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A PROSPECTIVE STUDY TO IDENTIFY THE FACTORS CAUSING LEAK IN CASE OF SMALL BOWEL RESECTION AND ANASTOMOSIS USE OF CRP AS AN EARLY PREDICTOR OF ANASTOMOTIC LEAK AFTER GASTROINTESTINAL REPAIR SURGERIES

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Abstract

Anastomotic leak is a major postoperative complication following gastrointestinal resection and anastomosis, with risk factors such as diabetes mellitus, hypoalbuminemia, and impaired wound healing contributing to its occurrence. This prospective observational study was conducted to identify factors associated with anastomotic leak and to evaluate the role of postoperative serum C-reactive protein (CRP) as an early predictive marker. A total of 100 patients undergoing gastrointestinal resection and primary anastomosis were studied, and CRP levels were measured on postoperative days 1, 3, and 5. Patients who developed anastomotic leak showed significantly higher CRP levels on postoperative days 3 and 5, while diabetes mellitus and hypoalbuminemia were found to be significantly associated with an increased risk of leakage. Serial postoperative CRP monitoring was found to be a simple, reliable, and cost-effective method for the early detection of anastomotic leak and may facilitate timely intervention and improved surgical outcomes.

Advancement of Knowledge

The present study reinforces the role of postoperative C-reactive protein (CRP) as a practical and reliable biomarker for the early prediction of anastomotic leak following gastrointestinal surgery. It

highlights the significance of serial CRP monitoring, particularly on postoperative days 3 and 5, in identifying patients at increased risk before the appearance of overt clinical signs. The study also emphasizes the contribution of diabetes mellitus and hypoalbuminemia as important risk factors for anastomotic failure, thereby supporting risk-stratified postoperative surveillance and timely intervention.

Keywords

Anastomotic Leak; C-Reactive Protein (CRP); Gastrointestinal Anastomosis; Intestinal Resection; Postoperative Complications; Biomarker; Diabetes Mellitus; Hypoalbuminemia; Early Prediction; Gastrointestinal Surgery.

Introduction

Anastomotic leak remains one of the most serious complications following gastrointestinal surgery and is associated with significant morbidity, prolonged hospital stay, increased healthcare costs, and mortality. Despite advancements in surgical techniques, perioperative care, and postoperative monitoring, the incidence of anastomotic leakage continues to pose a major challenge to surgeons worldwide. Early identification of patients at risk is crucial because delayed diagnosis often leads to sepsis, reoperation, and poor clinical outcomes [1,2].

An anastomotic leak is defined as a defect in the integrity of a surgical anastomosis resulting in communication between the intra- and extraluminal compartments. The reported incidence varies depending on the site of anastomosis, patient characteristics, and operative factors, ranging from 2% to 20% in different gastrointestinal procedures [3,4]. Several risk factors have been implicated in the development of anastomotic leakage, including advanced age, malnutrition, diabetes mellitus, smoking, emergency surgery, intraoperative contamination, poor tissue perfusion, and technical errors during anastomosis construction [5].

Clinical diagnosis of anastomotic leak is often difficult during the early postoperative period because signs such as fever, abdominal pain, tachycardia, and leukocytosis may be nonspecific. Conventional imaging modalities, although useful, may not always detect leaks in their initial stages and can delay intervention [6]. Therefore, there is growing interest in identifying reliable biochemical markers that can facilitate early detection and improve postoperative surveillance strategies.

C-reactive protein (CRP) is an acute-phase reactant synthesized by hepatocytes in response to inflammatory cytokines, particularly interleukin-6. Its concentration rises rapidly following tissue injury, infection, or inflammation, making it a useful marker of postoperative inflammatory response [7]. Following uncomplicated gastrointestinal surgery, CRP levels typically peak within the first few postoperative days and then gradually decline. Persistently elevated or rising CRP levels may indicate the presence of postoperative complications, including anastomotic leakage [8].

Several studies have investigated the predictive value of postoperative CRP measurements in patients undergoing gastrointestinal resections and anastomotic procedures. Elevated CRP levels during the early postoperative period have been associated with a significantly increased risk of anastomotic failure, suggesting that CRP may serve as a simple, inexpensive, and readily available biomarker for early leak detection [9]. Furthermore, serial CRP monitoring has demonstrated promising sensitivity and negative predictive value, allowing clinicians to identify low-risk patients and potentially facilitate safe early discharge protocols [10].

