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RESEARCH ARTICLE

C-Reactive Protein to Albumin Ratio: A Reliable Marker in Colorectal Cancer

Kolorektal Kanser Cerrahisinde Güvenilir Bir Belirteç: C-reaktif Proteinin Albümine Oranı

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ABSTRACT

Aim: Postoperative complications after colorectal cancer surgery result in increased treatment costs, prolonged hospital stays and poor prognosis and reduce quality of life of the patients. Here, we aim to contribute to the literature in terms of being a reliable marker of postoperative C-reactive protein (CRP) to albumin ratio (CAR) after colorectal cancer surgery.

Method: A total of 213 patients undergoing colorectal cancer surgery between 2013 and 2018 were analyzed in this study. Risk factors for the development of postoperative complications were analyzed using univariate and multiple logistic regression models. A receiver operating characteristic (ROC) curve analysis was used to analyze the association with the CRP and CAR variables, with the aim being to differentiate postoperative complications.

Results: Postoperative complications occurred in 87 (40.8%) patients. Based on the Clavien-Dindo classification, 25 (18.7%) patients developed major complications. Perioperative blood transfusion [odds ratio (OR)=1.3; 95% confidence interval (CI)=1.08-1.55] and postoperative CAR (OR=1.2; 95% CI=1.05-1.35) were independent risk factors for postoperative complications (p=0.005 for each). The cut-off value for CAR was 4.3 (sensitivity: 51.72; specificity: 71.43; and area under the curve: 0.642), meaning that CAR was found to be statistically significantly effective in differentiating postoperative complications (p<0.001). The (median) length of hospital stay was statistically significantly longer in the high CAR (>4.3) group (p=0.001), while the laparoscopic surgery rate was statistically significantly lower in the high CAR group (p=0.039).

Conclusion: CAR is a novel, reliable and independent marker. Moreover the ratio is useful for clinicians and provides the determination of early postoperative complications after colorectal cancer surgery.

Keywords: C-reactive protein to albumin ratio, colorectal cancer, postoperative complication

ÖZ

Amaç: Kolorektal kanser cerrahisi sonrası postoperatif komplikasyonlar, tedavi maliyetlerinin artmasına, hastanede kalış sürelerinin uzamasına ve kötü prognoza neden olur ve hastaların yaşam kalitesini düşürür. Burada kolorektal kanser cerrahisi sonrası postoperatif C-reaktif protein (CRP)/albümin oranının (CAR) güvenilir bir belirteci olması açısından literatüre katkıda bulunmayı hedefliyoruz.

Yöntem: Bu çalışmada 2013-2018 yılları arasında kolorektal kanser cerrahisi geçiren toplam 213 hasta analiz edildi. Postoperatif komplikasyonların gelişimi için risk faktörleri, tek değişkenli ve çoklu lojistik regresyon modelleri kullanılarak analiz edildi. Postoperatif komplikasyonları ayırt etmek amacıyla CRP ve CAR değişkenleri ile ilişkiyi analiz etmek için bir alıcı çalışma özelliği (ROC) eğri analizi kullanıldı.

Bulgular: Seksen yedi (%40,8) hastada ameliyat sonrası komplikasyon gelişti. Clavien-Dindo sınıflandırmasına göre 25 (%18,7) hastada majör komplikasyonlar gelişti. Perioperatif kan transfüzyonu [olasılık oranı (OO)= 1,3; %95 güven aralığı (GA)= 1,08-1,55] ve postoperatif CAR (OO= 1,2; %95 GA= 1,05-1,35) postoperatif komplikasyonlar için bağımsız risk faktörleriydi (her biri için p=0,005). CAR için cut-off değeri 4,3 idi (duyarlılık:

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51,72; özgüllük: 71,43; ve eğri altındaki alan: 0,642), yani CAR'nin postoperatif komplikasyonları ayırt etmede istatistiksel olarak anlamlı derecede etkili olduğu bulundu (p<0,001). Hastanede kalış süresi (ortanca) yüksek CAR (>4,3) grubunda istatistiksel olarak anlamlı derecede daha uzun iken (p=0,001), yüksek CAR grubunda laparoskopik cerrahi oranı istatistiksel olarak anlamlı derecede düşüktü (p=0,039).

Sonuç: CAR, yeni, güvenilir ve bağımsız bir belirteçtir. Ayrıca oran klinisyenler için yararlıdır ve kolorektal kanser cerrahisi sonrası erken postoperatif komplikasyonların belirlenmesini sağlar.

