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Is The Postoperative Day-7 C-Reactive Protein–to–Albumin Ratio Associated with Surgical Complications after Colorectal Cancer Surgery?

Postoperatif 7. Gün C-Reaktif Protein/Albümin Oranı ile Cerrahi Komplikasyonların Öngörülmesi: Kolon Kanseri Hastalarında Erken Risk Belirleme Aracı

Suat EVIRGEN, Meryem ÇETİN

Department of General Surgery, Faculty of Medicine, Amasya University, Amasya, Turkey

Abstract

Aim: This study aimed to evaluate the association and clinical utility of the C-reactive protein-to-albumin ratio (CAR), measured on postoperative day 7, for identifying patients at risk of surgical complications after elective colorectal cancer surgery.

Material and Method: A retrospective analysis was conducted of 200 patients who underwent curative colorectal resection between January 2017 and December 2023. Demographic and perioperative data, as well as 30-day postoperative complications, were reviewed. C-reactive protein (CRP) and albumin levels were assessed preoperatively and on postoperative day 7. CAR was calculated as CRP (mg/L) divided by albumin (g/dL). Complications were classified according to the Clavien–Dindo system.

Results: Postoperative complications occurred in 40% of patients. On postoperative day 7, patients with complications had significantly higher CRP levels, lower albumin levels, and higher CAR values (mean CAR: 5.07±2.05 vs. 2.31±1.12; p<0.001). A CAR value ≥ 3.2 was associated with a notably higher complication rate. In addition, patients with complications had a significantly longer hospital stay (median: 12 vs. 7 days; p<0.001).

Conclusion: The postoperative day-7 CAR is a simple and cost-effective biomarker that may help identify patients at higher risk of surgical complications after colorectal cancer surgery. Monitoring CAR in the early postoperative period may support risk stratification and guide clinical decision-making.

Keywords: Colorectal cancer, C-reactive protein, albumin, C-reactive protein-to-albumin ratio, postoperative complications

Öz

Amaç: Bu çalışma, elektif kolorektal kanser cerrahisi sonrası gelişebilecek cerrahi komplikasyonların öngörülmesinde, postoperatif 7. gün ölçülen C-reaktif protein/albumin oranının (CAR) prediktif değerini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Ocak 2017 ile Aralık 2023 tarihleri arasında küratif amaçlı kolorektal rezeksiyon uygulanan 200 hasta retrospektif olarak incelendi. Demografik ve perioperatif veriler ile 30 günlük postoperatif komplikasyonlar değerlendirildi. CRP ve albumin düzeyleri, ameliyat öncesi ve postoperatif 7. günde ölçüldü. CAR, CRP (mg/dL) değerinin albumin (g/dL) değerine bölünmesiyle hesaplandı. Komplikasyonlar Clavien–Dindo sınıflamasına göre değerlendirildi.

Bulgular: Hastaların %40'ında postoperatif komplikasyon gelişti. Komplikasyon gelişen grupta postoperatif 7. gün CRP düzeyleri daha yüksek, albumin düzeyleri ise daha düşük bulundu; buna bağlı olarak CAR değeri anlamlı düzeyde yüksekti (ortalama CAR: 5,07±2,05 vs. 2,31±1,12; p<0,001). CAR değeri ≥3,2 olan hastalarda komplikasyon oranı belirgin olarak yüksekti. Ayrıca, komplikasyon gelişen hastalarda hastanede kalış süresi daha uzundu (medyan: 12 gün vs. 7 gün; p<0,001).

Sonuç: Postoperatif 7. gün ölçülen CAR değeri, kolorektal kanser cerrahisi sonrası gelişebilecek komplikasyonları öngörmede basit, düşük maliyetli ve etkili bir biyobelirteç olabilir. CAR takibi, erken dönemde yüksek riskli hastaların belirlenmesine yardımcı olarak klinik yönetim kararlarının şekillendirilmesine katkı sağlayabilir.

