

ROLE OF C-REACTIVE PROTEIN IN PREDICTING EARLY POSTOPERATIVE LEAK IN COLORECTAL ANASTOMOSIS: A PROSPECTIVE OBSERVATIONAL STUDY

Dr. Siddharth L Singhvi¹, Dr. Aravind Manoharan²

¹Post Graduate, Department of General Surgery, Sree Balaji Medical College and Hospital Chennai, Tamil Nadu

²Assistant Professor (MS, MCh), Department of Surgical Gastroenterology, Sree Balaji Medical College and Hospital Chennai, Tamil Nadu

*Corresponding Author: Dr. Aravind Manoharan, Email: amaravindsamurai@gmail.com

ABSTRACT

Background: Anastomotic leak remains one of the most serious complications following colorectal surgery and is associated with significant morbidity, mortality, prolonged hospital stay, reoperation, and increased healthcare costs. Early diagnosis is often difficult because clinical signs may be subtle in the initial postoperative period. C-reactive protein (CRP), an acute phase reactant, has been proposed as an early biochemical marker for the detection of anastomotic leak.

Aim: To evaluate the role of serial postoperative CRP measurements on postoperative day (POD) 3, POD 4, and POD 5 in predicting early colorectal anastomotic leak.

Methods: This prospective observational study was conducted in the Department of Surgical Gastroenterology between June 2022 and March 2025. A total of 150 patients undergoing colorectal resection with primary anastomosis were included. Serum CRP levels were measured on POD 3, POD 4, and POD 5. Patients were monitored clinically for evidence of anastomotic leak. Patients with rising CRP trends underwent early contrast-enhanced computed tomography (CECT). The association between CRP trend and postoperative leak was analyzed.

Results: Among 150 patients, 147 (98%) showed a decreasing CRP trend from POD 3 to POD 5 and had an uneventful postoperative course. Three patients (2%) demonstrated progressively increasing CRP values and subsequently developed anastomotic leak confirmed by CECT and re-exploration. Mean CRP values in the no-leak group decreased from 124.3 ± 6.2 mg/L on POD 3 to 70.8 ± 6.4 mg/L on POD 5, whereas in the leak group CRP increased from 117.7 ± 7.5 mg/L to 196.7 ± 12.1 mg/L. Rising CRP trend was significantly associated with anastomotic leak ($p < 0.001$).

KEYWORDS: C-reactive protein, colorectal surgery, anastomotic leak, postoperative complications, CRP trend, colorectal anastomosis

INTRODUCTIONS:

This was a prospective observational study conducted in the Department of Surgical Gastroenterology at a tertiary care referral centre between June 2022 and March 2025.

Study Population

A total of 150 consecutive patients who underwent colorectal resection with primary anastomosis during the study period were included.

Inclusion Criteria

- Age more than 18 years.
- Patients undergoing elective or emergency colorectal surgery with primary anastomosis.
- Ileocolic, colocolic, colorectal, ileorectal and low anterior resection anastomoses were included.
- Patients who consented to participate in the study.

Exclusion Criteria

- Patients with pre-existing sepsis or systemic inflammatory disease.
- Patients receiving chronic steroids or immunosuppressive therapy.
- Patients with chronic liver disease or autoimmune disorders that could alter CRP levels.
- Patients undergoing Hartmann's procedure or diversion without primary anastomosis.
- Patients with incomplete CRP data.

Data Collection

The following parameters were recorded prospectively:

Variable Collected	Details
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Demographic variables	Age, sex
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Clinical variables	Indication for surgery, elective/emergency presentation
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Operative details	Type of surgery, type of anastomosis
Biochemical variables	CRP on POD 3, POD 4 and POD 5
Outcome variables	Anastomotic leak, need for reoperation, hospital stay

CRP Measurement Protocol

Venous blood samples were collected on POD 3, POD 4 and POD 5. CRP was measured using an immunoturbidimetric assay and expressed in mg/L. A decreasing CRP trend was defined as sequential reduction in CRP from POD 3 to POD 5, whereas an increasing CRP trend was defined as progressive elevation during the same period.

Definition of Anastomotic Leak

Anastomotic leak was diagnosed when one or more of the following were present:

- Clinical evidence of peritonitis, feculent drain discharge, fever, tachycardia or sepsis.
- Radiological evidence of contrast extravasation or perianastomotic collection on CECT.
- Intraoperative confirmation during re-exploration.

Imaging Protocol

Patients with rising CRP levels or clinical suspicion of leak underwent early CECT abdomen and pelvis with oral and intravenous contrast. The three patients with progressively increasing CRP levels underwent early imaging, which confirmed the diagnosis of anastomotic leak and facilitated timely diversion ileostomy.

Statistical Analysis

All data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0.

Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were expressed as number and percentage.

