Original Research

THE ROLE OF C-REACTIVE PROTEIN AS A PREDICTOR OF COLORECTAL ANASTOMOTIC LEAKAGE - A PROSPECTIVE OBSERVATIONAL STUDY AT S.C.B MEDICAL COLLEGE

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ABSTRACT

Background: Colorectal anastomotic leakage (CAL) is a major postoperative complication associated with significant morbidity and mortality. Early detection remains challenging due to nonspecific clinical signs. C-reactive protein (CRP), an acute-phase reactant, has emerged as a potential biomarker for early prediction of CAL.
Aim: To evaluate the role of postoperative CRP levels in predicting colorectal anastomotic leakage and to determine its diagnostic accuracy.
Methods: This prospective observational study included **51 patients** undergoing colorectal anastomosis. Postoperative CRP levels were measured, particularly on Day 4, and correlated with the occurrence of anastomotic leakage and other complications. Statistical analysis included Chi-square test, logistic regression, Mann–Whitney U test, and ROC curve analysis.
Results: Anastomotic leakage occurred in 9 patients (17.6%). No significant association was found between leakage and gender, disease etiology, or surgical technique ($p > 0.05$). CRP levels were significantly associated with prolonged hospital stay ($p = 0.02$) and postoperative complications ($p = 0.01$). ROC analysis demonstrated excellent diagnostic accuracy of Day 4 CRP, with an AUC of 0.964, sensitivity of 88.9%, and specificity of 88.1% at a cut-off value of 154 mg/L.
Conclusion: Postoperative CRP is a reliable, cost-effective, and easily accessible biomarker for early prediction of colorectal anastomotic leakage. Routine monitoring can aid in early diagnosis, reduce complications, and optimize postoperative management.

Keywords: C-Reactive Protein, Colorectal Surgery, Anastomotic Leakage, Postoperative Complications, Biomarker.

INTRODUCTION

Colorectal anastomotic leakage (CAL) remains one of the most serious and feared complications following colorectal surgery, contributing significantly to postoperative morbidity, prolonged hospital stay, increased healthcare costs, and mortality [1]. Despite advances in surgical techniques, perioperative care, and stapling devices, the incidence of CAL continues to range between 3% and 20%, depending on patient-related and procedure-related factors [2]. Early detection of anastomotic leakage is crucial, as delayed diagnosis is associated with sepsis, multi-organ dysfunction, and poor oncological outcomes, particularly in patients undergoing surgery for colorectal malignancy [3]. However, the clinical diagnosis of CAL is often challenging due to its nonspecific presentation, which may include fever, tachycardia, abdominal pain, or subtle biochemical changes, thereby necessitating the use of reliable biomarkers for early prediction [4].

C-reactive protein (CRP), an acute-phase reactant synthesized by hepatocytes in response to inflammatory cytokines such as interleukin-6, has emerged as a promising biomarker in the postoperative setting [5]. CRP levels typically rise following surgical trauma, peaking within 48–72 hours, and subsequently decline in uncomplicated recoveries. Persistent elevation or secondary rise in CRP levels beyond the expected postoperative period may indicate ongoing inflammation or infectious complications, including anastomotic leakage [6]. Due to its wide availability, low cost, and reproducibility, CRP has been extensively investigated as a predictive tool for early detection of CAL.

Several studies have demonstrated that postoperative CRP levels, particularly on postoperative days 3 to 5, have high sensitivity and negative predictive value for excluding anastomotic leakage [7]. This allows clinicians to identify low-risk patients suitable for early discharge under enhanced recovery after surgery (ERAS) protocols while prompting further investigation or

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intervention in high-risk individuals [8]. Various cut-off values have been proposed in the literature, with most studies suggesting that elevated CRP levels above specific thresholds are strongly associated with the development of postoperative complications, especially CAL [9]. Moreover, the use of CRP as part of a multimodal approach, including clinical assessment and imaging, has been shown to improve diagnostic accuracy and patient outcomes.

In addition to its diagnostic value, CRP also serves as a prognostic marker, correlating with the severity of complications and length of hospital stay. Elevated CRP levels have been associated with increased rates of reoperation, intensive care admission, and mortality [10]. Therefore, monitoring CRP trends in the postoperative period can aid in timely clinical decision-making, optimize resource utilization, and potentially reduce the burden of complications.