Anahtar Kelimeler: C-reaktif albümin oranı, kolorektal kanser, postoperatif komplikasyon

Introduction

Colorectal cancer is the third most commonly diagnosed form of cancer and the fourth leading cause of cancer-related death around the world.[1] The current curative treatment approach is still surgical resection, despite the improvements in colonoscopic interventions and chemotherapy.[2] Several complications occur after a surgical resection for colorectal cancer.[3,4] Such complications result in increased treatment costs, infections, prolonged hospital stays, delayed recovery times and poor prognosis.[5,6] Accordingly, early identification and the appropriate management of postoperative complications can improve clinical outcomes.

Many factors have been closely linked to cancer, including inflammation and wound healing.[7,8] Inflammation induces the release of cytokines, inhibits apoptosis and causes DNA injury, contributing to the growth, proliferation, invasion and metastasis of cancer cells.[9,10] Proinflammatory cytokines increase due to surgical trauma, resulting in changes in the acute phase reactants in the blood, such as albumin and the C-reactive protein (CRP).[11]

Systemic inflammatory response plays an important role in carcinogenesis and tumor progression, and a number of systemic inflammatory markers have been used for its identification, such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), Glasgow Prognostic Score (GPS), hemoglobin and albumin levels and lymphocyte and platelet count(HALP) and CRP. Recently, the preoperative CRP/albumin ratio (CAR) has come into use as a new inflammatory marker for various cancer types.[12,13,14,15] Literature contains several studies in which preoperative CAR has been used to determine complications following colorectal surgery, although researches investigating postoperative CAR are limited. Among these, the study by Ge et al.[11] demonstrated that the association between postoperative CAR after colorectal surgery with postoperative complications had a high diagnostic accurac.[11]

The present study contributes to literature by establishing the association of postoperative CAR with postoperative complications among patients who had undergone a curative resection due to colorectal cancer.

Methods

A retrospective examination was made of 213 patients who had been histopathologically diagnosed with colorectal cancer in a gastrointestinal surgery clinic between 2013 and 2018. The ethics committee of the hospital granted approval for the study (No: 2019.7/06-220), which was conducted in accordance with the principles of the Declaration of Helsinki (revised in 2013). All surgeries were performed by the same group of surgeons. The laboratory results of the preoperative period and the postoperative day 3 were evaluated. The study included patients aged 18 years and older who had been histopathologically diagnosed with colorectal adenocarcinoma, and who underwent curative surgical resection. The study excluded patients who had undergone an R1/R2 resection, and those with liver cirrhosis, those who had perioperatively received an intravenous albumin infusion, those with preoperative systemic infections, those who underwent an additional organ resection and those who underwent repeat surgery within postoperative three days. Data were acquired through demographic characteristics, laboratory tests and surgical characteristics. The demographic characteristics included gender, age, body mass index (BMI), comorbidities (diabetes mellitus [DM], hypertension [HT], coronary artery disease [CAD], chronic obstructive pulmonary disease [COPD]), smoking, American Society of Anesthesiologists (ASA) scores, laparoscopic or open technique, surgery type and sarcopenia. The laboratory tests included preoperative hemoglobin, hematocrit, serum albumin and CRP levels, and postoperative third day levels of CRP and serum albumin.

A recent review has demonstrated that perioperative immunonutrition prevents postoperative complications[16], and so patients who were administered perioperative immunonutrition in our clinic were also recorded according to the current guidelines.[17]

Furthermore, all patients who received a perioperative blood transfusion, as a possible cause of postoperative complications, were also recorded. The lengths of intensive care unit and hospital stay were recorded to evaluate clinical outcomes.

Definition of Postoperative Complications

Complications occurring within 30 days of surgery were defined as postoperative complications. All complications were categorized according to the Clavien-Dindo classification system.[18] Accordingly, grade I and II complications were classified as minor complications, and grade III and higher grade complications were classified as major complications. CAR was calculated by dividing the postoperative third day CRP value by the serum albumin value. A Receiver Operating Characteristics (ROC) curve analysis was used to determine the cut-off value for CAR.

