.3)	
Stage IV	111 (10.5)	39 (9.5)	
Neoadjuvant chemotherapy, n (%)			0.660
No	494 (46.6)	197 (48)	
Yes	566 (53.4)	213 (52)	
CEA, ng/mL (Q1,Q3)	4.0 (2, 10)	3.0 (2, 7)	0.029
CA19-9, kU/L (Q1,Q3)	9.0 (4, 23.2)	8.0 (4, 23.8)	0.911
CA72-4, U/mL (Q1,Q3)	3.0 (1, 6)	3.0 (1, 6)	0.558
CA125, U/mL (Q1,Q3)	12.0 (8, 18)	12.0 (8, 18)	0.656
NLR (Q1,Q3)	2.5 (1.8, 3.8)	2.5 (1.8, 3.6)	0.813
PLR (Q1,Q3)	150.5 (112, 217.9)	146.6 (107.6, 210.3)	0.357
LMR (Q1,Q3)	2.7 (2.4, 3)	2.8 (2.4, 3)	0.491
SII (Q1,Q3)	556.4 (354.6, 947.3)	513.6 (336.1, 934.2)	0.139

Table 1 (continued)

Characteristics	Training set ($n=1060$)	Validation set ($n=410$)	*P* value
PNI (Q1,Q3)	47.7 (43.4, 51.6)	47.1 (42.9, 51.2)	0.361
ALRI (Q1,Q3)	12.8 (9.4, 19.1)	12.8 (9.4, 17.9)	0.824
ALBI, n (%)			0.338
1	655 (61.8)	238 (58)	
2	399 (37.6)	171 (41.7)	
3	6 (0.6)	1 (0.2)	
MELD, Median (Q1,Q3)	6.5 (6.4, 6.7)	6.5 (6.4, 6.7)	0.916
Obstruction, n (%)	142.0 (13.4)	56.0 (13.7)	0.963
The time span (days)	4.42 ± 2.61	4.95 ± 3.72	0.653

Abbreviations: *BMI* body mass index (calculated as weight in kilograms divided by height in meters squared), *CEA* carcino-embryonic antigen, *CA19-9* carbohydrate antigen 19–9, *CA72-4* carbohydrate antigen 72–4, *CA125* carbohydrate antigen 125, *NLR* neutrophil to lymphocyte ratio, *PLR* platelet to lymphocyte ratio, *LMR* lymphocyte monocyte ratio, *SII* systemic immune inflammation index, *PNI* prognostic nutritional index, *ALRI* aspartate aminotransferase to lymphocyte ratio index, *ALBI* albumin bilirubin index, *MELD* model for End-stage Liver Disease

Decision Curve Analysis (DCA) is a newly proposed method for visualizing the potential clinical value of risk prediction models. Therefore, the DCA method was used to compare the consequences of predicting column charts in the current study.

Statistical analysis

All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA), SPSS 23.0 (SPSS Inc., Chicago, IL, USA), and R 4.0.0 software (Institute for Statistics and Mathematics, Vienna, Austria) for data analysis. Categorical variables are presented as numbers (percentage), while continuous variables are expressed as mean ± standard deviation or median (interquartile range). Univariate and multivariate logistic regression analyses were employed to analyze the relationship between clinical features, hematologic biochemical indicators, STM level, specific inflammatory factors, and obstruction. Subsequently, a receiver operating characteristic (ROC) curve was generated to assess the predictive ability of relevant inflammatory indicators for intestinal obstruction occurrence in patients. R software was utilized to construct a graph illustrating essential factors linked to intestinal obstruction. Internal validation of line diagrams, along with the assessment of model discrimination and calibration, was performed. The model's predictive value was evaluated based on the concordance index (C-index), involving repeated extraction of the same number of samples from the given database, followed by repeated training and internal verification of the resolution of the line graph model in the generated new dataset. Finally, an ROC curve was drawn. To further assess the accuracy of the column chart in predicting survival, a calibration curve was generated to compare the observations with the predictions.

