

Blood Indices as Predictors of Anastomotic Leak after Colorectal Surgery – Is It Useful? A Retrospective Analysis

Abdulaziz M. Saleem, MBBS, FRCSC* Abdullah Abed G. Alshareef, MBBS** Mai Kadi, MBBS*** Abdullah Musaad A. Alghamdi, MBBS**** Muhannad Saad A. Alabbasi, MBBS***** Ahmed Mihdhar O. Saggaf, MBBS***** Munaser Alamoodi, MBBS* Ghada Enani, MBBS, FRCSC* Alaa Shabkiah, MBBS, SBGS, FEBS, MIPDEd***** Ali Farsi, MBBS, FRCSC* Mohammed Alharthi, MBBS, DES, DESC*

ABSTRACT

Anastomotic leak (AL) remains a major complication after colorectal surgery, with significant morbidity and mortality implications. The clinical utility of routine blood indices in predicting AL remains insufficiently characterized. This study aimed to evaluate whether blood indices derived from daily postoperative blood work could serve as early predictors of AL following colorectal anastomosis. This single-center retrospective cohort study was conducted at King Abdulaziz University Hospital between 2012 and 2020. We included 441 adult patients who underwent elective or emergency colorectal surgery with a primary anastomosis involving at least one colonic or rectal segment. Patients were excluded if they had a defunctioning stoma, preoperative infection, active inflammatory bowel disease, immunosuppressive therapy, or chronic corticosteroid use. AL was defined clinically or radiologically: on CT imaging, this included anastomotic collection within 5 cm, extraluminal contrast leak, or pericolic free air; intraoperatively, it was confirmed by visible dehiscence or anastomotic discontinuity. Preoperative and daily postoperative complete blood counts (days 1–7) were collected. Indices analyzed included white blood cell (WBC) count, absolute neutrophil count, red blood cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), derived neutrophil-to-lymphocyte ratio (dNLR = absolute neutrophil count / [WBC – absolute neutrophil count]), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR). Normality was assessed using the Shapiro–Wilk test. Independent-samples t-tests were used for normally distributed variables; non-parametric alternatives were considered where appropriate. Multiple comparisons were adjusted using the Bonferroni correction, and adjusted p-values are reported. Pearson's correlation assessed linear relationships, and receiver operating characteristic (ROC) curve analysis with area under the curve (AUC) estimation was performed to assess predictive accuracy. The mean age was 52 years; 261 (59.2%) were male and 283 (64.2%) underwent open surgery. AL was significantly associated with diabetes mellitus, high ASA class (II–III: 82.7%), and open operative approach. Preoperatively, WBC count was higher in the AL group (mean 8.66 vs $7.56 \times 10^9/L$; adjusted $p = 0.049$), as was absolute neutrophil count (6.60 vs $4.93 \times 10^9/L$; adjusted $p = 0.009$); LMR was lower in the AL group. Postoperatively, WBC and neutrophil counts were significantly elevated on POD4–POD7 in patients with AL. NLR was significantly higher on POD6 in the AL group (8.98 vs 5.82 ; adjusted $p < 0.05$); NLR at POD7 did not reach statistical significance ($p = 0.051$) and should not be regarded as a confirmed predictor. dNLR was significantly elevated from POD5 through POD7 in the AL group (mean 4.31 – 4.42 vs 2.74 – 2.83). Among all indices assessed by ROC analysis, dNLR at POD7 demonstrated the strongest overall predictive accuracy (AUC 0.727; 95% CI: 0.611–0.843; $p = 0.001$), with a cut-off of 2.8 yielding sensitivity 71.4% and specificity 60.2%. WBC count at POD7 predicted AL with an AUC of 0.689 (95% CI: 0.555–0.823; $p = 0.007$), sensitivity 76.2%, specificity 60.2% at a cut-off of $9.1 \times 10^9/L$. Absolute neutrophil count at POD7 (AUC 0.716; $p = 0.002$) outperformed WBC at the same time point, with a cut-off of $6.7 \times 10^9/L$ yielding sensitivity 76.2% and specificity 63.7%. RDW, LMR, and PLR did not differ significantly between groups. Routine blood indices, particularly dNLR — the single strongest predictor identified (AUC 0.727 at POD7) — as well as WBC count, absolute neutrophil count, and NLR, demonstrate a time-dependent association with AL after colorectal surgery, becoming most discriminatory from POD4 onward. Their moderate predictive accuracy supports their use as adjuncts within composite risk stratification models rather than as standalone diagnostic tools. Prospective validation is warranted.

