

Prognostic Value of C-reactive Protein in Anastomotic Leakage within Three Days After Colorectal Surgery

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Abstract

Background: C-reactive protein (CRP) has been used as an indicator of postoperative complications. Considering the accuracy of this marker, in this study, we studied the diagnostic value of serum level of CRP as a marker for early detection of anastomotic leakage after colorectal surgery.

Materials and Methods: In this retrospective study, 214 patients underwent colorectal surgery were included. Based on the presence or absence of anastomotic leakage, these patients were divided into two groups: 17 patients in the group with anastomotic leakage and 197 patients in another group without anastomotic leakage. The two groups were compared for the serum CRP value that was measured and recorded on the third day after surgery.

Results: According to the acquired results, no significant differences were observed between the two groups in terms of disease (cancer or other diseases), type of surgery, height, and body mass index. Comparison between the two groups showed that the CRP value in the group with anastomotic leakage (127 ± 17.586) was significantly higher than that in the group without anastomotic leakage (49.81 ± 11.466) ($P = 0.000$).

Conclusion: The results of this study indicated that early assessment of CRP value after colorectal surgery is a special marker for the presence or absence of anastomotic leakage with high sensitivity and specificity.

Key Words: C-reactive protein, anastomotic leakage, colorectal surgery, prognostic value

Introduction

Anastomotic leakage is a serious complication after colorectal surgery, which is associated with increased death and complications after surgery, staying longer in the hospital, and higher costs of treatment (1-4). There are several risk factors that are associated with anastomotic leakage. But prediction of this complication in patients is still a challenging and important issue (5-7). In spite of the increasing knowledge about the risk factors regarding anastomosis and the improving surgical techniques, this complication is still a major challenge and occurs without any clear

indications and specific symptoms in some patients. The diagnosis of anastomotic leakage should occur at the earliest possible time to reduce its related mortality (8-10). The C-reactive protein (CRP) is an acute phase protein synthesized by the liver. This protein is known as an important indicator of postoperative anomalies for abdominal surgery. Due to its half-life, CRP is a valid marker for the secondary response to systemic infection for the surgical procedure and even an appropriate marker for tracking patients' recovery. Recently, this protein has been identified as an early indicator of abdominal septic abnormalities after esophageal anomalies, and pancreas and rectal anastomotic leakage. This protein, as a special marker, can make diagnosis of anastomotic leakage in a timely manner, thus reducing the mortality rate (11-13). To identify the diagnostic value of CRP protein measurement for anastomotic leakage, we designed the study to analyze the serum CRP value within 3 days after surgery and its diagnostic value for anastomotic leakage.

Materials and Methods

This was a retrospective study. The study population included all patients who referred to Shahid Sadoughi, Shahid Rahmemon, and Morteza Hospital during 2015-2016 and underwent colon or rectal surgery with intestinal anastomosis.

Patients were divided into two groups: anastomotic leakage and non-anastomotic leakage. Exclusion criteria were the absence of serum CRP value and/or the presence of preoperative infection. The two groups were compared in terms of pathological variables, weight, height, surgical method, and serum CRP level after surgery (third day after surgery). Anastomotic leakage was diagnosed based on the clinical indications of peritonitis or clinical evidence associated with fecal fluid in the abdomen or in the surgical drains, which was documented in patients' records. Collected data were analyzed with statistical software SPSS (version 22). The data were analyzed for the sensitivity and specificity of the positive and negative predictive values and diagnostic accuracy.

Results

Totally, 228 cases were extracted by investigation of the records in the hospital files. Of them, 14 cases had no CRP values. Therefore, these cases were excluded. A total of 214 patients were included and investigated. The 214 patients were divided into two groups, which did not differ significantly between two groups in terms of height and BMI.