The present study aims to evaluate the role of C-reactive protein (CRP) as an early and reliable biomarker for the detection of colorectal anastomotic leakage in the postoperative period. By systematically analyzing postoperative CRP trends, the study seeks to identify clinically significant threshold values that can aid in the timely recognition of anastomotic complications before the onset of overt clinical signs. Furthermore, the objective is to establish evidence-based CRP cut-off levels that can be utilized in routine clinical practice to stratify patients according to risk, thereby facilitating safe early discharge in uncomplicated cases while ensuring prompt intervention in high-risk individuals following elective colorectal surgery.

MATERIALS & METHODS

Study Design and Setting

- Prospective observational study
- Conducted at S.C.B Medical College (tertiary referral center)
- Study duration: 18 months
- Approved by Institutional Review Board and Ethics Committee

Study Population

- Adults ≥18 years undergoing elective colorectal surgery with primary intestinal anastomosis
- Patients recruited consecutively from surgical operation registry

Inclusion Criteria

- Age ≥18 years
- Provided informed consent
- Undergoing large intestinal anastomosis (e.g., hemicolectomy, sigmoid resection, anterior resection, Hartmann's reversal, colostomy closure, ileorectal anastomosis)

Exclusion Criteria

- Emergency surgery
- Pre-existing active infection
- Re-exploration or leak before postoperative day 4
- Acute/chronic liver failure
- Autoimmune disorders (SLE, dermatomyositis, scleroderma)
- Inflammatory bowel disease
- Leukemia

Sample Size

- Planned: 80 patients (based on audit data)
- Recruited: 55 patients
- Final analyzed: 51 patients

Statistical Analysis: We put the data into Microsoft Excel and then used SPSS software version 27.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5 to look at it. Mean ± standard deviation was used to show continuous variables, and frequencies and percentages were used to show categorical variables. The unpaired t-test was utilized to examine continuous variables between independent groups, whereas the paired t-test was employed for comparisons within the same group. The Chi-square test or Fisher's exact test was used to look at categorical variables, depending on which one was better. A p-value of less than 0.05 was seen to be statistically important.

RESULT

Table 1: Baseline Characteristics

Parameter	Value
Total patients	51
Anastomotic leaks	9 (17.6%)
No leaks	42 (82.4%)
Mean age	55.5 years
Age range	23–84 years
Mean hospital stay	14 ± 7.39 days
Male	36 (70.6%)
Female	15 (29.4%)

Table 2: Disease and Surgical Profile

Parameter	Value

Malignancy	19
Infective etiology	6
Others	26
Hartmann's reversal	33%
LAR + Stoma reversal	50%
Other procedures	Remaining

Table 3: Postoperative Outcomes

Parameter	**Value**
Total leaks	9
Detected during admission	7 (77.8%)
Readmitted with leak	2 (22.2%)
Non-leak complications	29%
Wound infection	9.80%
Pneumonia	11%
UTI	5.80%

Table 4: Statistical Associations

Variable	**Test**	**p-value**	**Result**
Gender vs leak	Chi-square	>0.05	Not significant
Disease vs leak	Chi-square	>0.05	Not significant
Surgery type vs leak	Chi-square	>0.05	Not significant
Technique vs leak	Chi-square	>0.05	Not significant
CRP vs hospital stays	Logistic regression	0.02	Significant
CRP vs complications	Mann-Whitney U	0.01	Significant

Table 5: CRP Diagnostic Accuracy (ROC Analysis)

Parameter	**Value**
Mean Day 4 CRP	116.57 mg/L
AUC	0.964
95% CI	0.918 – 1.000
p-value	<0.001
Cut-off value	154 mg/L
Sensitivity	88.90%
Specificity	88.10%
Youden Index	0.642

