#### **Review Article**

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# Is C-Reactive Protein (CRP) A Reliable Marker for Postoperative Complications in Gastrointestinal and Colorectal Surgery?

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## Key Messages:

We need more prospective studies in this field to decide the main purpose and role of CRP in postoperative period.

#### 1. Abstract

**1.1. Background:** There are many markers that have been studied in the prediction of the immune and inflammatory response postoperatively; among them the most common one is CRP.

## 2. Summary

CRP seems to be a good marker of the inflammatory response after colorectal, gastric, and bariatric operations, and in combination with the clinical picture of the patient can predict postoperative complications, but it is nonspecific and there is a need to wait minimally 48 hours until its peak level reached.

#### 3. Introduction

It very essential to be able to predict the complications that can arise after surgical, this is crucial to accelerate the recovery of patients, intervene in the appropriate time, and decrease pain. Different markers of surgical stress have been studied; one of them is C-reactive protein (CRP) measurement during the postoperative period in different gastrointestinal and colorectal procedures [1-3].

It is well known now that the laparoscopic approach has a less stress effect on the human body after surgery than the open approach for the same kind of procedure [4]. Multiple studies examined CRP to check the stress response of the patients after the surgical operations and then study the degree of an inflammatory response postoperatively [5, 6]. The higher its value, the higher the probability of Systemic Inflammatory Response Syndrome (SIRS). Evaluation of the level of CRP done before surgery and in the postoperative days. If the value of it increased during the postoperative days this will indicate greater inflammatory response and maybe early complications

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## [7, 8].

There are two main approaches for gastrointestinal and colorectal surgery, which are minimally invasive approach which includes robotic or laparoscopic and open surgery approach. Although multiple studies showed that the laparoscopic approach is more beneficial for the patients and their recovery in comparison with the open approach [9, 10], some studies compared the two approaches through observing the postoperative immune response which showed discrepancies in the results [11-14].

There are many markers that have been studied in the prediction of the immune and inflammatory response postoperatively; among them the most common one is CRP. Most of these studies found that CRP levels postoperatively are lower in the laparoscopic approach if we compare it to open surgery [15-17]. The aim of this mini-review is to verify the reliability of CRP or other markers in the prediction of postoperative complications.

#### 4. CRP and Colorectal Cancer Surgery

McDermott et al in their review agreed that CRP concentrations exceeding 150mg/L on a postoperative day 3 should alert surgeons to possible postoperative complications, including anastomotic leak [18]. With the current postoperative regimes, anastomotic leaks are usually diagnosed by CT scan. The median day of diagnosis varies between postoperative days 8 and 13 [19-21]. A recent review shows that more than 50% of colorectal anastomotic leaks were at the highest severity when diagnosed, which requires relaparotomy [22]. These facts would indicate that CRP is a good marker of the inflammatory response and early prediction of complications. So, CRP is of great value in the prediction of complications postoperatively in colorectal operations, of course, it should be correlated with the clinical picture of the patient.

## 5. CRP and Bariatric Surgery

Anastomotic leak after bariatric procedures especially sleeve gastrectomy can be a devastating complication, however, if diagnosed early can improve the management and prognosis.

CRP level is one of the markers used for this purpose in multiple studies. Albanopoulos et al. observed, based on an analysis of177 patients undergoing sleeve gastrectomy, that a highly increased CRP level on the 1<sup>st</sup> and 3<sup>rd</sup> postoperative day may indicate early septic complications [23]. They determined the CRP cut-off as 150 mg/l on the 1st day with 83.2% sensitivity and 100% specificity; furthermore, on the 3rd postoperative day, the cut-off was 200 mg/l with 100% sensitivity and specificity. Similar conclusions were drawn by Warschkow et al. [24] and Williams's et al. [25] analyzing patients after laparoscopic Roux-en-Y gastric bypass surgery. Warschkow et al. determined the CRP cut-off as 229 mg/l on the 2nd postoperative day with 53% sensitivity and 100% specificity, while Williams reported 127 mg/l with 93% sensitivity and 64% specificity, suggesting that further radiological investigation should be done in patients who reach this CRP level. According to researchers CRP on the 2ndpostoperative day is a good predictor of complications after Roux-en-Y gastric bypass.

The CRP peak is not reached until minimally 48 hours postoperatively, so if the patient will be discharged on the first postoperative day the peak may not be detected.

#### 6. CRP and Gastrectomy for Malignancy

It has been suggested by some studies that measuring the magnitude of the postoperative systemic inflammatory response may be useful in determining when to discharge the patient after gastrectomy [26]. CRP was investigated in multiple studies as a measurement of SIRS and prediction of postoperative complications following gastrectomy [27, 28].

Shishido et al reported that CRP on the 3<sup>rd</sup> postoperative day predicted infectious complications following gastric cancer resection [29]. On the other hand, a meta-analysis found that CRP could not predict these complications after gastroesophageal cancer surgery [27]. It is unclear whether the prediction of postoperative complications using CRP values is applicable for all patients.

## 7. Other Predictors

Many studies examined other markers to identify the stress response and the complications postoperatively [30]. IL-6, Cortisol and White Blood Cells (WBC) count are the main inflammatory markers that have been studied [31]. IL-6 was similar to the results of CRP but with earlier peak response until maximum of 24 hours [32]. Cortisol has been examined too and it can get to peak in a maximum time of 4 hours which is noticeably short. However, cortisol concentrations have not been associated with the magnitude of surgical stress and that is why it is not suitable for the prediction of postoperative complications [33]. The same applies to the WBC count because the detection of its peak is before CRP, at 24 hours. However, there is a variable range of results that will not allow for assessment and prediction of the magnitude of the surgical stress and, postoperative complications [34]. Other studies examined more markers such as serum cytokines, alpha-defensins, and TNF- in a trial to find more specific markers [35]. However, their measurements are more complicated than CRP, and the results obtained do not provide much additional information. In summary, we can conclude from the previous review that CRP is reasonably simple to measure; it is a routine check before and after surgical procedures in many centers, and, its level increase in accordance with the degree of surgical stress.

#### 8. Conclusion

CRP seems to be a good marker of the inflammatory response after colorectal, gastric, and bariatric operations, and in combination with the clinical picture of the patient can predict postoperative complications, but it is nonspecific and there is a need to wait minimally 48 hours until its peak level reached.

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