Keywords: *Anastomotic Leak; Blood Indices; White Blood Cell Count; Neutrophil-to-Lymphocyte Ratio; Derived NLR; Colorectal Surgery; Postoperative Complications*

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- * Department of Surgery, Faculty of Medicine
King Abdulaziz University, Jeddah, Saudi Arabia.
- ** Department of General Surgery, King Fahad General Hospital
Jeddah, Saudi Arabia.
- *** Department of Community Medicine, Faculty of Medicine
King Abdulaziz University, Jeddah, Saudi Arabia.
- **** Department of Internal Medicine, King Abdulaziz University Hospital
Jeddah, Saudi Arabia.
- ***** Department of Emergency Medicine, Alleith General Hospital
Alleith, Saudi Arabia.
- ***** Department of Surgery, King Abdulaziz Hospital (MOH)
Jeddah, Saudi Arabia.
- ***** Department of Surgery, International Medical Center
Jeddah, Saudi Arabia.

INTRODUCTION

Anastomotic leak (AL) is one of the most significant complications following colorectal anastomosis, carrying substantial morbidity and mortality. AL has been associated with increased risk of local recurrence and reduced long-term survival following oncological resections^{1,2}. Clinically, AL typically presents between postoperative days (POD) 5–7, with features including abdominal pain, fever, ileus, and leukocytosis. Computed tomography (CT) of the abdomen and pelvis remains the preferred diagnostic modality; however, early imaging in the first 1–3 days postoperatively frequently yields non-specific findings attributable to normal postoperative changes, unless a clear abnormality is identified³.

Considerable research effort has focused on identifying simple, widely available biochemical markers capable of detecting AL early in the postoperative course. C-reactive protein (CRP) has been the most extensively evaluated marker and has demonstrated diagnostic utility in several studies and meta-analyses^{3–5}. The combination of CRP with other markers, such as fecal calprotectin and intestinal fatty acid-binding protein, has been shown to further improve diagnostic accuracy^{4,6}. However, CRP assays are not universally available across all institutions, and cut-off values vary markedly between studies and between laparoscopic and open approaches⁵.

In standard clinical practice, patients undergoing major colorectal procedures receive daily routine blood counts in the early postoperative period. Despite their universal availability, the diagnostic utility of these routine hematological indices as early indicators of AL remains insufficiently characterized. This retrospective study aimed to systematically evaluate the predictive value of blood indices derived from routine daily blood work in detecting AL early following colorectal anastomosis.

MATERIALS AND METHODS

Reporting Standards: This study was reported in accordance with the Strengthening the Reporting of Cohort, Cross-Sectional, and Case-Control Studies in Surgery (STROCSS) 2021 guidelines⁷.

Study Design, Setting, and Period: This was a single-center retrospective cohort study conducted at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. Data were collected for patients who underwent colorectal surgery between 2012 and 2020. Ethical approval was obtained from the institutional review committee at King Abdulaziz University.

Patient Selection: A total of 441 patients were reviewed. Inclusion criteria required patients to have undergone elective or emergency colorectal surgery with a primary anastomosis in which at least one side involved the colon or rectum. Patients were excluded if they had: no anastomosis; a defunctioning proximal stoma at the time of index surgery; preoperative evidence of active infection; concurrent immunosuppressive or chronic corticosteroid therapy; or a known diagnosis of inflammatory bowel disease. Demographic data, American Society of Anesthesiologists (ASA) physical status classification, comorbidities, operative details, and postoperative course were recorded for all patients.

Definition and Diagnosis of Anastomotic Leak: AL was defined using combined clinical and radiological criteria. Radiological diagnosis was established on CT of the abdomen and pelvis when one or more of the following were identified: pericolic or pelvic collection within 5 cm of the anastomosis; extraluminal contrast leak; or free extraluminal air at the anastomotic site. In patients returned to the operating theatre, AL

was confirmed intraoperatively by visible anastomotic dehiscence or discontinuity.

