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ABOUT COVER

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The primary aim of *World Journal of Gastrointestinal Surgery* (WJGS, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc.*

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Retrospective Study

Preoperative neutrophil-to-lymphocyte ratio predicts symptomatic anastomotic leakage in elderly colon cancer patients: Multicenter propensity score-matched analysis

Chao-Yang Wang, Xiao-Long Li, Xiao-Long Ma, Xiong-Fei Yang, Yong-Yong Liu, Yong-Jiang Yu

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Abstract

BACKGROUND

The neutrophil-to-lymphocyte ratio (NLR), a composite inflammatory biomarker, is associated with the prognosis in patients with colorectal tumors. However, whether the NLR can be used as a predictor of symptomatic postoperative anastomotic leakage (AL) in elderly patients with colon cancer is unclear.

AIM

To assess the role of the NLR in predicting the occurrence of symptomatic AL after surgery in elderly patients with colon cancer.

METHODS

Data from elderly colon cancer patients who underwent elective radical colectomy with anastomosis at three centers between 2018 and 2022 were retrospectively analyzed. Receiver operating characteristic curve analysis was performed to determine the best predictive cutoff value for the NLR. Twenty-two covariates

were matched using a 1:1 propensity score matching method, and univariate and multivariate logistic regression analyses were used to determine risk factors for the development of postoperative AL.

RESULTS

Of the 577 patients included, 36 (6.2%) had symptomatic AL. The optimal cutoff value of the NLR for predicting AL was 2.66. After propensity score matching, the incidence of AL was significantly greater in the ≥ 2.66 NLR subgroup than in the < 2.66 NLR subgroup (11.5% *vs* 2.5%; $P = 0.012$). Univariate logistic regression analysis revealed statistically significant correlations between blood transfusion intraoperatively and within 2 d postoperatively, preoperative albumin concentration, preoperative prognostic nutritional index, and preoperative NLR and AL occurrence ($P < 0.05$); multivariate logistic regression analysis revealed that an NLR ≥ 2.66 [odds ratio (OR) = 5.51; 95% confidence interval (CI): 1.50-20.26; $P = 0.010$] and blood transfusion intraoperatively and within 2 d postoperatively (OR = 2.52; 95% CI: 0.88-7.25; $P = 0.049$) were risk factors for the occurrence of symptomatic AL.

CONCLUSION

A preoperative NLR ≥ 2.66 and blood transfusion intraoperatively and within 2 d postoperatively are associated with a higher incidence of postoperative symptomatic AL in elderly patients with colon cancer. The preoperative NLR has predictive value for postoperative symptomatic AL after elective surgery in elderly patients with colon cancer.

Key Words: Age; Colon cancer; Anastomotic leak; Neutrophil-to-lymphocyte ratio; Propensity score-matched

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Core Tip: The relationship between the preoperative neutrophil-to-lymphocyte ratio (NLR) and postoperative symptomatic anastomotic leakage (AL) in elderly patients with colon cancer was investigated in this study primarily. The findings showed that a higher preoperative NLR corresponded to a greater incidence of postoperative symptomatic AL. Moreover, in elderly patients with colon cancer after elective surgery, the preoperative NLR may serve as a predictor of postoperative symptomatic AL.

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INTRODUCTION

Older patients with colon cancer are becoming more common as the global elderly population continues to grow[1]. Increasing age also increases the risk of complications during and after colorectal surgery. Anastomotic leakage (AL) is a serious complication after colorectal surgery and may increase the risk of postoperative death in elderly patients[2] and severely affect the prognosis. Therefore, early prediction of the probability of AL occurrence and timely preventive measures are important for ensuring surgical safety and patient prognosis.

In recent years, various inflammatory response markers, such as the C-reactive protein-to-albumin ratio, platelet-to-lymphocyte ratio, and neutrophil-to-lymphocyte ratio (NLR), have been shown to be highly useful for predicting postoperative complications and prognosis in patients with colorectal cancer[3-5]. The effect of elevated peripheral blood NLRs on postoperative complications, cancer prognosis, and patient survival related to colorectal cancer has been confirmed by previous studies[6-9]. However, there are few data related to the role of the NLR in predicting the postoperative occurrence of AL in elderly patients with colon cancer. Therefore, in this study, we evaluated the role of the preoperative NLR as a predictive marker for symptomatic AL after radical resection in elderly patients with colon cancer.