Anahtar Kelimeler: Kolorektal kanser, C-reaktif protein, albümin, C-reaktif protein-albümin oranı, ameliyat sonrası komplikasyonlar

Corresponding *(İletişim)*: Suat EVIRGEN, Department of General Surgery, Faculty of Medicine, Amasya University, Amasya, Turkey
E-mail *(E-posta)*: opdrse@gmail.com
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INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy worldwide and ranks second in cancer-related mortality.[1] Surgical resection remains the cornerstone of curative treatment in localized disease. However, postoperative complications continue to pose a significant clinical challenge. These complications can prolong hospital stay, increase healthcare costs, and—particularly in the case of anastomotic leakage—adversely affect long-term oncologic outcomes.[2–6]

Early identification of patients at higher risk is essential to reduce failure-to-rescue rates and allow timely clinical interventions.[7] The systemic inflammatory response triggered by surgical trauma has been closely associated with postoperative morbidity.[8,9] In this context, acute-phase reactants play a pivotal role: while positive reactants such as C-reactive protein (CRP) increase, negative reactants like albumin tend to decrease.[10]

CRP typically rises after surgery, peaking around postoperative day 2 or 3, and then gradually declines under normal healing conditions. A lack of decline—or a secondary rise—may signal an underlying complication or infection.[11–13] Numerous studies have demonstrated that CRP levels measured between postoperative days 3 and 5 are useful for predicting complications, especially anastomotic leakage.[14,15]

While CRP reflects the intensity of the inflammatory process, serum albumin levels indicate nutritional and physiological status. The ratio of CRP to albumin (CAR) therefore integrates two key indicators—systemic inflammation and patient resilience—into a single metric.[15–18] In recent years, CAR has gained attention as a potential predictor of postoperative complications, particularly in gastrointestinal surgery. Several studies evaluating CAR between postoperative days 3 and 5 have reported promising results.[19,20]

However, with the increasing adoption of Enhanced Recovery After Surgery (ERAS) protocols, many patients are discharged by postoperative day 4 or 5, potentially before complications become clinically evident. As a result, the predictive value of laboratory assessments performed on postoperative day 7 may be increasingly important in current surgical practice.

Based on these considerations, the present study aims to investigate the clinical utility of postoperative day-7 CAR for identifying patients at risk of 30-day surgical complications following elective, curative colorectal cancer surgery.

MATERIAL AND METHOD

Study Design

This retrospective observational study included patients who underwent elective, curative-intent colorectal cancer surgery between January 2017 and December 2023 at Amasya University Şerefeddin Sabuncuoğlu Training and Research Hospital. All patients had histologically confirmed colorectal adenocarcinoma. The study protocol was approved by the Amasya University Clinical Research Ethics Committee (Approval No: E-76988455-050.01-263366; Date: May 23, 2025), and all procedures were conducted in accordance with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Patients were eligible if they were aged 18 years or older, had a diagnosis of colorectal adenocarcinoma, underwent elective curative surgery (right/left hemicolectomy, anterior resection, or abdominoperineal resection), and completed at least 30 days of postoperative follow-up.

Exclusion criteria were: emergency surgery; presence of preoperative infection or sepsis; diagnosis of inflammatory bowel disease; reoperation within the first 7 postoperative days; and preoperative albumin supplementation.

Surgical and Perioperative Management

All surgeries were performed in accordance with standard oncologic principles. The choice of surgical approach (laparoscopic or open) was based on surgeon preference and patient suitability. Prophylactic antibiotics were administered preoperatively in all cases. Postoperative care followed institutional routines; enhanced recovery protocols were not systematically implemented for all patients and were not included in the analysis.

Data Collection

Patient data were collected from hospital records, including demographics (age, sex, body mass index, and comorbidities), ASA (American Society of Anesthesiologists) classification, surgical approach, operative time, intraoperative blood loss, perioperative transfusion requirement, and pathological staging.

Laboratory values for C-reactive protein (CRP, mg/L) and albumin (g/dL) were recorded preoperatively and on postoperative day 7. The CRP-to-albumin ratio (CAR) was calculated by dividing CRP (mg/L) by albumin (g/dL). Postoperative day-7 CAR was used for all analyses.

Outcomes

The primary outcome was the occurrence of any postoperative complication within 30 days. Complications were classified according to the Clavien–Dindo classification: grades I–II were considered minor, and grade III or higher was considered major.[21] Evaluated complications included surgical site infection, anastomotic leakage, intra-abdominal abscess, ileus, urinary or pulmonary infection, thromboembolic events, and cardiovascular complications. Length of hospital stay and 30-day mortality were also recorded.