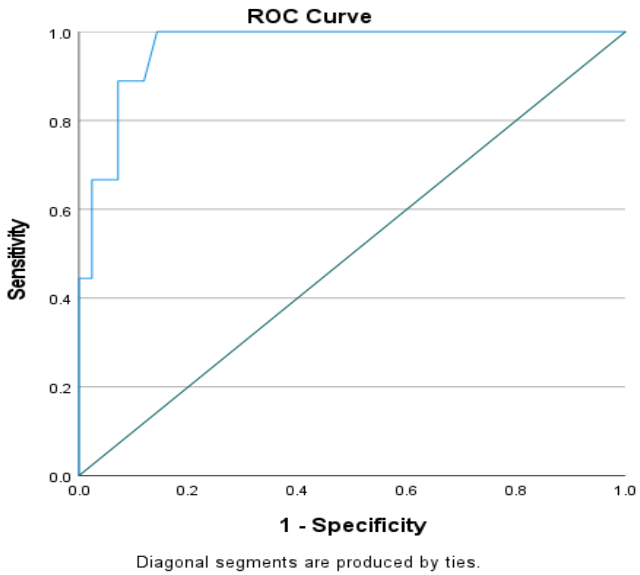

Figure: 1. ROC Curve for CRP in Predicting Anastomotic Leak

Table 1: Baseline Characteristics

The present study included a total of 51 patients who underwent colorectal anastomosis. Among them, 9 patients (17.6%) developed anastomotic leaks, while the remaining 42 patients (82.4%) had no evidence of leakage. The mean age of the study population was 55.5 years, with a wide age distribution ranging from 23 to 84 years, indicating inclusion of both young and elderly patients. The mean duration of hospital stay was 14 ± 7.39 days, reflecting moderate variability in postoperative recovery.

Gender distribution showed a predominance of males, with 36 patients (70.6%), compared to 15 females (29.4%), suggesting a higher representation of male patients in this cohort.

Table 2: Disease and Surgical Profile

With respect to disease etiology, malignancy was the most common indication, observed in 19 patients, followed by infective causes in 6 patients, while 26 patients were categorized under other etiologies, including benign and inflammatory conditions.

Regarding the type of surgical procedures performed, Hartmann's reversal accounted for 33% of cases, while low anterior resection (LAR) with stoma reversal constituted 50%, representing the majority of procedures. The remaining cases underwent other surgical interventions, indicating a diverse operative profile within the study population.

Table 3: Postoperative Outcomes

Out of the 9 cases of anastomotic leakage, the majority (7 patients; 77.8%) were diagnosed during the same hospital admission, whereas 2 patients (22.2%) presented later and required readmission, highlighting the importance of postoperative surveillance.

Non-leak postoperative complications were observed in 29% of patients, with pneumonia being the most common (11%), followed by wound infection (9.8%) and urinary tract infection (5.8%). These findings indicate a considerable burden of postoperative morbidity beyond anastomotic leakage.

Table 4: Statistical Associations

Statistical analysis revealed that gender, disease etiology, type of surgery, and surgical technique did not show a significant association with the occurrence of anastomotic leak (Chi-square test, $p > 0.05$ for all variables), suggesting that these factors were not independent predictors in this cohort.

However, C-reactive protein (CRP) levels demonstrated significant associations with clinical outcomes. There was a statistically significant correlation between CRP levels and duration of hospital stay (logistic regression, $p = 0.02$), indicating that higher CRP levels were associated with prolonged hospitalization. Additionally, CRP levels were significantly higher in patients who developed complications compared to those without complications (Mann–Whitney U test, $p = 0.01$), reinforcing its role as an inflammatory marker in postoperative prognosis.

Table 5: CRP Diagnostic Accuracy (ROC Analysis)

Receiver operating characteristic (ROC) curve analysis demonstrated that Day 4 CRP levels had excellent diagnostic accuracy in predicting anastomotic leakage. The mean CRP level on postoperative Day 4 was 116.57 mg/L. The area under the curve (AUC) was 0.964 (95% CI: 0.918–1.000; $p < 0.001$), indicating outstanding discriminatory ability.

A cut-off value of 154 mg/L was identified as optimal, yielding a sensitivity of 88.9% and specificity of 88.1%. The Youden Index of 0.642 further confirms the strong predictive performance of CRP at this threshold. These findings support the utility of Day 4 CRP as a reliable biomarker for early detection of anastomotic leakage.

DISCUSSION

In the present study, the incidence of colorectal anastomotic leakage (CAL) was 17.6%, which falls within the higher range reported in literature (3–20%). This relatively elevated incidence may be attributed to the heterogeneity of the study population, including both malignant and benign etiologies, as well as varied surgical procedures. A similar incidence was reported by Matthiessen et al., who observed a leakage rate of approximately 19% in low anterior resection cases, emphasizing that distal anastomoses carry a higher risk [11]. In contrast, Kingham and Pachter reported a lower incidence of around 6%, possibly reflecting differences in patient selection and perioperative protocols [12]. The higher leak rate in our study may also reflect real-world clinical variability rather than strictly controlled trial settings.