MATERIALS AND METHODS

Patients and data collection

Clinical data from elderly patients (≥ 65 years old) with primary colon cancer who underwent radical colon cancer surgery at the First Hospital of Lanzhou University, the Second Hospital of Lanzhou University, or Gansu Provincial People's Hospital from January 2018 to December 2022 were retrospectively collected. The clinicopathologic characteristics of these patients included the following: Basic information including sex, age, body mass index (BMI), smoking status, history of abdominal surgery, nonsteroidal drug use, hypertension, diabetes mellitus, pulmonary disease, and

neoadjuvant chemotherapy; surgical information including the American Society of Anesthesiologists (ASA) score, surgical approach (open/laparoscopic/robotic), anastomotic approach (end-to-end/end-to-lateral/lateral-to-lateral), and blood transfusion intraoperatively and within 2 d postoperatively; tumor pathological characteristics including tumor location, T-stage, N-stage, and tumor diameter; and serological examination including preoperative neutrophil count, preoperative lymphocyte count, preoperative hemoglobin, preoperative serum albumin (ALB) concentration, and carcinoembryonic antigen (CEA). The relevant preoperative serological indices were collected within 1 wk before surgery. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Medical Ethics Committee of the First Hospital of Lanzhou University (leading center of the study, approval No. LDYYLL-2023-363). The requirement for informed consent was waived by the Medical Ethics Committee of the First Hospital of Lanzhou University due to the retrospective nature of the study and the absence of any risk.

Definition

The diagnosis of AL included three main aspects: Clinical symptoms, drainage fluid characteristics, and abdominal computed tomography (CT) scans. Patients with clinical symptoms (such as fever) and signs of peritonitis underwent CT for further diagnosis. AL was classified as asymptomatic (grade A) or symptomatic (grades B and C) based on severity and clinical signs. Symptomatic AL required aggressive therapeutic intervention (such as drainage and irrigation, antibiotics, and endoscopic surgery) or secondary surgical treatment and was diagnosed if one of the following manifestations was present: (1) Abnormal fluid such as pus and intestinal contents draining from the postoperative abdominal drainage tube; or (2) Fluid or gas collection around the anastomosis seen on abdominal CT or contrast enema. The follow-up for AL was within 15 d postoperatively. NLR was calculated as neutrophil count ($10^9/L$)/lymphocyte count ($10^9/L$), and prognostic nutritional index (PNI) was calculated as serum ALB (g/L) + $5 \times$ lymphocyte count ($10^9/L$).

Inclusion and exclusion criteria

The inclusion criteria were as follows: ≥ 65 years of age, pathologically confirmed primary colon cancer, elective radical resection of colon cancer with one-stage anastomosis, and complete clinical and pathological data. The exclusion criteria were as follows: Patients with grade A AL without specific clinical management, patients with intraoperative prophylactic stoma, patients with postoperative pathologic results showing M1 stage, and patients with incomplete postoperative data.

Propensity score matching and statistical analysis

A database was created in Excel, a propensity score-matched (PSM) analysis was performed with R-Studio (2023.03.1 + 446), and the data analysis was performed with SPSS 26.0 software, with the significance set at $P < 0.05$. In all cohorts, the normality of the continuous variables was assessed by the Shapiro-Wilcoxon test, and continuous variables with a normal distribution are presented as the mean \pm SD. Continuous data not conforming to a normal distribution are presented as the median (interquartile range) and were further analyzed by the independent Student's *t* test or Mann-Whitney *U* test. Categorical variables are expressed as frequencies (percentages), and comparisons were made using the χ^2 test, Fisher's exact test, or rank sum test. Receiver operating characteristic (ROC) curve analysis was used to identify the best critical value for the NLR prediction of AL.

A 1:1 PSM analysis was performed using the nearest neighbor method. The caliper value was set to 0.2 times the standard deviation of the propensity score. To reduce selection bias and confounding factors, logistic regression analysis was used to calculate propensity scores for age, sex, BMI, smoking history, abdominal surgery history, nonsteroidal drug use, hypertension, diabetes mellitus, lung disease, neoadjuvant chemotherapy, tumor location, ASA classification, surgical approach, anastomosis, blood transfusion intraoperatively and within 2 d postoperatively, T stage, N stage, tumor diameter, CEA, preoperative hemoglobin, preoperative ALB, and preoperative PNI. The standardized mean difference (SMD) was measured to determine the balance between the two groups before and after propensity score matching. An SMD of < 0.2 indicated that an adequate balance was achieved between the two groups. After matching, covariates with $P < 0.05$ in the univariate logistic regression analysis were entered into the multivariate logistic regression analysis to determine the risk factors for the occurrence of postoperative symptomatic AL.

RESULTS

Study population and clinical characteristics

The study population enrollment process is shown in Figure 1. A total of 577 patients were ultimately included in the present study, 36 of whom (6.2%) developed symptomatic AL. The basic, preoperative, intraoperative, and postoperative data of the patients are shown in Table 1. Sex, blood transfusion intraoperatively and within 2 d postoperatively, N stage, preoperative ALB level, preoperative NLR, and preoperative PNI were significantly different between the AL group and the group without AL ($P < 0.05$).