Results

Clinical characteristics of patients

A total of 1470 patients from Wuhan Union Medical College Hospital participated in this study, comprising 876 males and 594 females, with approximately 53% aged over 60 years. Of these patients, 198 experienced intestinal obstruction, constituting 13.5% of all patients. Table 1 lists the clinicopathological characteristics of CRC patients in the training and verification sets. The data from the two groups were comparable, with no statistically significant difference found in all indicators ($P>0.05$). We categorized on CRC patients with intestinal obstruction based on the degree of obstruction. A higher proportion of patients in the complete obstruction had tumors located in the left colon compared to the incomplete obstruction group. At the same time, the histological grade, T stag, LMR and PNI are different in two group ($P<0.05$; Table 2).

All tumor markers and inflammatory indicators considered in this study exhibited statistical correlations with obstruction in CRC patients ($P<0.05$; Table 3).

Construction of peculiar inflammation score for CRC

Logistic regression analysis revealed specific inflammatory markers significantly associated with intestinal obstruction. These markers were utilized in developing the CPIS using logistic regression, focusing on factors displaying an evident relationship with obstruction. The results indicated that NLR ($\beta=0.079$, odds ratio [OR] $=1.082$, $P<0.001$), PLR ($\beta=0.005$, OR $=1.005$, $P<0.001$), LMR ($\beta=$-1.706, OR $=0.182$, $P<0.001$), SII ($\beta=0.000$, OR $=1.000$, $P<0.001$), Lg (SII) ($\beta=1.533$, OR $=4.630$, $P<0.001$), ALRI ($\beta=0.032$, OR $=1.033$, $P<0.001$), ALBI 2 ($\beta=1.048$, OR $=2.852$, $P<0.001$), MELD ($\beta=0.120$, OR $=1.127$, $P<0.001$), and PNI ($\beta=-0.109$, OR $=0.896$, $P<0.001$)

Table 2 Clinicopathological characteristics of all patients

Characteristics	Incomplete obstruction ($n=110$)	Complete obstruction ($n=88$)	*P* value
Age (years), n (%)			0.897
≥ 60 1	66 (60.0)	52 (59.1)	
< 60 0	44 (40.0)	36 (40.9)	
Gender, n (%)			0.584
Male	62 (56.4)	53 (60.2)	
Female	48 (43.6)	35 (39.8)	
BMI, Kg/m^2 (Q1,Q3)	21.92 (19.94, 23.56)	21.86 (19.72, 24.04)	0.830
Smoker, n (%)			0.119
No	88 (80.0)	62 (70.5)	
Yes	22 (20.0)	26 (29.5)	
Primary.site, n (%)			0.018
Left colon	29 (26.4)	39 (44.3)	
Right colon	49 (44.5)	34 (38.6)	
Rectum	32 (29.1)	15 (17.0)	
Family history of cancer, n (%)			0.110
No	102 (92.7)	86 (97.7)	
Yes	8 (7.3)	2 (2.3)	
Histological grade, n (%)			0.008
Well differentiated	21 (19.1)	6 (6.8)	
Moderately differentiated	77 (70.0)	62 (70.5)	
Poorly differentiated	12 (10.9)	20 (22.7)	
Tumor size, n (%)			0.690
< 2 cm	1 (0.9)	1 (1.1)	
2-5 cm	58 (52.7)	41 (46.6)	
≥ 5 cm	51 (46.4)	46 (52.3)	
T stage, n (%)			< 0.001
T1	1 (0.9)	5 (5.7)	
T2	3 (2.7)	23 (26.1)	
T3	62 (56.4)	33 (37.5)	
T4	44 (40.0)	27 (30.7)	
N stage, n (%)			0.320
N0	47 (42.7)	45 (51.1)	
N1	43 (39.1)	33 (37.5)	
N2	20 (18.2)	10 (11.4)	
M stage, n (%)			0.265
M0	106 (96.40)	87 (98.9)	
M1	4 (3.6)	1 (1.1)	
TNM stage, n (%)			0.408
Stage I	3 (2.7)	0 (0)	
Stage II	40 (36.4)	32 (36.4)	
Stage III	59 (53.6)	47 (53.4)	
Stage IV	8 (7.3)	9 (10.2)	
Adjuvant chemotherapy, n (%)			0.607
No	61 (55.5)	52 (59.1)	
Yes	49 (44.5)	36 (40.9)	
CEA, ng/mL (Q1,Q3)	4.7 (2.37, 12.75)	5.85 (2.92, 23.65)	0.093
CA19-9, kU/L (Q1,Q3)	12.1 (2.6, 12.1)	9.4 (4.3, 35.1)	0.833
CA72-4, U/mL (Q1,Q3)	1.5 (1.0, 3.7)	1.8 (1.0, 10.4)	0.223
CA125, U/mL (Q1,Q3)	21.4 (10.9, 43.6)	27.6 (15.7, 67.0)	0.051