Furthermore, the widely-accepted Charlson Comorbidity Index (CCI) was used to assess the effects of patient comorbidities. CCI is mostly used to estimate survival in cancer patients, although a number of researchers have found it to be useful also for estimating the clinical outcomes of colon cancer patients.[19,20]

Statistical Analysis

The study data were summarized as tabular descriptive statistics and expressed as mean ± standard deviation or median (IQR) for continuous variables. Categorical variables were expressed as numbers and percentages. Numerical variables were tested for normality using a Kolmogorov-Smirnov test. An Independent Samples t-test and a Mann-Whitney U test were used for the comparison of two independent groups for normally and non-normally distributed numerical variables, respectively. Pearson's Chi-Square or Fisher's Exact Tests were used to compare categorical variables for differences. Risk factors for the development of postoperative complications were analyzed using univariate and multiple logistic regression models, and the results were presented as odds ratio and at a 95% confidence interval.

A ROC curve analysis was used to analyze the association with the CRP and CAR variables, with the aim being to differentiate postoperative complications. The optimal cut-off values, 95% confidence interval and area under the curve (AUC) were calculated based on Youden's index using DeLong's method in the MedCalc Statistical Software Trial version (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2015) program. Statistical analyses were carried out using Jamovi (Version 1.0.7) and JASP (version 0.11.1) software, and a p-value of 0.05 was considered significant in the statistical analyses.

Results

The mean age of study participants was 61.3±13.2 years. Among study participants, there were 119 male and 94 female patients. Postoperative complications occurred in 87 (40.8%) patients. Based on the Clavien-Dindo classification, 25 (18.7%) patients developed major complications. Additionally, 42 (19.7%) patients developed surgical site infections. The median length of hospital stay was 8 days.

Table 1 presents a comparison of certain demographic and clinical characteristics and the development of postoperative complications. A univariate analysis revealed that the development of complications was statistically significantly associated with length of stay in the intensive care unit, the length of hospital stay, perioperative blood transfusion and laparoscopic surgery. Patients with postoperative complications had longer stays in both intensive care and hospital. Furthermore, postoperative complications were statistically significantly associated with lower postoperative albumin levels and higher postoperative third day CRP and CAR levels (p=0.032, p=0.001, respectively). None of the other comparisons revealed any statistically significant differences (p>0.05 for each, Table 1).

Table 2 presents the cut-off values, calculated using a ROC analysis based on the CRP and CAR variables and the influence on postoperative complication development. Accordingly, the cut-off value for CRP was 7.9 (sensitivity: 86.21; specificity: 36.51; and AUC: 0.646), meaning that CRP was statistically significantly effective in differentiating postoperative complications (p<0.001) (Figure 1). Furthermore, the cut-off value for CAR was 4.3 (sensitivity: 51.72; specificity: 71.43; and AUC: 0.642), meaning that CAR was found to be statistically significantly effective in differentiating postoperative complications (p<0.001). The comparison of the AUC values for CPR and CAR revealed no superiority between the two (p=0.769).

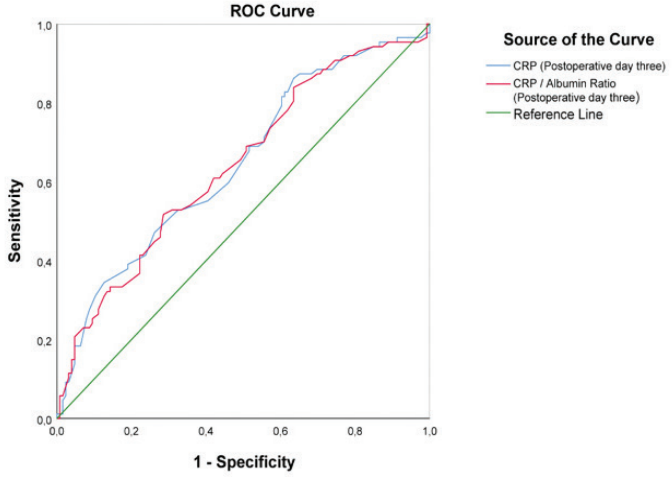


Figure 1. ROC curve analysis of postoperative 3rd day CRP and CAR values

CRP: C-reactive protein, CAR: C-reactive protein to albumin ratio

Table 1. Comparison of certain demographic and clinical characteristics and the development of postoperative complications