NLR

The continuous variable NLR was used as the test variable, and the dichotomous variable AL was used as the outcome variable. ROC curve analysis revealed that the area under the curve for the preoperative NLR was 0.683 [95% confidence interval (CI): 0.612-0.755]. For all patients, the sensitivity (0.861), specificity (0.543), and Youden index (0.405) of the NLR in predicting the occurrence of postoperative symptomatic AL in elderly patients undergoing radical resection for colon

Table 1 Patient clinical characteristics, *n* (%)

Variable	All patients (<i>n</i> = 577)	Non-AL patients (<i>n</i> = 541)	AL patients (<i>n</i> = 36)	Statistical value	<i>P</i> value
Gender				$\chi^2 = 6.189$	0.013
Female	276 (47.8)	266 (49.2)	10 (27.8)		
Male	301 (52.2)	275 (50.8)	26 (72.2)		
Age (yr)	71.0 (10.0)	71.0 (10.0)	72.0 (8.5)	$Z = -1.005$	0.315
BMI (kg/m ²)	22.81 \pm 3.43	22.79 \pm 3.44	23.16 \pm 3.25	$t = -0.627$	0.531
Smoking				$\chi^2 = 0.866$	0.352
No	393 (68.1)	371 (68.6)	22 (61.1)		
Yes	184 (31.9)	170 (31.4)	14 (38.9)		
History of abdominal surgery				$\chi^2 = 0.086$	0.770
No	413 (71.6)	388 (71.7)	25 (69.4)		
Yes	164 (28.4)	153 (28.3)	11 (30.6)		
Nonsteroidal drug use				$\chi^2 = 0.000$	1.000
No	524 (90.8)	491 (90.8)	33 (91.7)		
Yes	53 (9.2)	50 (9.2)	3 (8.3)		
Lung disease				$\chi^2 = 0.061$	0.804
No	316 (54.8)	297 (54.9)	19 (52.8)		
Yes	261 (45.2)	244 (45.1)	17 (47.2)		
Hypertension				$\chi^2 = 2.362$	0.124
No	381 (66.0)	353 (65.3)	28 (77.8)		
Yes	196 (34.0)	188 (34.7)	8 (22.2)		
Diabetes mellitus				$\chi^2 = 1.203$	0.273
No	486 (84.2)	458 (84.7)	28 (77.8)		
Yes	91 (15.8)	83 (15.3)	8 (22.2)		
Neoadjuvant chemotherapy				- ¹	0.124
No	567 (98.3)	533 (98.5)	34 (94.4)		
Yes	10 (1.7)	8 (1.5)	2 (5.6)		
Tumor location				- ¹	0.422
Right hemicolon	276 (47.8)	261 (48.2)	15 (41.7)		
Transverse colon	29 (5.0)	28 (5.2)	1 (2.8)		
Left hemicolon	64 (11.1)	57 (10.5)	7 (19.4)		
Sigmoid colon	208 (36.1)	195 (36.1)	13 (36.1)		
ASA classification				$\chi^2 = 1.389$	0.499
1	9 (1.6)	9 (1.7)	0 (0.0)		
2	429 (74.4)	404 (74.7)	25 (69.4)		
3	139 (24.0)	128 (23.6)	11 (30.6)		
Surgical approach				$\chi^2 = 4.110$	0.128
Open	171 (29.6)	155 (28.7)	16 (44.4)		
Laparoscopic	354 (61.4)	337 (62.2)	17 (47.2)		
Robotic	52 (9.0)	49 (9.1)	3 (8.4)		
Anastomosis				$\chi^2 = 0.055$	0.973

End-to-end anastomosis	198 (34.3)	185 (34.2)	13 (36.1)		
End-lateral anastomosis	248 (43.0)	233 (43.1)	15 (41.7)		
Lateral anastomosis	131 (22.7)	123 (22.7)	8 (22.2)		
Blood transfusion intraoperatively and within 2 d postoperatively				$\chi^2 = 20.869$	< 0.001
No	427 (74.0)	412 (76.2)	15 (41.7)		
Yes	150 (26.0)	129 (23.8)	21 (58.3)		
T stage				$\chi^2 = 0.1$	0.444
1	36 (6.2)	36 (6.7)	0 (0.0)		
2	60 (10.4)	57 (10.5)	3 (8.3)		
3	371 (64.3)	346 (64.0)	25 (69.4)		
4	110 (19.1)	102 (18.8)	8 (22.3)		
N stage				$\chi^2 = 7.778$	0.020
0	355 (61.5)	340 (62.9)	15 (41.7)		
1	138 (23.9)	127 (23.5)	11 (30.6)		
2	84 (14.6)	74 (13.7)	9 (27.7)		
Tumor diameter (cm)	4.0 (3.0)	4.0 (3.0)	4.75 (2.6)	$Z = -0.660$	0.509
CEA (ng/mL)	3.78 (5.99)	3.66 (5.82)	5.11 (10.02)	$Z = -1.468$	0.142
Preoperative hemoglobin (g/L)	119.0 (40.0)	119.0 (40.0)	118.5 (32.75)	$Z = -0.476$	0.634
Preoperative albumin (g/L)	38.23 \pm 4.69	38.40 \pm 4.69	35.68 \pm 3.81	$t = 4.076$	< 0.001
Preoperative NLR	2.62 (1.93)	2.55 (1.91)	3.36 (1.70)	$Z = -3.688$	< 0.001
Preoperative PNI	45.58 \pm 5.94	45.86 \pm 5.95	41.41 \pm 3.94	$t = 6.325$	< 0.001

¹Variables were tested using Fisher's exact probability method with no statistical values.