Table 2 (continued)

Characteristics	Incomplete obstruction ($n=110$)	Complete obstruction ($n=88$)	*P* value
NLR (Q1,Q3)	3.0 (1.9, 5.4)	3.5 (2.0, 5.2)	0.489
PLR (Q1,Q3)	187.2 (134.7, 283.6)	197.2 (148.6, 266.4)	0.513
LMR (Q1,Q3)	3.3 (1.9, 4.1)	2.6 (1.8, 3.3)	0.032
SII (Q1,Q3)	721.9 (456.9, 1356.8)	864.3 (507.8, 1437.6)	0.423
PNI (Q1,Q3)	44.6 (40.0, 47.7)	41.8 (39.1, 45.9)	0.027
ALRI (Q1,Q3)	14.3 (9.9, 26.3)	14.1 (11.3, 14.2)	0.451
ALBI, n (%)			0.055
1	49 (44.5)	25 (28.4)	
2	59 (53.6)	62 (70.5)	
3	2 (1.8)	1 (1.1)	
MELD, Median (Q1,Q3)	7.3 (6.6, 8.2)	7.5 (6.6, 8.7)	0.179
The time span, days (Q1,Q3)	4 (3, 5)	4 (6, 8)	0.005

Abbreviations: *BMI* body mass index (calculated as weight in kilograms divided by height in meters squared), *CEA* carcino-embryonic antigen, *CA19-9* carbohydrate antigen 19–9, *CA72-4* carbohydrate antigen 72–4, *CA125* carbohydrate antigen 125, *NLR* neutrophil to lymphocyte ratio, *PLR* platelet to lymphocyte ratio, *LMR* lymphocyte monocyte ratio, *SII* systemic immune inflammation index, *PNI* prognostic nutritional index, *ALRI* aspartate aminotransferase to lymphocyte ratio index, *ALBI* albumin bilirubin index, *MELD* model for End-stage Liver Disease

were prognostic factors for patients with intestinal obstruction. Multivariate logistic regression revealed that LMR ($\beta=-1.576$, OR = 0.207, $P<0.001$), ALRI ($\beta=0.018$, OR = 1.018, $P=0.015$), and PNI ($\beta=-0.067$, OR = 0.936, $P=0.009$) were independent risk factors for inflammation in patients with intestinal obstruction. The predictive model CPIS was generated as follows: CPIS = −1.576 × LMR − 0.067 × PNI + 0.018 ALRI. Using 50% (−7.18863) and 85% (−6.14368) of CPIS as cutoff values, three groups with different predictions were obtained (Table 3).