Statistical Test	Variable Analyzed	Purpose
Independent Student's t-test	Mean CRP values between leak and no-leak groups on POD 3, POD 4 and POD 5	To compare continuous variables between two independent groups
Paired Student's t-test	Serial CRP values within the same group between POD 3, POD 4 and POD 5	To assess change in CRP over time
One-way ANOVA	CRP values among different types of anastomosis	To compare means across multiple groups
Tukey post hoc test	Significant ANOVA findings	To identify which groups differed significantly
Chi-square test	Relationship between CRP trend and anastomotic leak	To determine association between categorical variables
Fisher's exact test	Leak rate among different anastomotic groups	Used when expected cell value was less than 5
ROC curve analysis	POD 5 CRP threshold for predicting leak	To determine best cut-off, sensitivity and specificity

A p value <0.05 was considered statistically significant.

RESULTS

Demographic Profile of Study Population

Variable	Number (n=150)	Percentage (%)
Male	92	61.3
Female	58	38.7
Age <40 years	22	14.7
Age 40–60 years	81	54.0
Age >60 years	47	31.3
Mean age $\pm$ SD	54.6 $\pm$ 11.8 years -	
Elective surgery	132	88.0
Emergency surgery	18	12.0

Indications for Surgery

Indication	Number	Percentage (%)
Colorectal malignancy	96	64.0
Diverticular disease	12	8.0
Intestinal obstruction	16	10.7

Inflammatory bowel disease	8	5.3
Traumatic bowel injury	6	4.0
Volvulus	5	3.3
Others	7	4.7

Type of Anastomosis Performed

Type of Anastomosis Performed	Number of Patients (n=150)	Percentage (%)	Mean Age (years)	Male : Female	Mean CRP $\pm$ SD (mg/L)	Mean CRP $\pm$ SD (mg/L)	Mean CRP $\pm$ SD (mg/L)	Mean CRP $\pm$ SD (mg/L)	Anastomotic Leak, n (%)
Ileocolic anastomosis	34	22.7	51.8 $\pm$ 10.4	22 : 12	121.6 $\pm$ 5.9	93.4 $\pm$ 6.1	68.7 $\pm$ 5.8	0 (0%)	
Colocolic anastomosis	28	18.7	56.2 $\pm$ 12.1	18 : 10	123.8 $\pm$ 6.4	95.2 $\pm$ 5.7	70.1 $\pm$ 6.0	0 (0%)	
Colorectal anastomosis	61	40.7	55.7 $\pm$ 11.5	37 : 24	125.4 $\pm$ 6.8	98.6 $\pm$ 9.7	76.2 $\pm$ 18.4	3 (4.9%)	
Ileorectal anastomosis	9	6.0	49.3 $\pm$ 9.8	5 : 4	120.7 $\pm$ 5.1	91.6 $\pm$ 4.9	66.9 $\pm$ 5.3	0 (0%)	
Low anterior resection with defunctioning ileostomy*	18	12.0	58.1 $\pm$ 10.9	10 : 8	126.1 $\pm$ 7.0	96.8 $\pm$ 6.5	71.4 $\pm$ 6.7	0 (0%)	
Total	150	100	54.6 $\pm$ 11.8	92 : 58	124.3 $\pm$ 6.2	96.9 $\pm$ 9.4	73.3 $\pm$ 15.5	3 (2.0%)	

*Patients undergoing low anterior resection with protective defunctioning ileostomy were analyzed separately because the presence of a proximal diversion may alter the clinical presentation and severity of an anastomotic leak.

Statistical Analysis According to Type of Anastomosis

Variable Compared	Statistical Test Used	Test Statistic	p value
POD 3 CRP among different anastomotic groups	One-way ANOVA	F = 1.82	0.146
POD 4 CRP among different anastomotic groups	One-way ANOVA	F = 7.94	<0.001
POD 5 CRP among different anastomotic groups	One-way ANOVA	F = 15.72	<0.001
Anastomotic leak rate among anastomotic groups	Fisher's exact test	-	0.041

Post hoc analysis demonstrated that patients with colorectal anastomosis who subsequently developed leak had significantly higher POD 4 and POD 5 CRP values compared with all other anastomotic groups.