AL: Anastomotic leakage; BMI: Body mass index; ASA: American Society of Anesthesiologists; CEA: Carcinoembryonic antigen; NLR: Neutrophil-to-lymphocyte ratio; PNI: Prognostic nutritional index.

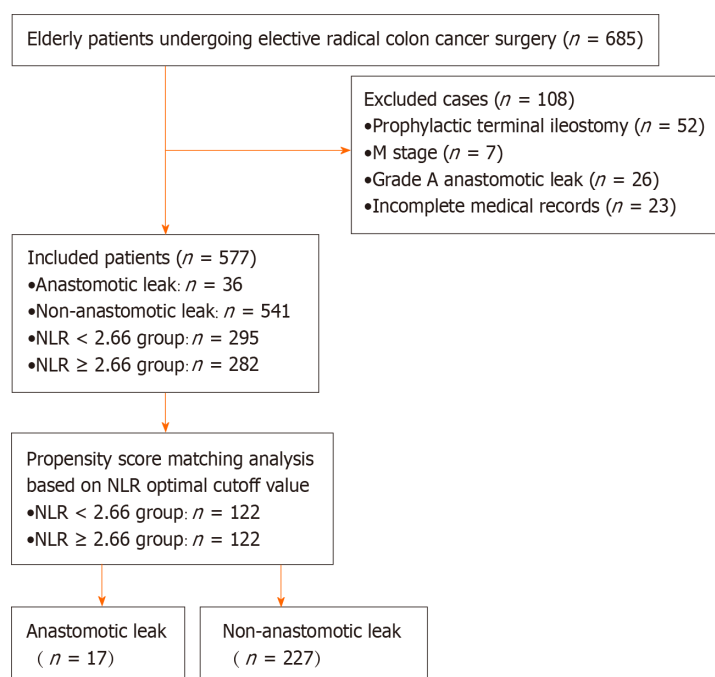


Figure 1 Study population enrollment process. NLR: Neutrophil-to-lymphocyte ratio.

cancer were highest when the NLR was 2.66 (Figure 2).

PSM based on the optimal cutoff value for the NLR

Of the 577 patients, 295 (51.1%) had an NLR < 2.66, and 282 (48.9%) had an NLR \geq 2.66 (Table 2). After 1:1 PSM, 122 matched pairs were generated, and patients were divided into NLR < 2.66 ($n = 122$) and NLR \geq 2.66 ($n = 122$) groups (Table 2). All covariates were well balanced with an SMD less than 0.2, and the difference between the NLR < 2.66 and NLR \geq 2.66 groups was not statistically significant (Table 2). Before (1.4% *vs* 11.3%, $P < 0.001$) (Figure 3A) and after (2.5% *vs* 11.5%, $P = 0.012$) (Figure 3B) PSM, the incidence of symptomatic AL was significantly lower in the NLR < 2.66 subgroup than in the NLR \geq 2.66 subgroup.

Analysis of risk factors associated with AL after PSM

According to the univariate logistic regression analysis, blood transfusion intraoperatively and within 2 d postoperatively, preoperative ALB concentration, preoperative PNI, and preoperative NLR were associated with the occurrence of postoperative AL (Table 3). Multivariate logistic regression analysis revealed that intraoperative blood transfusion and postoperative blood transfusion within 2 d [odds ratio (OR) = 2.52; 95%CI: 0.88-7.25; $P = 0.049$] and a high NLR (\geq 2.66) (OR = 5.51; 95%CI: 1.50-20.26; $P = 0.010$) were significantly associated with the occurrence of symptomatic AL after radical resection for colon cancer in elderly individuals.

DISCUSSION

The main finding of this study was that the incidence of postoperative symptomatic AL in 577 elderly patients who underwent radical colon cancer resection was 6.2%. The optimal cutoff value of the preoperative NLR for predicting symptomatic AL after radical colon cancer resection was determined by the ROC curve to be 2.66. After PSM, the incidence of AL was significantly greater in the \geq 2.66 NLR subgroup than in the < 2.66 NLR subgroup, and a preoperative NLR \geq 2.66 was significantly associated with the occurrence of AL after radical colon cancer resection. In addition, the incidence of postoperative symptomatic AL was greater in elderly colon cancer patients who were transfused intraoperatively and within 2 d postoperatively than in those in the nontransfused group.