Univariate and multivariate analyses of factors associated with intestinal obstruction

A single-factor logistic regression analysis of factors influencing intestinal obstruction occurrence revealed age (OR: 1.51, confidence interval [CI]: 1.06–2.15, $P=0.024$), BMI (OR: 0.89, CI: 0.84–0.95, $P<0.001$), tumor location (OR: 0.25, CI: 0.16–0.40, $P<0.001$), CA199 (OR: 1.01, CI: 1.00–1.02, $P=0.017$), CA125 (OR: 1.01, CI: 1.01–1.03, $P=0.001$), and CPIS (medium, OR: 3.60, CI: 2.20–5.89, $P<0.001$; high, OR: 12.45, CI: 7.45–20.79, $P<0.001$) as risk factors. Multifactor regression results showed that

Table 3 Logistic regression models of laboratory parameters in the training cohort

	Univariate			Multivariate		
	β	OR	P	β	OR	P
NLR	0.079	1.082	< 0.001	-0.033	0.968	0.270
PLR	0.005	1.005	< 0.001	0.001	1.001	0.714
LMR	-1.706	0.182	< 0.001	-1.576	0.207	< 0.001
SII	0.000	1.000	< 0.001			
Lg(SII)	1.533	4.630	< 0.001	0.618	1.855	0.254
ALRI	0.032	1.033	< 0.001	0.018	1.018	0.015
ALBI						
1	-	Ref	-	-	Ref	-
2	1.048	2.852	< 0.001	0.343	1.409	0.234
3	1.677	5.348	0.056	-0.209	0.968	0.842
MELD	0.120	1.127	0.088			
PNI	-0.109	0.896	< 0.001	-0.067	0.936	0.009

Abbreviations: *BMI* body mass index (calculated as weight in kilograms divided by height in meters squared), *NLR* neutrophil to lymphocyte ratio, *PLR* platelet to lymphocyte ratio, *LMR* lymphocyte monocyte ratio, *SII* systemic immune inflammation index, *PNI* prognostic nutritional index, *ALRI* aspartate aminotransferase to lymphocyte ratio index, *ALBI* albumin bilirubin index, *MELD* model for End-stage Liver Disease, *CRC-specific inflammatory score (CPIS)* -1.576 × LMR -0.067 × PNI + 0.018 × ALRI, *OR* Odds ratio

Table 4 Univariate and multivariate analyses of factors associated with obstruction

	Univariate analysis		Multivariate analysis	
	OR (95%CI)	**P**	**OR (95%CI)**	**P**
Age (years)				
≥ 60	1.51 (1.06–2.15)	0.024	1.28 (1.06–1.91)	0.035
< 60	Ref	-	Ref	-
Sex, female	1.16 (0.81–1.65)	0.425		
BMI	0.89 (0.84–0.95)	< 0.001	0.90 (0.72–1.16)	0.105
Smoker	1.25 (0.83–1.87)	0.282		
Primary site				
Left colon	Ref	-	Ref	-
Right colon	0.95 (0.62–1.45)	0.796	1.10 (0.69–1.77)	0.675
Rectum	0.25 (0.16–0.40)	< 0.001	0.32 (0.20–0.52)	< 0.001
Family history of cancer	2.00 (0.95–4.21)	0.067		
Histological grade				
Well differentiated	Ref	-		
Moderately differentiated	1.11 (0.70–1.77)	0.648		
Poorly differentiated	1.15 (0.58–2.28)	0.681		
Tumor size				
< 2 cm	Ref	-		
2-5 cm	3.72 (0.50–27.66)	0.200		
≥ 5 cm	6.06 (0.81–45.16)	0.079		
Neoadjuvant chemotherapy				
Yes	0.64 (0.45–0.91)	0.013	0.89 (0.60–1.34)	0.585
No	Ref	-	Ref	-
CEA (ng/mL)	1.00 (0.99–1.01)	0.928		
CA19-9 (kU/L)	1.01 (1.00–1.02)	0.017	1.00 (1.00–1.01)	0.206
CA72-4 (U/mL)	1.01 (1.01–1.03)	0.001	1.01 (0.97–1.03)	0.458
CA125 (U/mL)	1.00 (0.99–1.01)	0.717		
CPIS				
Low risk	Ref	-	Ref	-
Intermediate	3.60 (2.20–5.89)	< 0.001	3.18 (1.92–5.26)	< 0.001
High risk	12.45 (7.45–20.79)	< 0.001	10.00 (5.85–17.08)	< 0.001