Statistical Analysis

All analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Normality of distribution was assessed using the Shapiro–Wilk test. Continuous variables were analyzed using the Student's t-test or the Mann–Whitney U test, depending on distribution characteristics. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. The association between postoperative CAR and complication rates was evaluated using a cut-off value of 3.2, based on the observed distribution within the study cohort. Statistical significance was defined as $p<0.05$.

RESULTS

Patient Characteristics

Data from a total of 200 patients were retrospectively analyzed. Of these, 110 (55%) were male, and the mean age was 60.4±10.2 years (range: 38–82 years). Laparoscopic surgery was performed in 128 patients (64%), and open surgery in 72 patients (36%). The mean operative time was 180±45 minutes, and the mean intraoperative blood loss was 300±150 mL. Perioperative blood transfusions were required in 28 patients (14%). According to pathological staging, 15% of patients were stage I, 45% were stage II, and 40% were stage III.

Postoperative Complications

Within 30 days postoperatively, complications occurred in 80 patients (40%). Of these, 49 (61.3%) had a single complication, while 31 (38.8%) experienced multiple complications. Based on the Clavien–Dindo classification, 55 patients (68.8%) had minor complications (Grade I–II), and 25 (31.3%) had major complications (Grade ≥III). No 30-day mortality was observed.

The most frequently reported complications were superficial surgical site infection (17.5%), ileus (15%), intra-abdominal abscess (15%), and anastomotic leakage (10%). The median length of hospital stay was significantly longer in patients who developed complications than in those who did not (12 days [IQR: 9–18] vs. 7 days [IQR: 6–9]; $p<0.001$).

Comparison of Clinical and Laboratory Parameters

On postoperative day 7, patients with complications had significantly higher CRP levels and lower albumin levels ($p<0.001$ for both). Accordingly, the mean CAR value was also significantly higher in the complication group than in those without complications (5.07±2.05 vs. 2.31±1.12; $p<0.001$). In addition, patients who developed complications were older (63.5 vs. 58.2 years; $p=0.001$), had a higher rate of ASA score ≥3 (60.0% vs. 20.8%; $p<0.001$), and were more frequently operated on using an open surgical approach (43.8% vs. 22.5%; $p=0.002$).

No significant difference was found between the groups in terms of preoperative CRP and albumin levels ($p=0.200$ and $p=0.100$, respectively).

Table – Comparison of Clinical and Laboratory Parameters Between Patients With and Without Postoperative Complications

Variable	Complication (+) (n=80)	Complication (–) (n=120)	p-value
Age (years)	63.5±10.5	58.2±9.9	0.001
Male gender, n (%)	46 (57.5%)	64 (53.3%)	0.580
ASA Score ≥3, n (%)	48 (60.0%)	25 (20.8%)	<0.001
Open surgery, n (%)	35 (43.8%)	27 (22.5%)	0.002
Transfusion, n (%)	15 (18.8%)	13 (10.8%)	0.170
Preop. CRP (mg/L)	8.2±3.5	7.5±3.1	0.200
Preop. Albumin (g/dL)	3.8±0.52	3.91±0.43	0.100
Postop. Day-7 CRP (mg/L)	14.62±5.75	7.71±3.69	<0.001
Postop. Day-7 Albumin (g/dL)	2.93±0.41	3.37±0.29	<0.001
Postop. Day-7 CAR	5.07±2.05	2.31±1.12	<0.001
Length of hospital stay (days) median (IQR)	12 (9–18)	7 (6–9)	<0.001

CRP=C-reactive protein; CAR=C-reactive protein-to-albumin ratio; ASA=American Society of Anesthesiologists; Preop.=Preoperative; Postop.=Postoperative.

CAR Value and Risk of Complications

Among patients with a CAR value of ≥3.2 on postoperative day 7, the complication rate was 74.4%, compared with 14.0% in those with a CAR value below 3.2. This threshold was associated with an approximately five-fold higher risk of postoperative complications in unadjusted comparisons. These findings suggest that CAR is a simple and practical biomarker that may be useful for postoperative risk stratification after colorectal cancer surgery.