When inflammation and infection occur, neutrophils rapidly migrate to the site of inflammation, responding first to tissue damage and playing a key role in the host's resistance to infection[10]. Elevated peripheral blood neutrophil levels are characteristic of pathogenesis and are a hallmark of the inflammatory response. However, persistent neutrophilic infiltration is a hallmark of chronic inflammation and leads to tissue damage[11]. Furthermore, in one study, the number of lymphocytes involved in the immune state decreased with the progression of inflammatory disease, and this increase in lymphocyte count was a cause of decreased cellular immune function[12]. That is, cell-mediated immune responses are strongly dependent on lymphocytes. The NLR is an easily accessible marker identified as a good indicator of systemic inflammatory status in the general population[13]. The NLR has a better ability to predict systemic inflammation and prognosis than does the leukocyte, neutrophil, or lymphocyte count alone[14,15].

Previous studies have suggested that the post-colorectal AL may be associated with the NLR. First, Josse *et al*[16] reported that a preoperative NLR \geq 2.3 was significantly associated with postoperative complication rates and that the incidence of AL increased non-significantly. Subsequently, Miyakita *et al*[17] showed that a preoperative NLR \geq 2.21 was significantly associated with postoperative AL in patients with rectal cancer (OR = 4.51; $P = 0.0329$). In addition, Paliogiannis *et al*[9] showed that a higher NLR was associated with the occurrence of postoperative AL in patients undergoing elective colorectal surgery. According to our findings, high preoperative NLRs are a risk factor for the development of symptomatic AL after radical resection in elderly patients with colon cancer. The OR for the occurrence of symptomatic AL in the high NLR subgroup (\geq 2.66) was 5.51, indicating that the preoperative NLR may help to predict the risk of postoperative symptomatic AL in elderly patients with colon cancer before surgery, which could allow patients to take effective preventive measures. However, the predictive role of inflammatory indicators should be validated in larger clinical studies. In particular, for more effective prevention of AL occurrence, prevention methods should be explored through interventional prospective studies with risk stratification based on preoperative NLR values.

This study revealed that blood transfusion intraoperatively and within 2 d postoperatively was associated with the occurrence of postoperative symptomatic AL, which is consistent with previous findings[18,19]. Most of the transfusions were due to excessive surgical blood loss or severe anemia. Hemoglobin is associated with blood flow and oxygenation at the anastomotic margin and is an important factor in anastomotic healing. However, blood transfusion may lead to impaired blood rheology[20], which adversely affects microcirculation; transfusion may also induce immunosuppression [21], which increases the risk of infectious diseases around the anastomosis. Therefore, careful blood transfusion intraoperatively and within 2 d postoperatively may be an intervention to reduce the occurrence of postoperative AL in elderly patients undergoing radical colon cancer resection.

This study has several limitations. First, because this study was retrospective, we could not assess all the covariates that might have influenced the analysis. Therefore, our study may be affected to some extent by unavoidable selection bias. However, we performed a PSM analysis to minimize bias. Second, preoperative NLR values may be influenced by patients' infectious comorbidities, and there is no standard optimal cutoff value for the NLR. Therefore, these findings should be interpreted with caution. Third, further studies are needed to validate the relationship between the preoperative NLR and other postsurgical symptomatic ALs, as these parameters have not been specifically evaluated.

Table 2 Comparison of clinical characteristics before and after propensity score matching, *n* (%)

Variable	Before propensity score matching				After propensity score matching			
	NLR < 2.66 (<i>n</i> = 295)	NLR ≥ 2.66 (<i>n</i> = 282)	SMD	<i>P</i> value	NLR < 2.66 (<i>n</i> = 122)	NLR ≥ 2.66 (<i>n</i> = 122)	SMD	<i>P</i> value
Gender			0.237	0.005			0.131	0.305
Female	158 (53.6)	118 (41.8)			55 (45.1)	63 (51.6)		
Male	137 (46.4)	164 (58.2)			67 (54.9)	59 (48.4)		
Age (yr)	70.0 (9.0)	72.0 (9.0)	0.232	0.004	70.0 (9.8)	71.0 (7.8)	0.032	0.722
BMI (kg/m ²)	23.20 ± 3.49	22.40 ± 3.31	0.241	0.005	22.51 ± 3.20	22.67 ± 3.08	0.052	0.689
Smoking			0.230	0.004			0.119	0.118
No	217 (73.6)	176 (62.4)			82 (67.2)	93 (76.2)		
Yes	78 (26.4)	106 (37.6)			40 (32.8)	29 (23.8)		
History of abdominal surgery			0.065	0.443			0.076	0.560
No	207 (70.2)	206 (73.1)			88 (72.1)	92 (75.4)		
Yes	88 (29.8)	76 (26.9)			34 (27.9)	30 (24.6)		
Nonsteroidal drug use			0.022	0.795			0.063	0.641
No	267 (90.5)	257 (91.1)			111 (91.0)	113 (92.6)		
Yes	28 (9.5)	25 (8.9)			11 (9.0)	9 (7.4)		
Lung disease			0.214	0.010			0.117	0.364
No	177 (60.0)	139 (49.3)			67 (54.9)	74 (60.7)		
Yes	118 (40.0)	143 (50.7)			55 (45.1)	48 (39.3)		
Hypertension			0.047	0.573			0.018	0.891
No	198 (67.1)	183 (64.9)			82 (67.2)	83 (68.0)		
Yes	97 (32.9)	99 (35.1)			40 (32.8)	39 (32.0)		
Diabetes mellitus			0.100	0.207			0.022	0.864
No	254 (86.1)	232 (82.3)			101 (82.8)	102 (83.6)		
Yes	41 (13.9)	50 (17.7)			21 (17.2)	20 (16.4)		
Neoadjuvant chemotherapy			0.128	0.376			0.065	1.000
No	288 (97.6)	279 (98.9)			119 (97.5)	120 (98.4)		
Yes	7 (2.4)	3 (1.1)			3 (2.5)	2 (1.6)		
Tumor location			0.210	< 0.001			0.045	0.211
Right hemicolon	126 (42.7)	150 (53.2)			59 (48.4)	59 (48.4)		
Transverse colon	8 (2.7)	21 (7.5)			2 (1.6)	8 (6.6)		
Left hemicolon	30 (10.2)	34 (12.1)			17 (13.9)	19 (15.5)		
Sigmoid colon	131 (44.4)	77 (27.2)			44 (36.1)	36 (29.5)		
ASA classification			0.118	0.147			0.096	0.272
1	6 (2.0)	3 (1.1)			0 (0.0)	3 (2.5)		
2	227 (77.0)	202 (71.6)			98 (80.3)	93 (76.2)		
3	62 (21.0)	77 (27.3)			24 (19.7)	26 (21.3)		
Surgical approach			0.279	< 0.001			0.099	0.330
Open	65 (22.0)	106 (37.6)			37 (30.3)	36 (29.5)		
Laparoscopic	201 (68.2)	153 (54.3)			76 (62.3)	70 (57.4)		
Robotic	29 (9.8)	23 (8.1)			9 (7.4)	16 (13.1)		