Abbreviations: *BMI* body mass index (calculated as weight in kilograms divided by height in meters squared), *CEA* carcino-embryonic antigen, *CA19-9* carbohydrate antigen 19–9, *CA72-4* carbohydrate antigen 72–4, *CA125* carbohydrate antigen 125, *CPIS* CRC-specific inflammatory score, *OR* Odds ratio

age (OR: 1.28, CI: 1.06–1.91, $P=0.035$), tumor location (rectum, OR: 0.32, CI: 0.20–0.52, $P<0.001$), and CPIS (medium, OR: 3.18, CI: 1.92–5.26, $P<0.001$; high, OR: 10.0, CI: 5.85–17.08, $P<0.001$) were independent predictors of intestinal obstruction (Table 4).

Predictive performance of CPIS

ROC curve analysis was further applied to evaluate the predictive effect of CPIS on the occurrence of intestinal obstruction. The predictive ability of CPIS measured using the area under the curve (AUC) was 0.770 (95% CI: 0.728–0.811) in the training set (Fig. 2A) and 0.754 (95% CI: 0.685–0.824) in the validation set (Fig. 2B).

Construction and verification of intestinal obstruction prediction diagram

From the multivariate logistic regression results, age, tumor location, and CPIS were selected as three preoperative valuable factors for establishing the prediction model (Fig. 3). The predictive power of the obstruction line chart measured using the area under the ROC curve was 0.813 (95% CI: 0.777–0.850) in the training set (Fig. 2A) and 0.806 (95% CI: 0.752–0.860) in the validation set (Fig. 2B). The calibration curve of the predictive model for intestinal obstruction demonstrated good agreement between predicted outcomes and observed outcomes in both the training and validation

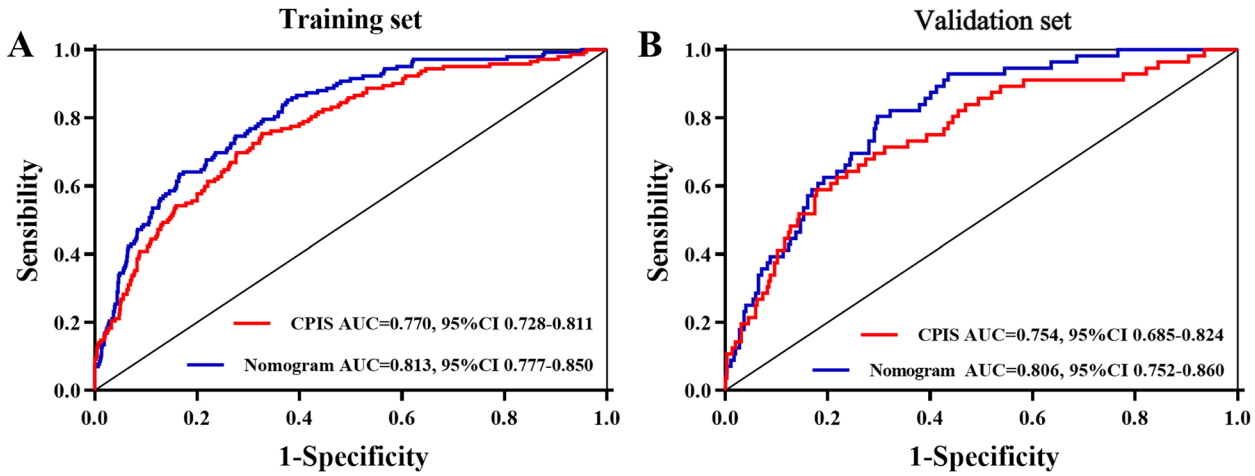

Fig. 2 Receiver operating characteristic (ROC) curve of nomogram and CPIS. The AUC values of ROC predicted obstruction rates of Nomogram and CPIS in the training cohorts (**A**); The AUC values of ROC predicted obstruction rates of Nomogram and CPIS in the validation cohorts (**B**)