		Postoperative complication		
	All (n=213)	**No (n=126)**	**Yes (n=87)**	**p-value**
Age	61.3±13.2	60.2±12.3	62.9±14.3	0.158*
Gender (%)				
Male	119 (55.9)	71 (56.3)	48 (55.2)	0.976**
Female	94 (44.1)	55 (43.7)	39 (44.8)	
BMI (%)				
<25	69 (32.4)	45 (35.7)	24 (27.6)	0.273**
≥25	144 (67.6)	81 (64.3)	63 (72.4)	
Smoking (%)	56 (26.4)	37 (29.6)	19 (21.8)	0.270**
Perioperative immunonutrition (%)	103 (48.4)	65 (51.6)	38 (43.7)	0.319**
Sarcopenia (%)	82 (42.7)	47 (41.2)	35 (44.9)	0.724**
HT (%)	69 (32.4)	37 (29.4)	32 (36.8)	0.323**
DM (%)	45 (21.1)	27 (21.4)	18 (20.7)	0.999**
COPD (%)	14 (6.6)	5 (4.0)	9 (10.3)	0.118**
CAD (%)	42 (19.7)	24 (19.0)	18 (20.7)	0.904**
Intensive care unit stay (day), (median)	1.0 [1.0- 1.0]	1.0 [1.0- 1.0]	1.0 [1.0- 1.0]	**0.001****
Length of hospital stay (day), (median)	8.0 [7.0- 14.0]	7.0 [6.0- 8.0]	15.0 [12.0- 20.0]	**0.001****
Operation time (min), (median)	210.0 [160.0- 250.0]	220.0 [166.2- 250.0]	210.0 [160.0- 260.0]	0.931***
Perioperative blood transfusion (median)	0.0 [0.0- 2.0]	0.0 [0.0- 2.0]	1.0 [0.0- 2.5]	**0.003****
Anterior resection (%)	42 (19.7)	24 (19.0)	18 (20.7)	0.904**
Low anterior resection (%)	74 (34.7)	43 (34.1)	31 (35.6)	0.936**
Right hemicolectomy (%)	57 (26.8)	32 (25.4)	25 (28.7)	0.701**
Left hemicolectomy (%)	19 (8.9)	13 (10.3)	6 (6.9)	0.538**
Subtotal colectomy (%)	5 (2.3)	2 (1.6)	3 (3.4)	0.401**
Total colectomy (%)	1 (0.5)	1 (0.8)	0 (0.0)	0.999**
Transverse colectomy (%)	3 (1.4)	3 (2.4)	0 (0.0)	0.272**
Loop ileostomy (%)	45 (21.1)	23 (18.3)	22 (25.3)	0.287**
Miles (%)	12 (5.6)	8 (6.3)	4 (4.6)	0.765**
Harttman (%)	2 (0.9)	1 (0.8)	1 (1.1)	0.999**
Laparoscopic (%)	52 (24.4)	39 (31.0)	13 (14.9)	**0.012****
ASA ≥3 (%)	141 (66.2)	81 (64.3)	60 (69.0)	0.574**
Charlson Comorbidity Index (median)	3.0 [2.0- 4.0]	3.0 [2.0- 4.0]	4.0 [2.0- 5.0]	0.057***
Charlson Comorbidity Index (%)				
≥2	174 (81.7)	101 (80.2)	73 (83.9)	0.606**
<2	39 (18.3)	25 (19.8)	14 (16.1)	0.606**
Preoperative hematocrit	34.9±5.6	35.4±5.8	34.3±5.3	0.188*
Preoperative albumin (mg/dL)	4.1±0.5	4.1±0.5	4.1±0.4	0.580*
Preoperative CRP (mg/dL), (median)	0.7 [0.3- 1.7]	0.6 [0.3- 1.4]	0.8 [0.3- 1.9]	0.252***
Albumin (Postoperative 3rd day)	3.0±0.4	3.1±0.4	3.0±0.4	**0.032***
CRP (Postoperative 3rd day), (median)	11.0 [7.8- 16.0]	10.0 [6.0- 14.0]	13.0 [9.0- 19.5]	**0.001*****
CAR (Postoperative 3rd day), (median)	3.6 [2.4- 5.3]	3.2 [1.9- 4.8]	4.4 [2.8- 6.2]	**0.001*****

BMI: Body mass index, HT: Hypertension, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, CRP: C-reactive protein

Based on the CAR cut-off value, 132 patients were classified as low CAR (≤4.3) and 81 patients as high CAR (>4.3) groups. Table 3 presents a comparison of certain clinical parameters by CAR. Accordingly, the (median) length of hospital stay was statistically significantly longer in the high CAR (>4.3) group (p=0.001), while the laparoscopic surgery rate was statistically significantly lower in the high CAR group (p=0.039).

A multivariate analysis model was then applied to determine the risk factors from the univariate analysis that were independently associated with postoperative complications (Table 4). First, a univariate logistic regression model was analyzed, and all variables included in the model were found to be statistically significant (p<0.05 for each, Table 4). An analysis of the multiple logistic regression model revealed that perioperative blood transfusion (OR=1.3; 95% CI=1.08-1.55) and CAR (OR=1.2; 95% CI=1.05-1.35) were independent risk factors for postoperative complications (p=0.005 for each).