Anastomosis			0.194	0.078			0.091	0.786
End-to-end anastomosis	114 (38.6)	84 (29.8)			40 (32.8)	35 (28.7)		
End-lateral anastomosis	117 (39.7)	131 (46.5)			52 (42.6)	55 (45.1)		
Lateral anastomosis	64 (21.7)	67 (23.7)			30 (24.6)	32 (26.2)		
Blood transfusion intraoperatively and within 2 d postoperatively			0.318	< 0.001			0.000	1.000
No	240 (81.3)	187 (66.3)			91 (74.6)	91 (74.6)		
Yes	55 (18.7)	95 (33.7)			31 (25.4)	31 (25.4)		
T stage			0.339	< 0.001			0.066	0.944
1	27 (9.2)	9 (3.2)			6 (4.9)	8 (6.6)		
2	36 (12.2)	24 (8.5)			11 (9.0)	12 (9.8)		
3	197 (66.8)	174 (61.7)			85 (69.7)	82 (67.2)		
4	35 (11.8)	75 (26.6)			20 (16.4)	20 (16.4)		
N stage			0.147	0.191			0.116	0.655
0	192 (65.1)	163 (57.8)			75 (61.5)	68 (55.7)		
1	63 (21.4)	75 (26.6)			29 (23.8)	34 (27.9)		
2	40 (13.5)	44 (15.6)			18 (14.7)	20 (16.4)		
Tumor diameter (cm)	4.00 (2.00)	5.00 (2.50)	0.427	< 0.001	4.00 (3.0)	4.75 (3.0)	0.051	0.824
CEA (ng/mL)	3.33 (4.74)	4.32 (6.97)	0.107	0.008	3.52 (5.57)	4.21 (5.59)	0.118	0.560
Preoperative hemoglobin (g/L)	126.00 (39.00)	109.50 (37.00)	0.332	< 0.001	119.5 (43.5)	117.5 (43.5)	0.035	0.711
Preoperative albumin (g/L)	39.00 ± 4.16	37.42 ± 5.06	0.311	< 0.001	38.34 ± 4.29	38.29 ± 4.77	0.009	0.944
Preoperative PNI	48.02 ± 5.22	43.04 ± 5.58	0.892	< 0.001	45.31 ± 4.99	45.16 ± 5.26	0.030	0.812

SMD: Standardized mean difference; BMI: Body mass index; ASA: American Society of Anesthesiologists; CEA: Carcinoembryonic antigen; NLR: Neutrophil-to-lymphocyte ratio; PNI: Prognostic nutritional index.

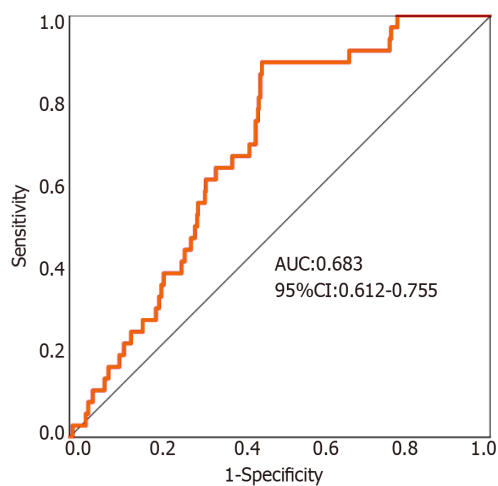


Figure 2 Receiver operating characteristic curve analysis of the ability of preoperative neutrophil-to-lymphocyte to predict symptomatic anastomotic leakage. AUC: Area under the curve; CI: Confidence interval.