sets, indicating no bias and high credibility (Fig. 4A-B). DCA is a new strategy treatment method for evaluating alternative predictions, which is superior to AUROC in clinical practice. The training and validation sets of the developed nomogram DCA curve are shown in Figs. 4C and D.

Discussion

Our findings reveal a close association between CRC complicated with intestinal obstruction and inflammatory indicators. CPIS, as a CRC-specific inflammatory prediction score, based on a combination of inflammation-related indicators, emerged as a robust indicator of intestinal obstruction. The integration of preoperative inflammatory markers with other clinical factors significantly enhances the diagnosis and management of CRC patients with intestinal obstruction.

Numerous researchers have confirmed the dual role of inflammatory responses in tumor development. First, chronic inflammation can lead to the accumulation of monocytes, platelets, and neutrophils, secreting cytokines that promote tumor angiogenesis and metastasis. Second, an increase in monocytes and lymphocytes creates resistance to tumor invasion [24]. Vakkila et al. reported that inflammation is associated not only with carcinogenesis but also with cancer progression [25, 26]. Invading white blood cells produce inflammatory cytokines and chemokines that stimulate tumor growth, and these cells are themselves stimulated by the tumor, thus contributing to elevated inflammatory markers such

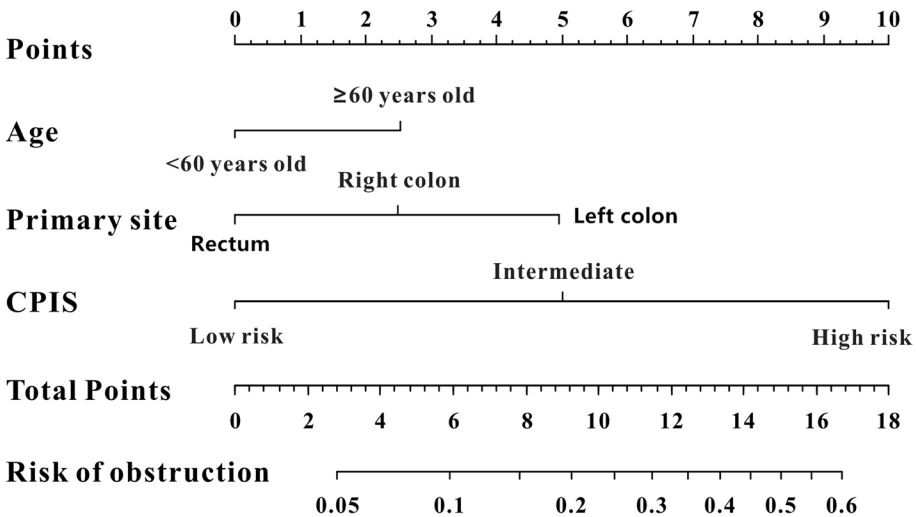

Fig. 3 Evaluation of obstruction rates associated nomograms for patients with colorectal cancer. The nomogram integrating the Age, Tumor primary site, and CPIS for predicting the risk of obstruction