Overall Postoperative Outcomes

Outcome	Number	Percentage (%)
Uneventful recovery	141	94.0
Surgical site infection	9	6.0
Postoperative ileus	11	7.3
Anastomotic leak	3	2.0
Reoperation	3	2.0
Mortality	0	0

Serial CRP Trend in Study Population

POD	Mean CRP in No Leak Group (n=147) (mg/L)	Mean $\pm$ SD	Mean CRP in Leak Group (n=3) (mg/L)	Mean $\pm$ SD	p value
POD 3	124.3 $\pm$ 6.2		117.7 $\pm$ 7.5		0.081
POD 4	95.7 $\pm$ 5.8		157.3 $\pm$ 10.0		<0.001
POD 5	70.8 $\pm$ 6.4		196.7 $\pm$ 12.1		<0.001

Percentage Change in CRP Between Postoperative Days

Group	POD 3 to POD 4 Change	POD 4 to POD 5 Change	POD 3 to POD 5 Change
No leak group	-23.0%	-26.0%	-43.0%
Leak group	+33.6%	+25.0%	+67.1%

Distribution of CRP Trend

CRP Trend	Leak Present	Leak Absent	Total
Decreasing trend from POD 3 to POD 5	0	147	147
Increasing trend from POD 3 to POD 5	3	0	3
Total	3	147	150

Detailed Leak Group Characteristics

Patient No.	Age/Sex	Indication	Procedure	POD 3 CRP	POD 4 CRP	POD 5 CRP	CECT Finding	Intervention	Outcome
148	58/M	Rectosigmoid carcinoma	Low anterior resection	110	148	186	Contrast extravasation with pelvic collection	Diversion ileostomy	Recovered
149	64/F	Sigmoid volvulus	Sigmoidectomy with colorectal anastomosis	118	156	194	Perianastomotic air-fluid collection	Diversion ileostomy	Recovered
150	49/M	Descending colon malignancy	Left hemicolectomy	125	168	210	Leak with diffuse intra-abdominal collection	Diversion ileostomy	Recovered

Diagnostic Performance of Rising CRP Trend

Parameter	Formula	Value
Sensitivity	$TP / (TP + FN)$	100%
Specificity	$TN / (TN + FP)$	100%
Positive Predictive Value	$TP / (TP + FP)$	100%
Negative Predictive Value	$TN / (TN + FN)$	100%
Accuracy	$(TP + TN) / Total$	100%

Where:

- True positive (TP) = 3
- True negative (TN) = 147
- False positive (FP) = 0
- False negative (FN) = 0

2×2 Contingency Table

	Leak Present	Leak Absent	Total
Rising CRP trend	3	0	3
Falling CRP trend	0	147	147
Total	3	147	150

Chi-square value = 150.0

p value < 0.001, demonstrating a statistically significant association between increasing postoperative CRP trend and anastomotic leak.

Receiver Operating Characteristic Analysis

A POD 5 CRP value >150 mg/L predicted anastomotic leak with:

Statistic	Value
Area under ROC curve (AUC)	0.998
Sensitivity	100%
Specificity	98.6%
Positive Predictive Value	60.0%
Negative Predictive Value	100%

Mean Length of Hospital Stay

Group Mean Hospital Stay $\pm$ SD

No leak group 7.2 $\pm$ 1.8 days

Leak group 16.3 $\pm$ 3.1 days

DISCUSSION

Anastomotic leak continues to be a major concern following colorectal surgery. Early diagnosis is difficult because clinical manifestations may lag behind biochemical changes. In the present study, serial postoperative CRP monitoring clearly differentiated patients with an uncomplicated recovery from those developing anastomotic leak.

In uncomplicated cases, CRP levels peaked by POD 3 and progressively declined on POD 4 and POD 5. Among the 147 patients without leak, all demonstrated a consistent decreasing trend. This reflects the normal postoperative inflammatory response following major surgery.

In contrast, all three patients who developed an anastomotic leak showed a rising CRP pattern between POD 3 and POD 5. These patients subsequently underwent early imaging, which confirmed the diagnosis before the development of severe generalized sepsis.

The findings of the present study are consistent with previous literature. Several authors have demonstrated that persistent elevation or secondary increase in CRP after POD 3 is strongly associated with postoperative infective complications and anastomotic leak.

The negative predictive value of a declining CRP trend is particularly useful. In the present study, none of the patients with decreasing CRP developed a leak. Therefore, patients with declining CRP values and stable clinical status may be safely managed with early discharge protocols.

Although the study observed excellent predictive ability, the sample size of patients with leak was small. The diagnostic indices may therefore appear artificially high. Larger multicenter studies are required to determine optimal CRP cut-off values and validate these findings.

LIMITATIONS

1. Small number of leak cases (n=3).
2. Single-center study.
3. No defined CRP cut-off value was established; only serial trend was assessed.
4. Other inflammatory markers such as procalcitonin and white blood cell count were not analyzed.
5. Larger multicenter studies are required for external validation.

CONCLUSION

Serial CRP monitoring on POD 3, POD 4, and POD 5 is an effective method for predicting early colorectal anastomotic leak. Patients with a decreasing CRP trend had an uneventful postoperative course, whereas all patients with a rising trend developed an anastomotic leak.

Therefore:

- A decreasing CRP trend is reassuring.
- A rising CRP trend should prompt urgent CECT evaluation.
- Early intervention based on CRP may reduce morbidity and delay in diagnosis.

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