The types of surgery were also assessed between the two groups (right, left or total colectomy). As shown in this Table 1, the most common type of surgery in both groups was left colectomy. The two groups did not show a significant difference in

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Table 1. Frequency and comparison for the type of surgery and CRP level between two groups

Group	Left colectomy	P value	Right colectomy	P value	Total colectomy	P value	CRP level	P value
Anastomotic leakage	146 (74.1%)	0.097	43 (21.8%)	0.018	8 (4.1%)	0.045	49.81±11.466	0.000
None	16 (94.1%)		0 (0%)		1 (5.9%)		127±17.586	

the type of left colectomy. Regarding the right colectomy and total colectomy, there was a significant difference between the two groups.

The CRP levels were compared between the two groups, and the results are summarized in Table 1. The results showed that there was a higher level of CRP value in the anastomotic leakage group than in non-anastomotic leakage group. Statistical difference was significant between the two groups. The ROC chart was generated based on the CRP value on the third day after surgery (Figure 1). The curve was analyzed for the optimal cut-off calculation of CRP by sensitivity and specificity association. In this chart, the displacement and deviation of the curve from the reference line represented the high accuracy of the test. The CRP related cut-off value in this test was 97 based on statistical analysis. Based on ROC chart and statistical calculation, the sensitivity of the method was 94.1% and its characteristic was 99%. The positive predictive value for this test was 92.1% and the negative impact value was 99.5%.

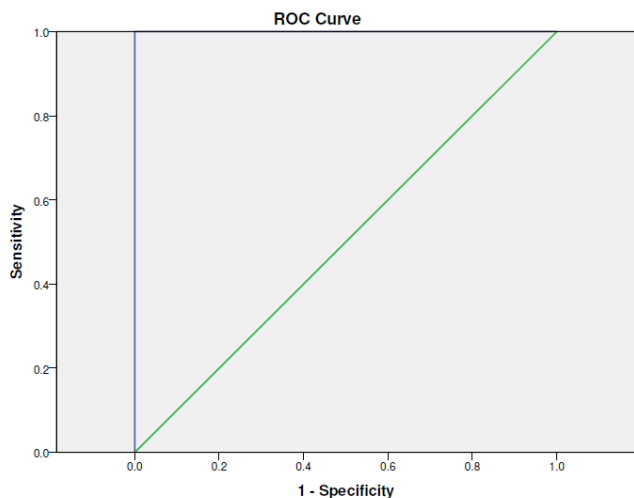


Fig. 1. ROC curve based the sensitivity and specificity of CRP values.

Discussion

The aim of this study was to determine the diagnostic value of CRP protein level for anastomotic leakage after colorectal surgery. Therefore, patients underwent colorectal surgery were categorized into two groups, anastomotic leakage and non-anastomotic leakage, and were evaluated for the serum CRP level. The two groups had similar BMI without significant difference between

them. The prevalence of anastomotic leakage after colon and rectal surgery varies from 1% to 20%, and the incidence depends on the type of surgical procedure (1, 2). This problem is associated with a high mortality of the patient, and nearly one third of the deaths from colon and rectal surgery are due to anastomotic leakage (3, 14). In the present study, the mortality rate was not evaluated due to the lack of complete registration of the information. Of course, the urgency of a quick diagnostic method of anastomotic leakage is indispensable. The diagnosis is not always easy in the early postoperative period due to low clinical manifestations. This lack of early diagnosis leads to increased mortality (4, 15, 16). According to Loos *et al.*, a delayed diagnosis of anastomotic leakage (5 days after surgery) will increase mortality by 18%. But if this problem is detected before the 5th day, the mortality rate will be minimized (1). Early diagnosis of this problem is an urgent need for immediate initiation of treatment. CRP is a protein that is almost exclusively produced by liver cells as part of the acute phase response (2, 3). The half-life of this protein (approximately 19 hours) has led to the prescription of CRP as a valuable marker for diagnosis of disease activity, inflammatory response, postoperative recovery, or postoperative problems. An increase in CRP level is considered as an independent diagnostic indicator of patients with colon, liver and pancreatic cancer (4). This inflammatory marker is also used to determine pancreatic necrosis and monitor the severity of patients with acute pancreatitis. CRP, along with clinical signs and other inflammatory markers, is considered as an undesirable scoring index for surgical and non-surgical complications. Recently, this protein has been identified as an early predictor of septic abnormalities after rectal, pancreatic and esophageal surgery. Given the potential side effects of anastomotic leakage in colon and rectal surgery, there is a special emphasis on the role of this protein (5). In this study, we observed that on the third day after surgery, the mean serum CRP in the group with anastomotic leakage was significantly higher, indicating the diagnostic value of this marker for assessing the prevalence of the complication of anastomotic leakage. The results of the present study are consistent with the results of other studies and it is suggested that early and stable assessment of postoperative CRP serum level is a predictor of anastomotic leakage in patients. They can also be used for other infectious complications (respiratory, urinary and surgical wounds) (5-8). Change observed in CRP protein level in patients with postoperative anastomotic leakage suggests that infectious processes and activation of the CRP synthesis are immediate after the surgical procedure and before the onset of clinical manifestations. The synthesis of this inflammatory marker only depends on the function of the liver and is not compromised by the defect of other organs. Therefore, the speed of production of this protein truly reflects the intensity of the inflammatory process. Ischemic tissue in the suture line seems to