CONCLUSION

Symptomatic AL is associated with a high preoperative NLR and blood transfusion intraoperatively and within 2 d postoperatively. In elderly patients who undergo radical colon cancer resection, a preoperative NLR ≥ 2.66 is significantly associated with the likelihood of postoperative symptomatic AL occurrence. We recommend the preoperative use of the NLR as a predictive marker for the risk of AL for better preoperative evaluation and selection of the best surgical and care plan for elderly patients undergoing elective radical colon cancer resection.

Table 3 Univariate and multivariate logistic regression analyses of risk factors associated with the occurrence of symptomatic anastomotic leakage after propensity score matching

Variable	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P value	OR (95%CI)	P value
Gender				
Female ¹				
Male	1.37 (0.50-3.72)	0.540		
Age (yr)	1.00 (0.91-1.09)	0.949		
BMI (kg/m ²)	0.98 (0.84-1.15)	0.812		
Smoking				
No ¹				
Yes	0.77 (0.24-2.44)	0.653		
History of abdominal surgery				
No ¹				
Yes	1.19 (0.40-3.51)	0.757		
Nonsteroidal drug use				
No ¹				
Yes	1.55 (0.33-7.31)	0.581		
Lung disease				
No ¹				
Yes	0.73 (0.26-2.05)	0.551		
Hypertension				
No ¹				
Yes	0.86 (0.29-2.54)	0.787		
Diabetes mellitus				
No ¹				
Yes	1.07 (0.29-3.89)	0.923		
Neoadjuvant chemotherapy				
No ¹				
Yes	3.48 (0.37-33.03)	0.277		
Tumor location				
Right hemicolon ¹				
Transverse colon	1.53 (0.17-13.61)	0.704		
Left hemicolon	1.25 (0.31-4.98)	0.752		
Sigmoid colon	0.92 (0.29-2.91)	0.883		
ASA classification				
< 2 ¹				
3	1.211 (0.377-3.887)	0.748		
Surgical approach				
Open ¹				
Laparoscopic	0.65 (0.22-1.94)	0.438		
Robotic	1.52 (0.35-6.60)	0.574		
Anastomosis				

End-to-end anastomosis ¹				
End-lateral anastomosis	1.43 (0.42-4.95)	0.568		
Lateral anastomosis	1.56 (0.40-6.07)	0.523		
Blood transfusion intraoperatively and within 2 d postoperatively				
No ¹				
Yes	2.85 (1.05-7.74)	0.040	2.52 (0.88-7.25)	0.049
T stage				
≤ 2 ¹				
≥ 3	0.822 (0.224-3.014)	0.768		
N stage				
0 ¹				
1	1.28 (0.41-4.00)	0.667		
2	1.28 (0.33-4.97)	0.725		
Tumor diameter (cm)	1.01 (0.81-1.26)	0.931		
CEA (ng/mL)	1.00 (0.99-1.01)	0.636		
Preoperative hemoglobin (g/L)	1.01 (0.99-1.03)	0.327		
Preoperative albumin (g/L)	0.85 (0.75-0.97)	0.013	0.99 (0.73-1.35)	0.946
Preoperative PNI	0.86 (0.76-0.96)	0.010	0.88 (0.66-1.17)	0.380
Preoperative NLR				
NLR < 2.66 ¹				
NLR ≥ 2.66	5.14 (1.44-18.38)	0.012	5.51 (1.50-20.26)	0.010

¹Control group.

BMI: Body mass index; ASA: American Society of Anesthesiologists; CEA: Carcinoembryonic antigen; NLR: Neutrophil-to-lymphocyte ratio; PNI: Prognostic nutritional index; OR: Odds ratio; CI: Confidence interval.