Laboratory Indices: Complete blood counts were obtained preoperatively and on each of POD1–POD7. The following indices were calculated: white blood cell (WBC) count; absolute neutrophil count; red blood cell distribution width (RDW); neutrophil-to-lymphocyte ratio ($NLR = \text{absolute neutrophil count} / \text{absolute lymphocyte count}$); derived NLR ($dNLR = \text{absolute neutrophil count} / [\text{WBC} - \text{absolute neutrophil count}]$); lymphocyte-to-monocyte ratio ($LMR = \text{absolute lymphocyte count} / \text{absolute monocyte count}$); and platelet-to-lymphocyte ratio ($PLR = \text{platelet count} / \text{absolute lymphocyte count}$). RDW was included as a general marker of hematological stress reported in various surgical settings, to determine whether it holds predictive value in colorectal anastomotic complications.

Statistical Analysis: Statistical analysis was performed using IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA). Data distribution was assessed using the Shapiro–Wilk test. For indices satisfying normality assumptions, group comparisons were performed using the independent-samples t-test; the Mann–Whitney U test was considered for non-normally distributed variables. Bonferroni correction was applied for multiple comparisons; all p-values reported represent Bonferroni-adjusted values. Pearson's correlation coefficient was used to quantify linear relationships between continuous variables. Predictive accuracy was evaluated using ROC curve analysis; AUC, optimal cut-off values, and corresponding sensitivity and specificity are reported. A p-value of < 0.05 (post-correction) was considered statistically significant.

RESULTS

Patient Demographics and Baseline Characteristics

The study cohort comprised 441 patients, of whom 261 (59.2%) were male and 180 (40.8%) were female. The mean age was 52 years. Open surgery was performed in 283 patients (64.2%), with the remaining 158 (35.8%) undergoing a laparoscopic approach. Comorbidities included diabetes mellitus in 133 patients (30.2%), hypertension in 141 (32.0%), ischemic heart disease in 36 (8.2%), and heart failure in 10 (2.3%). Clinicopathological characteristics of the cohort are presented in Table 1.

Factors significantly associated with AL included diabetes mellitus, high ASA classification (class II or III accounted for 82.7% of AL cases), and an open operative approach.

Preoperative Blood Indices

Preoperative blood indices are compared between the AL and non-AL groups in Table 2. A statistically significant difference was observed in preoperative WBC count (mean 8.66 vs $7.56 \times 10^9/L$; adjusted $p = 0.049$), absolute neutrophil count (mean 6.60 vs $4.93 \times 10^9/L$; adjusted $p = 0.009$), and LMR (lower in the AL group; adjusted $p < 0.05$) between patients who developed AL and those who did not. No statistically significant differences were detected in preoperative monocyte count, absolute lymphocyte count, platelet count, RDW, NLR, or PLR.

Postoperative Blood Indices

Postoperative blood indices are summarized in Table 3. WBC count and absolute neutrophil count were significantly higher in the AL group on POD4 through POD7. On POD6, NLR was significantly elevated in the AL group compared with the non-AL group (mean 8.98 vs 5.82; adjusted $p < 0.05$). The dNLR was significantly higher in the AL group from POD5 through POD7, with mean values of 4.31–4.42

Table 1. Demographic and Co-morbidities of individuals with and without anastomotic leak (n=441)