Recent evidence also supports the integration of CRP-based monitoring into enhanced recovery pathways, where early recognition of complications is essential for improving patient outcomes. Studies have shown that postoperative CRP trends correlate closely with the development of infectious and

anastomotic complications, highlighting its potential role as an objective adjunct to clinical assessment [11].

Given the substantial clinical impact of anastomotic leakage and the need for timely diagnosis, evaluating the utility of CRP as an early predictive marker is of considerable importance. This prospective observational study aims to assess the relationship between postoperative CRP levels and the occurrence of anastomotic leak following gastrointestinal anastomotic surgery, thereby contributing to improved postoperative monitoring and patient management.

Methodology

This prospective observational study was conducted in the Department of General Surgery at a tertiary care teaching hospital over a period of 18 months from January 2025 to June 2026 after obtaining approval from the Institutional Ethics Committee. The study was designed to evaluate the role of postoperative serum C-reactive protein (CRP) as an early predictor of anastomotic leak following gastrointestinal anastomotic surgery. All eligible patients were enrolled consecutively after obtaining written informed consent.

The study included adult patients aged 18 years and above who underwent elective or emergency gastrointestinal resection with primary anastomosis. Patients with pre-existing systemic inflammatory disorders, autoimmune diseases, chronic liver disease, active infection before surgery, malignancy receiving neoadjuvant chemotherapy, long-term steroid therapy, immunosuppressive treatment, or those undergoing stoma formation without intestinal anastomosis were excluded from the study. Patients who died within 48 hours of surgery due to causes unrelated to anastomotic failure were also excluded.

A total of 100 patients fulfilling the inclusion criteria were enrolled. Detailed demographic and clinical data were recorded for each patient, including age, sex, body mass index, smoking history, alcohol consumption, diabetes mellitus, hypertension, anemia, serum albumin level, indication for surgery, type of surgery, site of anastomosis, operative duration, intraoperative blood loss, degree of peritoneal contamination, and need for blood transfusion. Both emergency and elective gastrointestinal procedures involving gastric, small bowel, and colorectal anastomoses were included.

All operations were performed by consultant surgeons or under their direct supervision following standard surgical principles. Perioperative antibiotic prophylaxis and postoperative care were administered according to institutional protocols. Patients were closely monitored in the postoperative period for signs suggestive of anastomotic leak, including fever, tachycardia, abdominal pain, abdominal distension, prolonged ileus, wound infection, purulent or feculent drain discharge, generalized peritonitis, and sepsis.

Venous blood samples were collected under aseptic precautions for measurement of serum CRP levels on postoperative day (POD) 1, POD 3, and POD 5. Serum CRP concentration was measured using an immunoturbidimetric assay in the central biochemistry laboratory of the hospital, and values were expressed in mg/L. The postoperative trend of CRP levels was recorded and compared between patients who developed an anastomotic leak and those who had an uncomplicated postoperative course.

Anastomotic leak was defined as a defect in the integrity of the gastrointestinal anastomosis resulting in communication between the intra- and extraluminal compartments. The diagnosis was established based on clinical findings and confirmed by radiological investigations such as contrast-enhanced computed tomography of the abdomen, water-soluble contrast studies, ultrasonography-guided drainage findings, or re-exploration when required. Patients were categorized into two groups: the leak group and the non-leak group.

All patients were followed until discharge from the hospital or death. The primary outcome measure was the occurrence of anastomotic leak. Secondary outcome measures included postoperative morbidity, duration of hospital stay, requirement for re-intervention or reoperation, intensive care unit admission, and mortality. The relationship between postoperative CRP levels and the development of anastomotic leak was analyzed.

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using Student's t-test for continuous variables and Chi-square test or Fisher's exact test for categorical variables as appropriate. Receiver Operating Characteristic (ROC) curve analysis was performed to determine the optimal CRP cut-off value for predicting anastomotic leak. Sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve (AUC) were calculated. A p-value of less than 0.05 was considered statistically significant.

Confidentiality of patient information was maintained throughout the study. Participation was voluntary, and all procedures were carried out in accordance with the ethical principles of the Declaration of Helsinki and institutional research guidelines.

Results

A total of 100 patients undergoing gastrointestinal resection and primary anastomosis were included in the present study. The age of the patients ranged from 18 to 75 years, with a mean age of 47.3 ± 13.2 years. The majority of patients belonged to the 41–50 years age group (24%), followed by the 31–40 years age group (22%), as shown in **Table 1**. Male patients predominated in the study population, accounting for 68% of the cases, while females constituted 32% (**Table 2**).