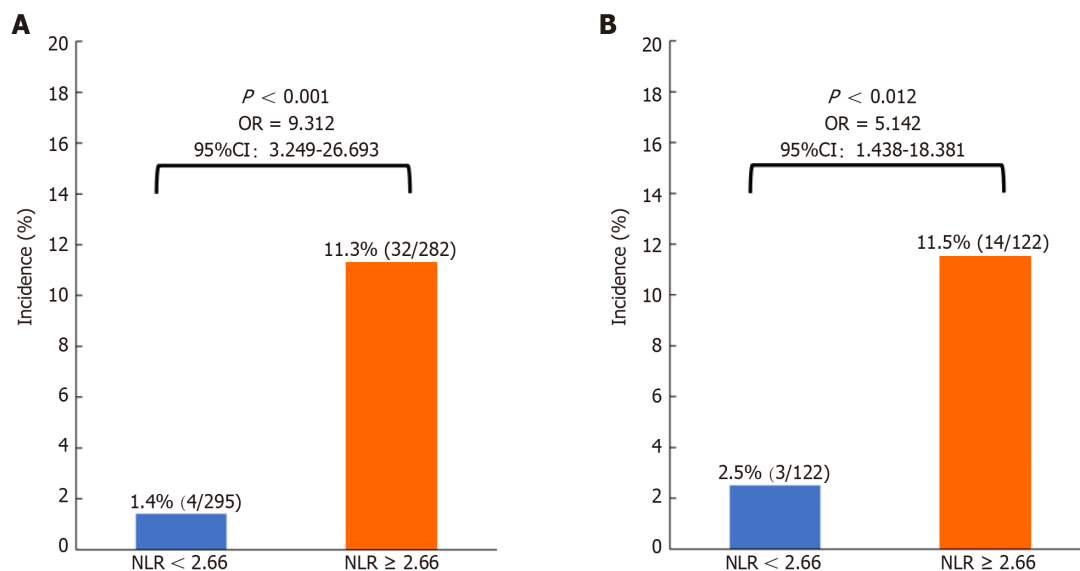


Figure 3 Comparison of the incidence of symptomatic anastomotic leakage between the neutrophil-to-lymphocyte ratio < 2.66 and neutrophil-to-lymphocyte ratio ≥ 2.66 groups before and after propensity score matching. A: Before propensity score matching; B: After propensity score matching. NLR: Neutrophil-to-lymphocyte ratio; OR: Odds ratio; CI: Confidence interval.

ARTICLE HIGHLIGHTS

Research background

The neutrophil-to-lymphocyte ratio (NLR) is a complex inflammatory biomarker that is associated with prognosis in patients with colorectal tumors. However, it is unclear whether NLR can be used as a predictor of postoperative symptomatic anastomotic leakage (AL) in elderly colon cancer patients.

Research motivation

The discovery of biomarkers able to predict AL early after colorectal surgery would bring consistent advantages in the management and outcomes of this complication. NLR is a low-cost, easy-to-perform, and widely available index. Here, we aimed to investigate the NLR as an early available predictive marker for AL.

Research objectives

To assess the role of preoperative NLR in predicting the development of symptomatic AL after surgery in elderly patients with colon cancer by using propensity score matched (PSM) analysis.

Research methods

We used a retrospective analysis to examine data from elderly colon cancer patients admitted between January 2018 and December 2022 at three large medical centers. The best predictive cutoff value for NLR was determined using the receiver operating characteristic curve. All covariates were matched using a 1:1 PSM method, and finally, all variables were analyzed using univariate and multivariate logistic regression analyses to determine the correlation between NLR and the occurrence of postoperative AL and other associated risk factors.

Research results

Among 577 patients, 36 (6.2%) experienced symptomatic AL. The optimal NLR cutoff for predicting AL was 2.66. After propensity score matching, the incidence of AL was significantly higher in the NLR ≥ 2.66 subgroup compared to the NLR < 2.66 subgroup (11.5% *vs* 2.5%; $P = 0.012$). Univariate logistic regression analysis showed significant differences in blood transfusion intraoperatively and within 2 d postoperatively, preoperative albumin concentration, preoperative prognostic nutritional index, and preoperative NLR regarding AL occurrence ($P < 0.05$); multivariate logistic regression analysis identified NLR ≥ 2.66 [odds ratio (OR) = 5.51; 95% confidence interval (CI): 1.50-20.26; $P = 0.010$] and blood transfusion intraoperatively and within 2 d postoperatively (OR = 2.52; 95% CI: 0.88-7.25; $P = 0.049$) as risk factors for symptomatic AL occurrence.

Research conclusions

High preoperative NLR (≥ 2.66) and intraoperative, as well as postoperative (within 2 d), blood transfusions are associated with increased postoperative symptomatic AL in elderly colon cancer patients. Preoperative NLR serves as a predictor for postoperative symptomatic AL after elective surgery for elderly colon cancer patients.

Research perspectives

In the future, we plan to further confirm the clinical applicability of NLR using a prospective randomized controlled trial approach.

FOOTNOTES

Author contributions: Wang CY and Li XL performed the study conceptualization and design, statistical analysis, and manuscript preparation; Wang CY, Ma XL, and Liu YY contributed to data acquisition; Yang XF, Liu YY, and Yu YJ contributed to data quality assessment; Li XL contributed to data interpretation; Wang CY drafted the initial manuscript; Yu YJ reviewed and revised the paper; and all authors have read and agreed to the published version of the manuscript.

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Informed consent statement: The requirement of informed consent was waived by the Medical Ethics Committee of the First Hospital of Lanzhou University due to the retrospective nature of the study and the absence of any risk.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: The data analyzed in this study is available from the corresponding author upon reasonable request.

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