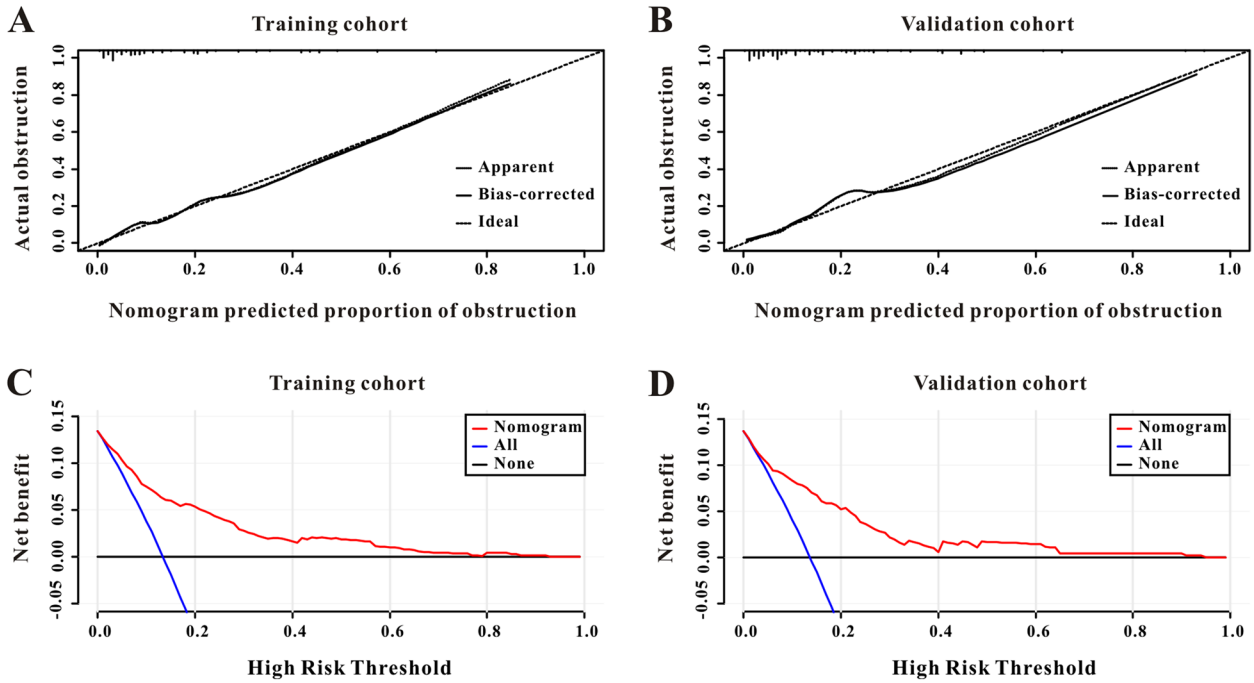

Fig. 4 The calibration curves and Decision curve analysis f the nomogram for the risk of obstruction predictions. Represents the calibration curve for predicting patients' the risk of obstruction in the training and the validation cohorts (**A**, **B**); Decision curve analysis of the nomogram for the risk of obstruction prediction of patients with colorectal cancer in the training and the validation cohorts (**C**, **D**)

as CRP and IL-6 in various malignant diseases. These markers are closely linked to the prognosis of patients with malignant diseases [27–29].

Currently, diagnosing intestinal obstruction remains a common and challenging issue in the clinical setting. The combination of imaging and endoscopic diagnosis is the main method for the preoperative diagnosis of intestinal obstruction. However, the varying levels of endoscopy at different hospitals owing to the large population in China, the uneven distribution of medical resources in different regions, and the high examination costs pose challenges. This leads to a lack of imaging and endoscopic diagnosis in some patients, resulting in delayed hospital visits and unfavorable prognoses. By contrast, traditional detection methods such as peripheral blood biochemical detection offer advantages in terms of rapid and simple sample collection, low cost, and preoperative detection before minor trauma. This method deserves attention in research [30]. Leveraging comprehensive experimental detection methods available in hospitals of all levels, we analyzed the relationship between systemic inflammatory indicators and CRC patients with intestinal obstruction. This study aimed to enhance the diagnostic rate of this condition by establishing a disease-predictive model for CRC complicated with intestinal obstruction.