Of the 100 patients studied, 12 patients developed an anastomotic leak, giving an overall leak rate of 12%, whereas 88 patients had an uneventful postoperative recovery (**Table 3**). Small bowel resection and anastomosis was the most commonly performed procedure, accounting for 52% of all operations, followed by ileocolic anastomosis (18%), colorectal anastomosis (16%), and gastrojejunostomy (14%) (**Table 4**).

Postoperative CRP levels were evaluated on postoperative day (POD) 1, POD 3, and POD 5. Although the mean CRP level on POD 1 was higher in patients who subsequently developed an anastomotic leak compared with those who did not, the difference was not statistically significant (118.4 ± 24.6 mg/L vs. 102.3 ± 21.8 mg/L; $p = 0.071$). However, a marked increase in CRP levels was observed among patients who developed anastomotic leakage on POD 3 and POD 5. On POD 3, the mean CRP level in the leak group was 196.7 ± 34.2 mg/L compared to 108.6 ± 26.4 mg/L in the non-leak group, and this difference was highly statistically significant ($p < 0.001$). Similarly, on POD 5, CRP levels remained significantly elevated in the leak group (178.5 ± 38.7 mg/L) compared to the non-leak group (62.4 ± 19.1 mg/L), with a highly significant p-value (<0.001), as shown in **Table 5**.

The association between diabetes mellitus and the occurrence of anastomotic leak was also analyzed. Among the 24 diabetic patients included in the study, 6 developed an anastomotic leak, whereas only 6 leaks occurred among the 76 non-diabetic patients. Statistical analysis demonstrated a significant association between diabetes mellitus and an increased risk of anastomotic leakage ($p = 0.020$), indicating that diabetic patients were more prone to postoperative anastomotic complications (**Table 6**).

Serum albumin levels were evaluated as a marker of nutritional status. Hypoalbuminemia (serum albumin <3.5 g/dL) was present in 28 patients, of whom 8 developed an anastomotic leak. In contrast, only 4 leaks occurred among the 72 patients with normal serum albumin levels. The incidence of leak was significantly higher in patients with hypoalbuminemia, and statistical analysis revealed a strong

association between low serum albumin levels and anastomotic failure (p = 0.001), as illustrated in **Table 7**.

Receiver Operating Characteristic (ROC) curve analysis was performed to assess the diagnostic performance of CRP in predicting anastomotic leakage. Postoperative day 3 CRP demonstrated excellent predictive accuracy with an area under the curve (AUC) of 0.91. A CRP cut-off value of 150 mg/L provided a sensitivity of 91.7% and specificity of 84.1% for predicting anastomotic leak. Furthermore, the negative predictive value was 98.7%, indicating that patients with CRP levels below the cut-off were highly unlikely to develop an anastomotic leak (**Table 8**).

Overall, the findings of the present study demonstrated that persistently elevated postoperative CRP levels, particularly on POD 3 and POD 5, were strongly associated with the development of anastomotic leak. In addition, diabetes mellitus and hypoalbuminemia emerged as significant risk factors for anastomotic failure. The high sensitivity and negative predictive value of CRP observed in this study suggest that serial postoperative CRP monitoring may serve as a reliable and cost-effective tool for the early detection and exclusion of anastomotic leakage following gastrointestinal anastomotic surgery.

Table 1. Distribution of Patients According to Age

Age Group (Years)	Number of Patients (n=100)	Percentage (%)
18–30	18	18.0
31–40	22	22.0
41–50	24	24.0
51–60	20	20.0
>60	16	16.0

The majority of patients belonged to the 41–50 years age group (24%), followed by the 31–40 years age group (22%). The mean age of the study population was 47.3 ± 13.2 years.

Table 2. Gender Distribution

Gender	Number	Percentage (%)
Male	68	68.0
Female	32	32.0

Male patients constituted 68% of the study population, whereas females accounted for 32%.

Table 3. Incidence of Anastomotic Leak

Outcome	Number	Percentage (%)
Leak Present	12	12.0

Outcome	Number	Percentage (%)
Leak Absent	88	88.0

Anastomotic leak occurred in 12% of patients undergoing gastrointestinal anastomotic surgery.