Discussion

The present study demonstrated postoperative CAR to be an independent and a significant risk factor for postoperative complications among 213 patients who underwent curative

Table 2. ROC analysis results of postoperative complication based on CRP and CAR variables

	AUC	Sensitivity	Specificity	Cut-Off	95% CI	p-value	Pairwise comparison of ROC curves p-value
CRP	0.646	86.21	36.51	>7.9	0.578–0.710	**<0.001**	0.769
CAR	0.642	51.72	71.43	>4.3	0.574- 0.706	**<0.001**	

CRP: C-reactive protein, CAR: C-reactive protein to albumin ratio, CI: Confidence interval, ROC: Receiver operating characteristic, AUC: Area under the curve

Table 3. Comparison of certain clinical parameters based on CAR levels of patients

		CAR		
	All (n=213)	**≤4.3 (n=132)**	**>4.3 (n=81)**	**p**
BMI (%)				
<25	69 (32.4)	45 (34.1)	24 (29.6)	0.600*
≥25	144 (67.6)	87 (65.9)	57 (70.4)	
Smoking (%)	56 (26.4)	35 (26.7)	21 (25.9)	0.999*
Perioperative immunonutrition (%)	103 (48.4)	64 (48.5)	39 (48.1)	0.999*
Sarcopenia (%)	82 (42.7)	50 (42.4)	32 (43.2)	0.999*
6th month survival (%)	6 (2.8)	3 (2.3)	3 (3.7)	0.676*
HT (%)	69 (32.4)	41 (31.1)	28 (34.6)	0.704*
DM (%)	45 (21.1)	28 (21.2)	17 (21.0)	0.999*
COPD (%)	14 (6.6)	10 (7.6)	4 (4.9)	0.639*
CAD (%)	42 (19.7)	24 (18.2)	18 (22.2)	0.588*
Intensive care unite (day), (median)	1.0 [1.0- 1.0]	1.0 [1.0- 1.0]	1.0 [1.0- 1.0]	0.775**
Length hospital stay (day), (median)	8.0 [7.0- 14.0]	8.0 [7.0- 11.0]	10.0 [7.0- 16.0]	**0.001****
Laparoscopic (%)	52 (24.4)	39 (29.5)	13 (16.0)	**0.039***
Charlson Comorbiditiy Index (%)				
≥2	174 (81.7)	103 (78.0)	71 (87.7)	0.114*
<2	39 (18.3)	29 (22.0)	10 (12.3)	
Clavian dindo (%)				
<3	109 (81.3)	65 (86.7)	44 (74.6)	0.119*
≥3	25 (18.7)	10 (13.3)	15 (25.4)	

BMI: Body mass index, HT: Hypertension, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease,

Table 4. Univariate and multiple logistic regression analyses of the factors affecting postoperative complication development

	Univariate LR		Multiple LR	
	OR. (95%CI)	p-value	OR. (95%CI)	p-value
Perioperative blood tx	1.35 [1.13-1.62]	**0.001**	1.3 [1.08-1.55]	**0.005**
Laparoscopic: Yes vs. No	0.39 [0.19-0.79]	**0.009**	0.48 [0.23-1.01]	0.055
Albumin (postoperative 3rd day)	0.47 [0.23-0.96]	**0.038**	1.18 [0.51-2.76]	0.698
CRP (postoperative 3rd day)	1.08 [1.03-1.12]	**< 0.001**	-	-
CAR (postoperative 3rd day)	1.21 [1.08-1.35]	**< 0.001**	1.2 [1.05-1.35]	**0.005**

Dependent variable: Presence of Post-op complication. Bold p values were considered statistically significant (p<0.05). OR: Odds ratio, LR: Logistic regression, CI: Confidence interval, CRP was not included in the multiple model due to multicollinearity problems.

CRP: C-reavtive protein

surgical resection due to colorectal cancer. Furthermore, the ROC analysis revealed that high CAR values prolonged the hospital stays, and that postoperative CAR was higher in patients who had not undergone laparoscopic surgery.