PNI was established by Japanese scholars, including Ono Temple, also known as the "Ono Temple Index." Initially designed to assess the nutritional and immune status of patients undergoing gastrointestinal surgery, PNI has evolved into a prognostic indicator for determining the prognosis of various diseases, such as gastrointestinal malignancies, gynecological tumors, and lung cancer. Additionally, its application in prognostic assessments for non-tumor patients, including those with fractures, heart failure, and cerebral infarction, has been increasing [31, 32]. Our findings indicate that PNI independently influences the occurrence of intestinal obstruction in patients, aligning with the findings of previous reports.

The first application of ALRI was in hepatocellular carcinoma patients due to liver cirrhosis, leading to elevated AST levels and decreased lymphocyte levels. Casadei Gardini et al.'s research revealed that high ALRI levels are associated with poor progression-free survival and overall survival compared with low ALRI levels in patients. They considered ALRI a noninvasive predictor of CRC patient prognosis [33]. Our results also highlight the high sensitivity of ALRI in predicting the occurrence of intestinal obstruction in patients.

Thus far, there have been limited reports on a predictive model for CRC-induced intestinal obstruction.

Eto et al. suggested that preoperative NLR is an effective predictor of CRC-induced intestinal obstruction [34]. We conducted group and regression analyses on tumor-related inflammatory indicators, constructing the CPIS for CRC-induced obstruction. This not only identified independent influencing factors for intestinal obstruction but also established a predictive model with an ROC of 0.806, surpassing traditional models.

To the best of our knowledge, this study is the first to develop a novel predictive model based on specific indicators of CRC inflammation, supported by a large-sample, single-center study with a noteworthy reference value. However, there are limitations. First, this study had a retrospective study design, and the inclusion of case data was inevitably biased. Second, we did not compare the outcomes of the two groups of patients or assess the effects of other therapies on the survival of the two groups of patients. At the same time, we did not compare models between patients with different degrees of obstruction. Finally, this single-center clinical study lacked effective external validation, necessitating a multicenter prospective study in the future to further verify our conclusions.

Conclusion

In this study, CRC complicated by intestinal obstruction is closely related to inflammatory indicators. Preoperative inflammatory-specific indicators, when combined with other clinical factors, significantly enhance the diagnosis and management of CRC patients with intestinal obstruction.

Abbreviations

CRC	Colorectal cancer
CRP	C-reactive protein
IL-6	Interleukin-6
CPIS	CRC peculiar inflammatory score
AJCC	American Joint Committee on Cancer
BMI	Body mass index
T	Tumor
N	Regional lymph node
M	Metastasis
STM	Serum tumor marker
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
CEA	Carcinoembryonic antigen
CA19-9	Carbohydrate antigen 19–9
CA125	Carbohydrate antigen 125
CA72-4	Carbohydrate antigen 72–4
NLR	Neutrophil to lymphocyte ratio
PLR	Platelet to lymphocyte ratio
LMR	Lymphocyte to monocyte ratio
SII	Systemic immune inflammation index
PNI	Prognostic nutritional index
ALRI	Alanine transaminase to lymphocyte ratio index
ALBI	Albumin bilirubin index
TB	Total bilirubin
MELD	Model end stage liver disease model
INR	International normalized ratio
ROC	Receiver operating characteristic
C-index	Consistency index
OR	Odds ratio
CI	Confidence interval
AUC	Area under curve
AUROC	Area under the receiver operating characteristic curve
DCA	Decision curve analysis

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Authors' contributions

Wentai Cai and Zhenzhou Li collected and integrated clinical data of patients of Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan. Wentai Cai fulfilled the whole statistical work and analysed the outcome validate the statistical value. Wentai Cai prepared tables and figures. Bo Liu and Yinghao Cao designed the program and applied for the funding, supervised and adjusted this research. Wentai Cai, Zhenzhou Li, Bo Liu and Yinghao Cao reviewed and edited the manuscript.

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Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Wuhan Union Hospital (No. 2018-S377).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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