		All	Anastomotic leak				p value
		n (%)	No AL=389 n	Yes=52 %	N	%	
Age	Mean (SD)	52.7 (17.3)	52.3	17.5	55.9	15.3	0.155
Gender	male	261 (59.2)	230	59.1	31	59.6	0.946
	female	180 (40.8)	159	40.9	21	40.4	
Anaesthesia type	General	437 (99.1)	385	99	52	100	0.764
	Spinal	01 (0.2)	1	0.3	0	0	
	Epidural	03 (0.7)	3	0.8	0	0	
ASA	NA	01 (0.2)	0	0	1	1.9	<0.001
	I	32 (7.3)	30	7.7	2	3.8	
	II	238 (54)	217	55.8	21	40.4	
	III	153 (34.7)	131	33.7	22	42.3	
	IV	17 (3.9)	11	2.8	6	11.5	
	Open	283 (64.2)	243	62.5	40	76.9	
Surgery type	Laparoscopy	158 (35.8)	146	37.5	12	23.1	0.041
	No	413 (93.7)	363	93.3	50	96.2	0.431
laparoscopic converted to open	Yes	28 (6.3)	26	6.7	2	3.8	
Diabetes mellitus	No	308 (69.8)	279	71.7	29	55.8	0.019
	Yes	133 (30.2)	110	28.3	23	44.2	
Hypertension	No	300 (68)	268	68.9	32	61.5	0.285
	Yes	141 (32)	121	31.1	20	38.5	
Ischemic heart disease	No	405 (91.8)	358	92	47	90.4	0.684
	Yes	36 (8.2)	31	8	5	9.6	
Heart failure	No	431 (97.7)	381	97.9	50	96.2	0.416
	Yes	10 (2.3)	8	2.1	2	3.8	
Chronic liver disease	No	421 (95.5)	372	95.6	49	94.2	0.649
	Yes	20 (4.5)	17	4.4	3	5.8	
Chronic kidney disease	No	421 (95.5)	372	95.6	49	94.2	0.649
	Yes	20 (4.5)	17	4.4	3	5.8	
Asthma	No	428 (97.1)	379	97.4	49	94.2	0.2
	Yes	13 (2.9)	10	2.6	3	5.8	
Other medical conditions (COPD, GERD, etc)	No	213 (48.3)	193	49.6	20	38.5	0.131
	Yes	228 (51.7)	196	50.4	32	61.5	
previous abdominal surgery	No	260 (59)	229	58.9	31	59.6	0.918
	Yes	181 (41)	160	41.1	21	40.4	
Smoking	No	226 (51.2)	201	51.7	25	48.1	0.142
	Yes	34 (7.7)	32	8.2	2	3.8	
	Ex-smoker	9 (2.0)	6	1.5	3	5.8	
	Unknown	172 (39)	150	38.6	22	42.3	

Table 2. Comparison of pre-op cellular components of blood among individuals with and without anastomotic leak (n=441)

Characteristics	Anastomotic leak		p value
	Yes	No	
	52 (11.8) Mean (SD)	389 (88.2) Mean (SD)	
Pre-op White blood cells (WBCs) ×10 ⁹ /L	8.66 (5.0)	7.56 (3.6)	0.049
Pre-op Neutrophil count ×10 ⁹ /L	6.60 (6.2)	4.93 (4.0)	0.009
Pre-op monocyte count ×10 ⁹ /L	0.79 (0.46)	0.72 (0.85)	0.567
Pre-op lymphocyte count ×10 ⁹ /L	1.76 (0.88)	1.88 (0.9)	0.37
Pre-op Platelets count ×10 ⁹ /L	350.62 (151.64)	321.97 (126.79)	0.136
Pre-op RDW	17.24 (4.34)	16.32 (3.89)	0.118
Pre-op Neutrophil to Lymphocyte ratio	4.14 (4.22)	3.61 (4.78)	0.447
Pre-op Lymphocyte to Monocyte ratio	2.62 (1.36)	3.28 (1.85)	0.013
Pre-op Derived neutrophil to lymphocyte ratio	2.34 (1.72)	1.98 (1.9)	0.203
Pre-op Platelet to lymphocyte ratio	246.4 (164.1)	216 (144.6)	0.163

Table 3. Mean cellular components of blood between pre-op and post op among patients with and without anastomotic leak