be responsible for the occurrence of a severe inflammatory response followed by an increase in the synthesis of CRP (17-20). In several studies on human and animal samples, the reduction of oxygen content of the anastomotic leakage tissue that causes changes in the healing process has been observed. A decrease in the pH of the anastomosis mucosa occurs in the first 24 hours after surgery with an increased risk of opening, and this theory proves that the weak tissue perfusion of an anastomosis begins very quickly and increases the risk of problems (21-25). Welsh *et al.* have found that the CRP level on the third day after surgery is higher than 140 mg/L in patients underwent rectal surgery and has a positive diagnostic value in predicting postoperative anomalies, especially anastomotic leakage. The sensitivity of this protein in this diagnosis is 80% and its specificity is 81% and its predictive value is 85.7% (6). From this perspective, our results are consistent with those of Welsh *et al.* Our study also demonstrated the diagnostic value of measuring CRP protein level on day 3 after surgery as an indicator of postoperative abnormalities. The results of our study and other similar studies on the diagnostic value of CRP were consistent. Various studies have compared the diagnostic value of serum leukocytes to detect postoperative abnormalities with that of CRP serum level. These studies have shown that the count of blood cells is not as good as measuring serum CRP levels in detecting anastomosis after surgery (6,7,16). In some studies, procalcitonin has been considered as a more appropriate marker than CRP as an indicator of inflammatory changes, but this marker indicates the magnitude of inflammatory response in the first 12 hours after surgery and should be interpreted with caution (7). Some patients may have little underlying clinical anastomotic leakage. Although these patients do not need medical intervention, the goal is to achieve early diagnosis of significant clinical abnormalities that can lead to increased mortality. Therefore, considering that the level of CRP protein increases until the third day after surgery, this protein appears to be more appropriate as the diagnostic indicator than other markers. As it is clear from the ROC chart, the displacement and deviation of the curve from the reference line represent the high accuracy of the test. The CRP related cut-off in this test was 97 based on statistical analysis. Waterland *et al.* calculated and compared the diagnostic value of this protein on the first, second, third, fourth, fifth, sixth and seventh days after laparoscopic and colorectal surgeries. The cut-off rates on the first day of open surgery and the fourth day in laparoscopic surgery are close to the calculated cutoff rate in our study (16). In the study by Waterland *et al.*, sensitivity is calculated at 90% and 87%, respectively. Because of the deviation of the ROC curve from the standard line, this indicates the high accuracy of the calculation of CRP values in the early detection of anastomotic leakage of colon and rectum surgery. Our study showed a good increase in this protein on the third day after surgery and emphasized the diagnostic value of this protein.

Conclusion

The results of this study suggested that CRP protein measurement could be used as an early diagnostic tool for the diagnosis of anastomotic leakage after colon and rectal surgery. The level of this protein on the third day after colon and rectal surgery in patients with anastomotic leakage had a significantly increase compared to that in patients without anastomotic leakage. Based on the ROC curve, the diagnostic accuracy of this protein was high. Therefore, the CRP protein level can be used as an accurate predictor of anastomotic leakage.

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