DISCUSSION

In this study, we demonstrated a significant association between the C-reactive protein-to-albumin ratio (CAR), measured on postoperative day 7, and the occurrence of surgical complications in patients undergoing elective surgery for colorectal cancer. According to our findings, patients with elevated CAR values had significantly higher complication rates and prolonged hospital stays.

Postoperative complications can prolong short-term recovery and negatively affect overall patient outcomes. Therefore, early identification of high-risk patients in the postoperative period is crucial for effective clinical management. CAR, as utilized in our study, stands out as a simple and cost-effective biomarker that may help address this clinical need.

CRP is a positive acute-phase reactant synthesized by the liver in response to tissue damage and inflammation, and it tends to rise in the early postoperative period after most surgical interventions.[10,11] Under normal healing processes, CRP typically peaks between postoperative days 3 and 5 and then declines.[12–14] Albumin, on the other hand, is a negative acute-phase reactant, and its plasma concentration decreases in inflammatory conditions.[15] The combination of these two parameters as CAR provides an integrated indicator of both systemic inflammatory burden and the patient's physiological reserve.[16–18]

Previous studies have primarily evaluated CAR between postoperative days 3 and 5 and reported its effectiveness in identifying patients at risk of postoperative complications.[19,20] However, during this period, many patients may already be discharged, and some complications may not yet be clinically evident. Therefore, our study focused on the predictive value of CAR on postoperative day 7. Our results showed a strong correlation between CAR values measured at this later time point and the risk of complications.

CRP levels were significantly higher and albumin levels significantly lower in patients who developed postoperative complications, explaining the significantly elevated CAR values in this group. In addition, we observed that patients who underwent open surgery, those of advanced age, and those with higher ASA scores were more likely to experience complications. These factors further support the clinical utility of CAR as a risk stratification tool.

In our cohort, a CAR cut-off value of ≥3.2 was associated with a complication rate of 74.4%. This finding aligns with prior studies that have reported the utility of CAR in predicting postoperative morbidity.[20] Other postoperative composite inflammation scores have also been associated with outcomes after colorectal cancer surgery.[22] The clinical applicability of CAR is further enhanced by its ease of calculation, no additional cost, and availability from routine laboratory parameters.

Study Limitations

Despite the statistically significant relationship observed between postoperative CAR and complications, this study has several limitations. First, it was retrospective and conducted at a single center, which may limit the generalizability of the findings. Second, we only evaluated CAR values on postoperative day 7 and did not assess dynamic changes during earlier postoperative days. Moreover, the CAR cut-off (≥3.2) was derived from the observed distribution in our cohort and should be externally validated in independent populations. In addition, we did not perform multivariable modeling or ROC-based performance analyses; therefore, the independent predictive performance of CAR and its discriminative accuracy could not be established. Finally, due to the relatively short follow-up period, the impact of complications on long-term oncologic outcomes could not be fully assessed. Therefore, prospective, multicenter studies with longer follow-up durations are needed to validate these findings and to define the optimal timing and cut-off values of CAR in clinical practice.

Future Recommendations

Further research involving multicenter, prospective cohorts and dynamic CAR tracking (from days 3 to 7) is warranted. Integration with clinical risk models and comparison with other biomarkers should also be considered to improve predictive accuracy and clinical utility.

CONCLUSION

This study demonstrated that the C-reactive protein-to-albumin ratio (CAR), measured on postoperative day 7, is associated with early postoperative complications in patients undergoing elective colorectal cancer surgery and may help identify patients at higher risk. CAR values were significantly higher in patients who developed complications, and a threshold of ≥3.2 was associated with a markedly increased risk of morbidity.

CAR is a simple and readily accessible parameter that reflects both inflammatory burden and the patient's physiological reserve. Therefore, incorporating CAR into postoperative monitoring may facilitate earlier identification of high-risk patients, enable more personalized follow-up strategies, and support timely use of advanced diagnostic interventions when necessary.

Nevertheless, to translate these findings into routine clinical practice, larger-scale, multicenter, prospective studies are required to confirm and refine the clinical utility of CAR.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study protocol was approved by the Amasya University Clinical Research Ethics Committee (Date: 22.05.2025, Decision No: 2025/74)

Informed Consent: Written informed consent was obtained from all participants prior to enrollment in the study.

Referee Evaluation Process: Externally peer-reviewed.

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