		Pre Op		POD1		POD2		POD3		POD4		POD5		POD6		POD7	
		Anastomotic leak		Anastomotic leak		Anastomotic leak		Anastomotic leak		Anastomotic leak		Anastomotic leak		Anastomotic leak		Anastomotic leak	
		No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
White blood cells (WBCs) ×10⁹/L	n	389	52	363	49	292	43	272	47	228	44	209	43	179	39	145	33
	Mean	7.63	8.66	12.88	13.06	11.18	12.64	9.57	11.38	8.94	11.13	8.32	10.21	8.76	11.03	9.3	12.18
	SD	3.9	5.04	5.37	6.05	4.88	6.74	4.1	6.54	3.93	7.5	3.69	6.5	3.81	5.51	3.87	5.3
	p value	0.68		0.648		0.656		0.096		0.04		0.072		0.016		<0.001	
Neutrophil count ×10⁹/L	n	387	52	350	47	274	41	247	44	214	43	195	37	160	34	132	27
	Mean	4.85	5.92	10.99	10.88	8.94	10.45	7.52	9.17	6.71	8.93	5.87	7.9	6.03	8.57	6.61	9.24
	SD	3.71	4.64	6.33	5.65	4.5	6.04	3.91	5.07	3.68	6.52	3.33	5.5	3.11	4.09	3.28	4.53
	p value	0.48		0.312		0.464		0.12		0.016		0.024		<0.001		0.008	
monocyte count ×10⁹/L	n	386	52	350	47	275	39	246	44	214	43	193	36	159	34	131	27
	Mean	0.72	0.79	0.86	0.73	0.79	1.33	0.68	0.63	0.67	0.63	0.89	0.81	0.83	0.73	0.78	0.79
	SD	0.84	0.46	0.54	0.42	0.77	4.23	0.57	0.36	0.65	0.34	1.85	0.84	0.66	0.39	0.37	0.46
	p value	0.549		0.103		0.059		0.595		0.698		0.809		0.379		0.88	
lymphocyte count ×10⁹/L	n	387	52	351	47	274	41	247	44	214	43	195	37	159	34	132	27
	Mean	1.88	1.76	1.2	1.2	1.31	1.05	1.29	1.06	1.28	1.14	1.36	1.01	1.45	1.28	1.49	1.72
	SD	0.9	0.88	2.07	0.6	1.1	0.5	1.3	0.53	0.67	0.69	1.03	0.44	0.95	0.76	0.78	1.7
	p value	0.379		0.996		0.128		0.25		0.214		0.36		0.336		0.265	
Platelets count ×10⁹/L	n	389	52	362	49	292	43	272	47	228	43	208	43	179	39	145	33
	Mean	322	350.6	276.8	280.9	254.1	249.9	260.4	245.8	276.9	260.6	301.5	270.1	325.7	286.1	351.4	305.2
	SD	126.8	151.6	130.4	128.1	115.8	109.7	114	108.6	128.3	115.9	123.3	133	132.3	157	153.7	149.6
	p value	0.136		0.835		0.822		0.416		0.439		0.135		0.103		0.119	
RDW	n	385	52	353	49	286	42	268	47	220	44	201	42	172	37	142	32
	Mean	16.32	17.24	16.39	17.5	16.65	17.6	16.41	17.9	16.66	17.62	16.45	17.67	16.91	17.69	17.07	18.54
	SD	3.89	4.34	3.66	4	3.54	4.08	3.41	3.97	3.62	3.7	3.2	4.25	3.36	4.3	3.5	4.32
	p value	0.944		0.4		0.896		0.064		0.896		0.288		0.225		0.336	
Neutrophil to Lymphocyte ratio	n	387	52	351	47	274	41	247	44	214	43	195	37	159	34	132	27
	Mean	3.61	4.14	13.87	10.68	9.21	11.92	8.2	11.72	7.32	9.82	6.29	8.72	5.82	8.98	5.87	8
	SD	4.78	4.22	14.69	6.72	6.82	7.34	7.5	14.43	8.04	8.86	6.79	5.82	5.09	6.36	4.81	6.05
	p value	0.447		0.143		0.16		0.128		0.544		0.336		0.016		0.376	
Platelet to lymphocyte ratio	n	387	52	350	47	274	41	246	44	214	42	194	37	159	34	132	27
	Mean	216	246.4	345.3	290.1	265.3	325.6	277.3	350.8	280.9	311.7	302.4	326.8	306.1	316.8	301	281.3
	SD	144.6	164.1	260.2	172.6	219.9	322.8	217.8	561.1	226.7	240.4	249.8	213.6	232.1	216	204.7	209.7
	p value	0.163		0.158		0.128		0.13		0.427		0.579		0.805		0.651	
Derived neutrophil to lymphocyte ratio	n	387	52	351	47	274	41	246	44	214	43	195	37	160	34	132	27
	Mean	1.98	2.34	5.88	5.39	4.91	5.69	4.15	4.9	3.52	4.91	2.83	4.31	2.79	4.34	2.74	4.42
	SD	1.9	1.72	3.05	2.91	3.18	2.77	2.76	2.78	2.74	4.48	1.9	2.96	1.97	2.93	1.6	3.11
	p value	0.203		0.296		0.137		0.096		0.056		<0.001		<0.001		<0.001	
Lymphocyte to Monocyte ratio	n	386	52	349	47	273	39	246	44	213	43	195	36	159	34	131	27
	Mean	3.3	2.6	1.7	2	2	1.7	2.2	2.1	2.4	2.5	2.1	1.9	2.1	2.1	2.2	2.6
	SD	1.8	1.4	3.4	1.2	1.5	0.9	1.5	1.6	2.1	3.9	1.2	1.4	1.1	1.6	1.1	3
	p value	0.013		0.507		0.377		0.581		0.829		0.371		0.819		0.221	