The demographic profile of our study demonstrated a male predominance (70.6%), although no statistically significant association was found between gender and leak occurrence. This finding is consistent with the observations of Boccola et al., who reported that while male gender has been suggested as a risk factor due to anatomical constraints such as a narrow pelvis, it was not independently associated with increased leak rates on multivariate analysis [13]. Similarly, Sciuto et al. found no significant correlation between gender and CAL, reinforcing the notion that gender alone may not be a reliable predictor [14].

With regard to disease etiology, although malignancy constituted a significant proportion of cases in our study, no statistically significant association was found between underlying pathology and anastomotic leakage. This is in agreement with findings by Frasson et al., who demonstrated that while malignancy is often

associated with complex resections, it does not independently predict leakage when adjusted for confounding factors such as nutritional status and intraoperative variables [15].

Analysis of surgical procedures in our cohort revealed that Hartmann's reversal and LAR with stoma reversal were the most commonly performed operations. However, no significant association was found between the type of surgery or surgical technique and leak rates, which aligns with the study by Vignali et al., who reported that technical factors alone, such as stapled versus hand-sewn anastomosis, do not significantly influence leakage rates when performed by experienced surgeons [16]. This suggests that patient-related and inflammatory factors may play a more critical role than operative technique alone.

Postoperative outcomes in our study showed that 77.8% of leaks were detected during the index admission, while 22.2% required readmission, highlighting the importance of vigilant postoperative monitoring. Comparable findings were reported by Bruce et al., who emphasized that a significant proportion of leaks may present after discharge, underscoring the need for reliable early predictors such as biomarkers [17]. Additionally, non-leak complications such as pneumonia, wound infection, and UTI were observed in our cohort, which is consistent with the findings of Tevis and Kennedy, who reported that postoperative infectious complications are common and often coexist with systemic inflammatory responses [18].

A key finding of our study was the significant association between CRP levels and both hospital stay ($p = 0.02$) and postoperative complications ($p = 0.01$). These findings are supported by Warschkow et al., who demonstrated that elevated postoperative CRP levels are strongly correlated with prolonged hospitalization and increased complication rates [19]. Similarly, Ortega-Deballon et al. found that persistently elevated CRP levels are indicative of septic complications and can serve as an early warning sign, enabling timely intervention [20].

Most notably, our ROC analysis revealed that Day 4 CRP had excellent diagnostic accuracy, with an AUC of 0.964, sensitivity of 88.9%, and specificity of 88.1% at a cut-off value of 154 mg/L. These findings are highly consistent with those of Singh et al., who reported high sensitivity and specificity of CRP in predicting CAL, particularly on postoperative days 3–5 [7]. Furthermore, Platt et al. also demonstrated that CRP is a reliable predictor of infective complications with comparable diagnostic performance [9]. The high AUC in our study further reinforces the robustness of CRP as a predictive biomarker.

Overall, the findings of this study are in strong agreement with existing literature, confirming that while demographic and surgical factors may not independently predict anastomotic leakage, postoperative inflammatory markers such as CRP play a pivotal role in early detection and risk stratification. Incorporating CRP monitoring into routine postoperative protocols may facilitate early diagnosis, reduce morbidity, and improve clinical outcomes.

CONCLUSION

The present study demonstrates that colorectal anastomotic leakage remains a significant postoperative complication, with an incidence of 17.6% in our cohort. While demographic factors, disease etiology, and surgical techniques did not show a significant association with leakage, postoperative inflammatory response, particularly C-reactive protein (CRP), proved to be a reliable predictor. Elevated CRP levels were significantly associated with increased postoperative complications and prolonged hospital stay. Notably, Day 4 CRP showed excellent diagnostic accuracy, with high sensitivity and specificity at an optimal cut-off value of 154 mg/L. These findings highlight the clinical utility of CRP as a simple, cost-effective, and widely available biomarker for early detection of anastomotic leakage. Routine postoperative monitoring of CRP can aid in timely diagnosis, facilitate early intervention, and improve patient outcomes, while also supporting safe early discharge in low-risk patients.

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