Table 4. Type of Surgery Performed

Type of Surgery	Number	Percentage (%)
Small Bowel Resection & Anastomosis	52	52.0
Ileocolic Anastomosis	18	18.0
Colorectal Anastomosis	16	16.0
Gastrojejunostomy	14	14.0

Small bowel resection and anastomosis was the most commonly performed procedure (52%).

Table 5. Comparison of CRP Levels Between Leak and Non-Leak Groups

Postoperative Day	Leak Group (n=12) Mean ± SD (mg/L)	Non-Leak Group (n=88) Mean ± SD (mg/L)	p-value
POD 1	118.4 ± 24.6	102.3 ± 21.8	0.071
POD 3	196.7 ± 34.2	108.6 ± 26.4	<0.001
POD 5	178.5 ± 38.7	62.4 ± 19.1	<0.001

Mean CRP levels were higher in patients who developed anastomotic leak at all postoperative time points. The difference was statistically significant on postoperative day 3 and postoperative day 5 ($p < 0.001$).

Table 6. Association of Diabetes Mellitus with Anastomotic Leak

Diabetes Status	Leak Present	Leak Absent	Total
Diabetic	6	18	24
Non-Diabetic	6	70	76

Statistical Test	Value
Chi-square	5.42
p-value	0.020

Diabetes mellitus was significantly associated with an increased risk of anastomotic leak (p=0.020).

Table 7. Association of Hypoalbuminemia with Anastomotic Leak

Serum Albumin	Leak Present	Leak Absent
<3.5 g/dL	8	20
≥3.5 g/dL	4	68

Statistical Test	Value
Chi-square	10.26
p-value	0.001

Patients with hypoalbuminemia showed a significantly higher incidence of anastomotic leak compared to patients with normal serum albumin levels.

Table 8. ROC Analysis of CRP on POD 3

Parameter	Value
Cut-off CRP	150 mg/L
Sensitivity	91.7%
Specificity	84.1%
Positive Predictive Value	44.0%
Negative Predictive Value	98.7%
AUC	0.91

ROC curve analysis demonstrated excellent predictive accuracy of CRP on postoperative day 3 for detecting anastomotic leak. A CRP value greater than 150 mg/L yielded a sensitivity of 91.7% and specificity of 84.1%.

Overall Interpretation

Among 100 patients included in the study, the incidence of anastomotic leak was 12%. Patients who developed a leak had significantly higher postoperative CRP levels compared to those without leak. The difference became highly significant from postoperative day 3 onwards. Diabetes mellitus and hypoalbuminemia were also identified as significant risk factors for anastomotic leakage. ROC curve analysis showed that postoperative day 3 CRP was an excellent predictor of leak, with high sensitivity and negative predictive value. These findings suggest that serial postoperative CRP monitoring may serve as a useful, inexpensive, and readily available tool for early detection of anastomotic leak following gastrointestinal anastomotic surgery.

Discussion

Anastomotic leak is one of the most serious complications following gastrointestinal resection and anastomosis and continues to be a major cause of postoperative morbidity and mortality despite significant advances in surgical techniques, perioperative care, and critical care management. Delayed diagnosis of an anastomotic leak often results in sepsis, prolonged hospital stay, reoperation, increased healthcare expenditure, and poor patient outcomes. Consequently, the identification of reliable biomarkers capable of detecting anastomotic leakage before the onset of overt clinical symptoms has become an important area of surgical research [1,2].

In the present study, the incidence of anastomotic leak was 12%. This finding is comparable to the leak rates reported in previous studies, which have ranged from 2% to 20% depending on patient selection, anatomical site of anastomosis, underlying pathology, and surgical technique [2,3,4]. Bruce et al. [2] highlighted that anastomotic leakage remains a major determinant of postoperative morbidity following gastrointestinal surgery, while Reinke et al. [4] demonstrated its significant impact on hospital stay and postoperative recovery. The leak rate observed in the present study therefore falls within the range reported in the available literature.

The demographic profile of the study population revealed a predominance of male patients with a mean age comparable to that reported by previous investigators studying gastrointestinal anastomotic outcomes [5,6]. Although age and gender have been suggested as potential contributors to impaired healing, the evidence remains inconsistent, and their direct influence on anastomotic leakage is often overshadowed by other factors such as nutritional status, comorbid conditions, and tissue perfusion [7].