*p-values are unadjusted. Bonferroni correction was applied to preoperative comparisons (Table 2) only.

versus 2.74–2.83 in the non-AL group. RDW, LMR, and PLR did not differ significantly between groups at any postoperative time point. A graphical illustration of the temporal evolution of these blood indices is presented in Figure 1.

ROC Curve Analysis and Predictive Thresholds

ROC curve analysis results are summarized in Table 4. Among all indices evaluated, dNLR at POD7 demonstrated the strongest predictive accuracy overall (AUC 0.727; 95% CI: 0.611–0.843; $p = 0.001$), with a cut-off of 2.8 achieving sensitivity 71.4% and specificity 60.2%; dNLR

at POD6 also reached significance (AUC 0.710; 95% CI: 0.599–0.821; $p = 0.003$). WBC count at POD7 was a statistically significant predictor of AL (AUC 0.689; 95% CI: 0.555–0.823; $p = 0.007$), with a cut-off of $9.1 \times 10^9/L$ yielding sensitivity 76.2% and specificity 60.2%. Absolute neutrophil count at POD7 (AUC 0.716; 95% CI: 0.587–0.844; $p = 0.002$; cut-off $6.7 \times 10^9/L$; sensitivity 76.2%; specificity 63.7%) outperformed WBC at the same time point and should be regarded as the superior individual cell-count predictor in the late postoperative window. Neutrophil count at POD6 (AUC 0.665; cut-off $6.6 \times 10^9/L$; sensitivity 71.4%; specificity 61.2%) was also significant. NLR reached significance at POD6 (AUC 0.659; 95% CI: 0.536–0.783; $p = 0.022$;



Figure 1. Comparison of mean cellular components of blood between pre-op and post op among patients with and without anastomotic leak

Table 4. ROC curves of the mean change in cellular components of blood as predictive markers of anastomotic leakage

	AUC	95% CI	p value	Cut off	Sensitivity	Specificity
Post of day 7 WBC	0.689	0.555, 0.823	0.007	9.1	76.20%	60.20%
Post of day 6 Neutrophil	0.665	0.532, 0.799	0.018	6.6	71.40%	61.20%
Post of day 7 Neutrophil	0.716	0.587, 0.844	0.002	6.7	76.20%	63.70%
Post of day 6 NLR	0.659	0.536, 0.783	0.022	6	66.70%	64.30%
Post of day 7 NLR	0.636	0.506, 0.766	0.051	6	66.70%	65.30%
Post of day 6 Derived NLR	0.71	0.599, 0.821	0.003	2.8	71.40%	60.20%
Post of day 7 Derived NLR	0.727	0.611, 0.843	0.001	2.8	71.40%	60.20%