CRP is an acute phase reactant that is synthesized by the liver. Elevated CRP serum levels induce the release of the inflammatory cytokines associated with cancer. In addition, serum albumin level is a commonly used marker for nutritional status, and is associated with the chronic inflammatory process that activates cytokines like IL-1 and TNF-α.[21,22] Recent studies have demonstrated that a systemic inflammatory response after surgical trauma is associated with poor outcomes, which was established with serum levels of CRP and albumin.[23,24] A recent study reported that CRP alone was not a sufficient determining factor indicating inflammation in the early postoperative period.[25]

Ge et al. conducted a study to determine postoperative complications in the early period after colorectal surgery, and established a ratio using CRP and albumin together. They found that the postoperative third day CAR value had a higher diagnostically accurate association with postoperative complications than CRP (predictive value [PPV] for CRP: 79.1%; PPV for CAR: 81.4%). Additionally, the CAR cut-off value was found to be 2.2, and an independent risk factor for postoperative complications (AUC of CAR was 0.779, sensitivity was 0.748, specificity was 0.695).[11] A recent study by Man et al., in turn, compared modified GPS, CAR, postoperative GPS and CRP values to determine postoperative complications after colorectal cancer surgery. The authors reported that the postoperative third day CAR value was more useful than the other markers among all of these scoring systems (AUC: 0.711, PPV: 83.2%); the cut-off value was 2.6 (sensitivity: 51.3%, specificity: 87.8%); and the postoperative complication rate was higher in those with high CAR (≥2.6) values.[26]

Our study had a larger sample size than the two similar studies identified, but established a postoperative complication rate that was lower than those two studies (40.8%).[11,26] Different to these studies, we found the CAR cut-off value to be 4.3 (sensitivity: 51.72, specificity: 71.43, and AUC: 0.642). Despite the lower specificity and AUC values, the multiple logistic regression analysis revealed CAR to be an independent risk factor for postoperative complications, which was consistent with other studies. Furthermore, an AUC value of >0.5 is statistically a good predictor of postoperative complications. Other studies.[11,26] found major and minor postoperative complications, based on the Clavien-Dindo classification, to be statistically significantly lower in the low CAR group, whereas no statistically significant association was identified between patients with postoperative minor and major complications, and CAR in the present study. On the other hand, our study reported longer hospital stays and lower laparoscopic surgery rates in the high CAR group.

Once again, the studies by Man et al.[26], and Ge et al.[11] failed to identify any statistically significant association between laparoscopic surgery and postoperative complications, while the present study identified a lower postoperative complication rate among patients undergoing laparoscopic surgery. In a similar vein, literature contains a number of studies reporting reduced postoperative complication rates and shortened hospital stays with laparoscopic surgery when compared to open surgery.[27,28]

Another point to emphasize about the present study is the identification of a perioperative blood transfusion as an independent risk factor for postoperative complications. In a recent meta-analysis it was indicated that transfusions can lead to infections, and pulmonary, cardiac, anastomotic and overall complications among patients undergoing colorectal cancer surgery.[29]

Although there was no statistically significant association between CCI and postoperative complications (p=0.057), postoperative complications were found to be more common among patients with a higher median CCI value (>3). Similar to the present study, Huang et al.[20] reported more postoperative complications in the group with CCI ≥3 among elderly colorectal cancer patients who had undergone laparoscopic surgery.[20]

Additionally, two recent meta-analyses reported high preoperative CAR to be associated with poor prognosis and disease-free survival in colorectal cancer patients.[30,31] Our study made no investigation of the link with survival, although further studies may analyze the relationship between postoperative CAR and prognosis and disease-free survival in colorectal cancer patients.

Study Limitations

There are some limitations in the present study, first and foremost among which is its retrospective, single-center design. Second, CAR was not compared with other inflammatory scoring systems, and so it could not be established whether or not it was superior to other markers. As such, there is a need for prospective, multi-center and large-scale studies with a larger sample size for the comparison of other markers.

Conclusion

Despite the lack of comparison with other inflammatory markers, CAR is an easy to use and independent ratio for clinicians that allows the early postoperative determination of complications. Especially today, when there are still high postoperative complication rates after colorectal surgery, it is of vital importance to identify and manage postoperative complications in the early period with a view to shortening hospital stays, decreasing hospital costs and improving the quality of life of patients.

Ethics

Ethics Committee Approval: The ethics committee of the hospital granted approval for the study (no: 2019.7/06-220), which was conducted in accordance with the principles of the Declaration of Helsinki (revised in 2013).

Informed Consent: The informed consent was given by all the participated patients.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Design: Ö.Z.S., E.P., M.D., Data Collection or Processing: H.B., T.Ö., E.A., O.U., Analysis or Interpretation: S.G., A.S.Z., Writing: Ö.Z.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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