The most important finding of the present study was the significant association between elevated postoperative CRP levels and the development of anastomotic leakage. While CRP values on postoperative day 1 were higher among patients who subsequently developed a leak, the difference was not statistically significant. However, a marked and statistically significant elevation of CRP levels was observed on postoperative day 3 and postoperative day 5 among patients with anastomotic leakage. This observation supports the hypothesis that persistent postoperative inflammatory response serves as an early indicator of occult septic complications and impaired anastomotic healing.

Several previous studies have demonstrated similar findings. Lee et al. [5] reported that postoperative CRP is a useful predictor of infectious complications following gastrointestinal surgery. Wiggins et al. [6] further demonstrated that elevated CRP levels possess good diagnostic accuracy for identifying patients at risk of postoperative complications, particularly anastomotic failure. Nugent et al. [7] emphasized the utility of serial CRP monitoring in postoperative surveillance and highlighted its role in early clinical decision-making.

The findings of the present study are also consistent with the observations of Huang et al. [8], who demonstrated that persistently elevated CRP levels following gastric surgery were significantly associated with anastomotic complications. Similarly, Li et al. [9] reported that postoperative CRP values could accurately predict major complications following gastrointestinal resection. Chen et al. [10] found that CRP measured during the early postoperative period had excellent sensitivity and specificity for identifying anastomotic leakage, while Fujisaki et al. [11] observed that CRP levels on postoperative day 3 could reliably identify patients likely to develop postoperative complications.

The predictive value of CRP has also been confirmed in several studies involving colorectal surgery. Qiu et al. [12] demonstrated that elevated postoperative CRP levels were strongly associated with an increased incidence of anastomotic leakage. Pequignot et al. [13] reported that CRP was an effective biomarker for identifying early postoperative complications after gastrointestinal reconstructive procedures. Similarly, van Helsdingen et al. [14] concluded that CRP remains one of the most extensively validated inflammatory markers for postoperative monitoring following gastrointestinal surgery.

Receiver Operating Characteristic (ROC) analysis performed in the present study demonstrated excellent predictive performance of postoperative day 3 CRP. Similar findings have been reported by Low et al. [15], who observed that postoperative CRP possesses high diagnostic accuracy and an excellent negative predictive value for excluding anastomotic leakage. Hamabe et al. [16] also found that CRP monitoring could facilitate early identification of high-risk patients and improve postoperative surveillance strategies.

The high negative predictive value observed in the present study is of particular clinical importance. Patients with CRP values below the established cut-off on postoperative day 3 were highly unlikely to develop an anastomotic leak. This finding supports the concept proposed by Zhang et al. [17], who demonstrated that low postoperative CRP levels can safely identify patients suitable for accelerated recovery and early discharge protocols. Similar conclusions were reached by Cauchy et al. [18], who emphasized the usefulness of CRP in reducing unnecessary investigations and optimizing postoperative resource utilization.

In addition to CRP, the present study identified diabetes mellitus as a significant risk factor for anastomotic leakage. Patients with diabetes exhibited a higher incidence of leak compared with non-diabetic individuals. Impaired microvascular circulation, delayed collagen synthesis, altered inflammatory response, and compromised wound healing associated with diabetes may explain this increased susceptibility. Similar observations have been reported in multiple studies evaluating risk factors for anastomotic failure [2,4,19].

Hypoalbuminemia was another factor significantly associated with anastomotic leakage in the present study. Patients with serum albumin levels below 3.5 g/dL experienced a substantially higher leak rate than patients with normal nutritional status. Nutritional deficiency adversely affects fibroblast proliferation, collagen deposition, angiogenesis, and tissue repair, thereby impairing anastomotic healing. Previous investigations have consistently identified hypoalbuminemia as an independent predictor of postoperative complications and anastomotic failure [5,6,19].

Recent evidence has further strengthened the role of CRP in postoperative monitoring. Mayank et al. [1] demonstrated that serial CRP measurements provide valuable information regarding the risk of anastomotic leakage and may facilitate earlier intervention. Rajabaleyan et al. [20] similarly reported that inflammatory biomarkers, particularly CRP, continue to play an important role in contemporary postoperative surveillance protocols and can contribute significantly to improved patient outcomes when incorporated into standardized clinical pathways.

The present study supports the growing body of evidence indicating that postoperative CRP is a simple, inexpensive, widely available, and reliable biomarker for the early detection of anastomotic leakage. Its routine use may allow clinicians to identify high-risk patients before the appearance of overt clinical manifestations, enabling timely diagnostic evaluation and intervention. Furthermore, patients with low CRP levels may benefit from enhanced recovery protocols and earlier discharge, thereby reducing healthcare costs and improving resource utilization.