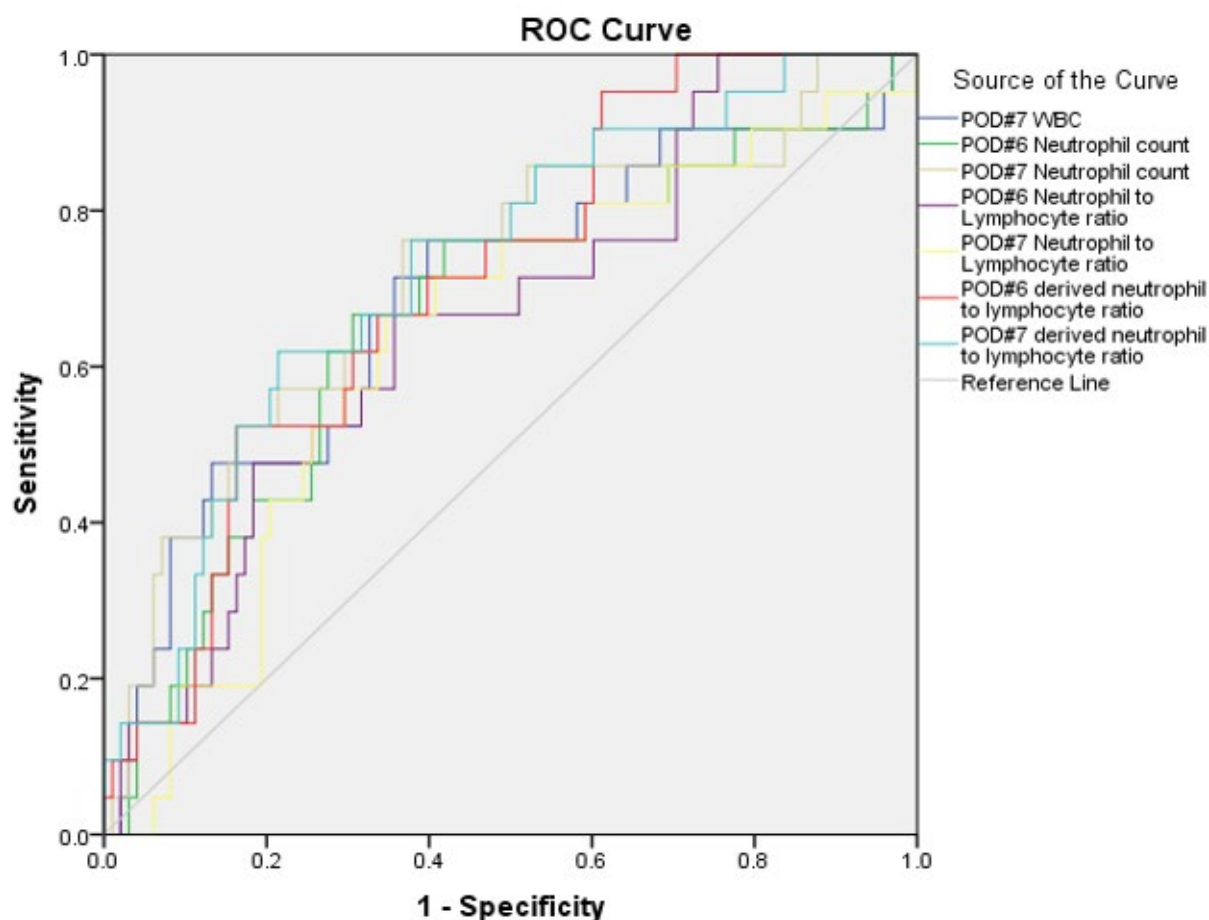


Figure 2. Receiver operating characteristics (ROC) curve and area under the curve (AUC) for pre and post-op cellular components of blood

cut-off 6.0; sensitivity 66.7%; specificity 64.3%); NLR at POD7 did not reach statistical significance (AUC 0.636; $p = 0.051$) and is not considered a confirmed independent predictor at that time point. ROC curves for preoperative and postoperative indices are shown in Figure 2.

DISCUSSION

AL remains one of the most consequential complications following colorectal surgery. While CT imaging is the standard diagnostic modality, its sensitivity in the early postoperative period is limited, and many institutions do not have routine access to more expensive biomarkers such as CRP or procalcitonin. This study evaluated whether hematological indices obtainable from universal daily blood counts could serve as early surrogate markers for AL.

Our findings demonstrate that WBC count and absolute neutrophil count were elevated in the AL group across POD4 through POD7, while NLR and dNLR became discriminatory from POD5–POD6 onward. This time-dependent pattern is clinically meaningful: early postoperative elevations in inflammatory markers are expected following surgical trauma and are therefore non-specific; persistent or secondary inflammatory escalation from POD4 is more likely to reflect pathological processes such as anastomotic dehiscence. This aligns with the biological timeline of AL, which most commonly manifests between POD5 and POD7.