However, the present study has certain limitations. It was conducted at a single tertiary care center and involved a relatively limited sample size. Variations in the type and location of gastrointestinal anastomoses may also influence leak rates and CRP kinetics. Therefore, larger multicentric studies involving standardized CRP measurement protocols are required to establish universally applicable cut-off values and strengthen the evidence supporting CRP-guided postoperative management.

Overall, the findings of the present study demonstrate that elevated postoperative CRP levels, particularly on postoperative days 3 and 5, are strongly associated with the development of anastomotic leakage following gastrointestinal surgery. The results are consistent with the findings reported by numerous investigators [1–20] and support the incorporation of serial CRP monitoring into routine postoperative care for the early detection and management of anastomotic complications.

Conclusion

Postoperative serum CRP is a reliable and cost-effective biomarker for the early prediction of anastomotic leak following gastrointestinal anastomotic surgery. Persistently elevated CRP levels, particularly on postoperative days 3 and 5, are significantly associated with the development of anastomotic leakage. Routine postoperative CRP monitoring may facilitate early diagnosis, timely intervention, and improved postoperative outcomes.

References

1. Shaswat Mayank, Cureus 2024 Oct 8;16(10):e71107, PMID: 39525122
2. J Bruce, Br J Surg 2001 Sep;88(9):1157-68. PMID: 11531861
3. Abbas MA.Dis Colon Rectum. 2010 Jun;53(6):859-60.PMID: 20484997
4. Reinke CE, .Dis Colon Rectum. 2013 May;56(5):638-44.PMID: 23575404
5. Lee S, J Gastrointest Surg. 2007 Jun;11(6):708-13.PMID: 17562118
6. Wiggins T, .Surg Oncol. 2015 Sep;24(3):181-6. Epub 2015 Jun 17.PMID: 26116395
7. Nugent TS, .Int J Colorectal Dis. 2021 Sep;36(9):1819-1829. Epub 2021 Apr 1.PMID: 33796958
8. Chang-Ming Huang, Medicine (Baltimore) 2015 May;94(17):e812. PMID: 25929938
9. Li P, Huang.Surg Endosc. 2016 Sep;30(9):4092-101. Epub 2015 Dec 23.PMID: 26701705
10. Chen K, Surg Laparosc Endosc Percutan Tech. 2018 Feb;28(1):e18-e23. PMID: 29176372
11. Fujisaki M,.Surg Endosc. 2016 Apr;30(4):1380-7. Epub 2015 Jun 27.PMID: 26123337
12. Qiu H, .J Cancer Res Ther. 2019;15(7):1450-1463.PMID: 31939422
13. Pequignot A, .Obes Surg. 2012 May;22(5):712-20. .PMID: 22328096
14. van Helsdingen CP, .World J Gastroenterol. 2020 Jun 21;26(23):3293-3303. PMID: 32684743
15. Low DE, .J Gastrointest Surg. 2010 Nov;14(11):1646-52. . Epub 2010 Sep 8.PMID: 20824376
16. Hamabe A, .Asian J Endosc Surg. 2018 Aug;11(3):220-226. Epub 2017 Dec 12.PMID: 29230964
17. Zhang W, .Int J Colorectal Dis. 2017 Oct;32(10):1431-1437. Epub 2017 Aug 2.PMID: 28766076
18. Cauchy F, .Int J Colorectal Dis. 2017 May;32(5):699-707. . Epub 2017 Jan 26.PMID: 28124742
19. Sciuto A, .World J Gastroenterol. 2018 Jun 7;24(21):2247-2260. d.PMID: 29881234
20. Rajabaleyan P, .Ann Coloproctol. 2024 Oct;40(5):431-439. Epub 2024 Oct 8.PMID: 39376121
21. Oh CK, .Ann Coloproctol. 2020 Aug;36(4):273-280. Epub 2019 Nov 13.PMID: 32054256
22. Tonini V, Zanni M.World J Gastrointest Surg. 2023 May 27;15(5):745-756. .PMID: 37342854
23. Scardino A, .Int J Colorectal Dis. 2024 Sep 27;39(1):152. PMID: 39331160
24. Shin HH, .Biomimetics (Basel). 2023 Nov 12;8(7):542. .PMID: 37999183
25. Ishiyama Y, .Asian J Surg. 2021 Feb;44(2):485-487. Epub 2020 Nov 21.PMID: 33229124