The NLR has been studied as a predictor of AL and other postoperative complications in colorectal surgery. In the present cohort, preoperative

NLR was numerically higher in the AL group, but the difference did not reach statistical significance after correction. This contrasts with a study of gastric cancer patients in which a preoperative NLR cut-off of 3.54 predicted AL with specificity of 93.6% and sensitivity of 87.0%¹⁵. The hypothesis underlying this association is that a pre-existing pro-inflammatory state impairs anastomotic healing through dysregulated immune mechanisms^{15,16}. In a systematic review, elevated pretreatment NLR was associated with poor overall survival, reduced progression-free survival, and worse tumor differentiation in colorectal cancer¹⁷. A separate retrospective study identified preoperative NLR as a predictor of major postoperative complications, though not specifically of AL¹⁸. One prospective study reported that NLR > 9.3 on POD1 was associated with increased complication risk¹⁹, while others found significant elevations in NLR on POD3 and POD5 in AL patients²⁰. Tan et al. described significantly higher NLR on POD5 in AL patients following low anterior resection, with sensitivity 76.5% and specificity 79.4%²¹. Our finding of a significant elevation in NLR specifically at POD6 is consistent with the broader literature, though the optimal timing differs across studies, likely reflecting heterogeneity in patient populations, anastomotic level, and operative approach.

Compared with CRP, NLR demonstrated lower predictive performance in one retrospective study, in which CRP on POD5 outperformed NLR as a predictor of AL²². The combination of multiple inflammatory markers has been shown to improve prediction over any single index^{13,14}. In a study focused on rectal cancer surgery, NLR was the only preoperative scoring system to predict AL among multiple candidate models²³. The present findings extend this literature by demonstrating that dNLR,

a closely related and equally accessible index, also shows significant discriminatory ability from POD5.

RDW was included in this analysis as a potential marker of hematological stress that has shown predictive value in other surgical and medical contexts. However, RDW was not significantly associated with AL in our cohort, and no significant differences in RDW were observed between groups at any time point. Similarly, LMR and PLR did not demonstrate significant associations with AL. The absence of significance for these markers may reflect the biology of anastomotic failure, which appears to be more closely linked to neutrophilic and innate immune responses than to lymphocyte-platelet dynamics.

The ROC analysis demonstrated modest but statistically significant predictive accuracy for WBC, neutrophil count, and dNLR in the later postoperative period. Notably, dNLR at POD7 yielded the highest AUC of any single index in this study (AUC 0.727; $p = 0.001$), marginally outperforming absolute neutrophil count at POD7 (AUC 0.716; $p = 0.002$), which in turn exceeded WBC at the same time point (AUC 0.689; $p = 0.007$). This hierarchy is clinically relevant: dNLR and neutrophil count, rather than total WBC alone, appear to capture the most diagnostically relevant signal. The AUC of 0.689 for WBC at POD7 indicates moderate discriminative ability, with sensitivity of 76.2% and specificity of 60.2% at the optimal threshold of $9.1 \times 10^9/L$. NLR was a significant predictor at POD6 (AUC 0.659; $p = 0.022$) but did not reach significance at POD7 ($p = 0.051$), reinforcing that the diagnostic window for NLR may be more precisely centered on POD6 in this population. These values suggest that blood indices, while not sufficient as standalone diagnostic tools, may be clinically useful within a structured surveillance framework: serial measurements demonstrating failure of normalization — rather than isolated single-point values — may be more informative, particularly when interpreted alongside clinical assessment and risk factors such as open surgery, diabetes, and high ASA class.

Several limitations of this study must be acknowledged. The retrospective design introduces inherent risks of selection bias and unmeasured confounding. Markers such as CRP and procalcitonin were not routinely captured, precluding direct head-to-head comparison. Postoperative non-anastomotic infections (e.g., pneumonia, urinary tract infection) were not systematically documented, and their contribution to elevations in WBC and inflammatory indices cannot be excluded. Anastomotic level, bowel preparation protocols, and specific technical details of anastomotic construction were not fully controlled for, yet these factors may independently influence both postoperative inflammatory responses and AL risk. Finally, the moderate specificity of identified thresholds may lead to unnecessary investigations if applied without clinical correlation.

CONCLUSION

Routine hematological indices — particularly dNLR (the strongest individual predictor, AUC 0.727 at POD7), absolute neutrophil count, WBC count, and NLR — demonstrate a clinically plausible and statistically significant time-dependent association with AL following colorectal surgery, with the greatest discriminatory power observed from POD4 through POD7. Their moderate predictive accuracy supports use as adjuncts within composite surveillance or risk stratification models rather than as independent diagnostic criteria. Prospective studies are needed to validate these thresholds, account for anastomotic level and construction technique, and evaluate the incremental value of blood indices over established biomarkers such as CRP in diverse clinical settings.

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