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Research Article

Analysis of prognostic factors in metastatic colon cancer

Metastatik kolon kanserinde prognostik faktörlerin analizi

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Abstract

Aim: Colorectal cancer (CRC) ranks as the second leading cause of cancer-related deaths and the third most common cancer globally. However, due to the complexity of tumor biology, identifying reliable prognostic factors remains crucial.

Material and Methods: We conducted a retrospective analysis of 71 patients with metastatic colon cancer who were followed at Balikesir Ataturk City Hospital. The platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII) were calculated. Survival analysis was performed using the Kaplan-Meier method and prognostic factors were evaluated with Cox regression analysis.

Results: The median overall survival (OS) was 34.8 months. Survival was significantly shorter in patients with a BMI <20 kg/m^2 (21 months; p = 0.001). An Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≥2, the presence of de novo metastases, and peritoneal metastases were all associated with poorer survival. In univariate analysis, elevated PLR (HR: 1.81) and elevated SII (HR: 2.16) were significantly associated with increased mortality. Among tumor markers, elevated carbohydrate antigen 19-9 (CA 19-9) (HR: 1.86) and, more prominently, elevated carcinoembryonic antigen (CEA) (HR: 3.83) negatively impacted survival. In the multivariate Cox regression analysis, ECOG performance status ≥2, the presence of peritoneal metastasis, elevated systemic immune-inflammation index (SII), and elevated carcinoembryonic antigen (CEA) were identified as independent prognostic factors for overall survival.

Conclusion: Clinical factors (ECOG PS, BMI), metastasis characteristics (peritoneal, de novo), inflammatory markers (PLR, SII), and tumor markers (CA 19-9, CEA) are significant predictors of survival in metastatic colon cancer. CEA, in particular, emerged as a strong independent prognostic factor.

Keywords: colorectal cancer, metastatic, prognostic factors, platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII)

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Öz

Amaç: Kolorektal kanser (CRC), kansere bağlı ölümlerin ikinci önde gelen nedeni ve dünya genelinde en sık görülen üçüncü kanser türüdür. Bununla birlikte, tümör biyolojisinin karmaşıklığı nedeniyle, güvenilir prognostik faktörlerin belirlenmesi hayati önem taşımaktadır.

Gereç ve Yöntemler: Balikesir Ataturk Şehir Hastanesi'nde takip edilen metastatik kolon kanseri olan 71 hastanın retrospektif analizi gerçekleştirildi. Trombosit-lenfosit oranı (PLR), nötrofil-lenfosit oranı (NLR) ve sistemik immün-enflamasyon indeksi (SII) hesaplandı. Sağkalım analizi Kaplan-Meier yöntemi kullanılarak yapıldı ve prognostik faktörler Cox regresyon analizi ile değerlendirildi.

Sonuçlar: Ortalama genel sağkalım (OS) 34,8 ay idi. Vücut kitle indeksi (BMI) <20 kg/m^2 olan hastalarda sağkalım anlamlı derecede daha kısaydı (21 ay; p = 0,001). Doğu Kooperatif Onkoloji Grubu Performans Durumu (ECOG PS) ≥2, de novo metastaz varlığı ve periton metastazları, daha kötü sağkalımla ilişkiliydi. Tek değişkenli analizde, yüksek PLR (HR: 1,81) ve yüksek SII (HR: 2,16) anlamlı olarak artmış mortalite ile ilişkiliydi. Tümör belirteçleri arasında, yüksek karbonhidrat antijeni 19-9 (CA 19-9) (HR: 1,86) ve daha belirgin olarak yüksek karsinoembriyonik antijen (CEA) (HR: 3,83) sağkalımı olumsuz etkiledi. Çok değişkenli analiz, ECOG PS ≥2, periton metastazı, yüksek SII ve yüksek CEA'yı bağımsız prognostik faktörler olarak tanımladı. Yaş, cinsiyet, tümör yeri, mutasyon durumu ve karaciğer metastazı istatistiksel olarak anlamlı prognostik faktörler değildi.

Sonuç: Klinik faktörler (ECOG PS, BMI), metastaz özellikleri (peritoneal, de novo), inflamatuar belirteçler (PLR, SII) ve tümör belirteçleri (CA 19-9, CEA), metastatik kolon kanserinde sağkalımın önemli belirleyicileridir. Özellikle CEA, güçlü bir bağımsız prognostik faktör olarak ortaya çıkmıştır.

Anahtar Kelimeler: kolorektal kanser, metastatik, prognostik faktörler, trombosit-lenfosit oranı (PLR), sistemik immün-enflamasyon indeks (SII)

Introduction

Colorectal cancer (CRC) ranks as the second leading cause of cancer-related deaths and the third most commonly diagnosed cancer globally [1,2]. Approximately 20% of patients present with stage 4 disease at initial diagnosis, and nearly 50–60% of all CRC patients will eventually develop metastases [3,4]. The prognosis for metastatic CRC (mCRC) remains poor, with a five-year survival rate of approximately 14% [5].

While combination chemotherapy serves as the backbone of systemic therapy for most patients, treatment for mCRC is increasingly guided by biomarker profiling [6]. Research focusing on key pathways—including vascular endothelial growth factor (VEGF), epidermal growth factor receptor (EGFR), human epidermal growth factor receptor 2 (HER2), and mutations in KRAS, NRAS, and BRAF, as well as microsatellite instability has led to the development of numerous targeted therapies [7]. Clinical studies have demonstrated that tailoring treatment based on the molecular characteristics of the tumor improves overall survival (OS) [3]. Despite these advances, the complex and diverse molecular pathways involved in CRC tumorigenesis necessitate continued research to optimize prognostic stratification and therapeutic outcomes [8].

The role of systemic inflammation in cancer prognosis is increasingly recognized [9]. Prognostic indices such as the NLR, PLR, and SII, which reflect the systemic inflammatory response, have been extensively evaluated in various cancers, including CRC. However, a lack of standardization and conflicting evidence regarding their prognostic utility have prevented their widespread adoption into routine clinical practice [9-16].

This study aims to investigate potential prognostic factors in patients with mCRC. We evaluated clinicopathological features and survival outcomes in conjunction with systemic inflammation-based prognostic indicators, including the SII, NLR, and PLR.

Material and Methods

The protocol for this retrospective study was approved by the local ethics committee (Non-Invasive Clinical Research Ethics Committee of Balıkesir Atatürk City Hospital, Approval No: E-30041352-514.19.99-281272412 2025/06/62, Date: 19.06.2025). Since this study was a retrospective archive search, informed consent was not obtained from the patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

This study included patients aged 18 to 85 years with stage IV CRC who were followed at the Medical Oncology Clinic of Balıkesir Atatürk City Hospital. Patients diagnosed with

metastatic colon cancer between January 2018 and January 2024 were included in the study. Exclusion criteria included renal failure, liver failure, a diagnosis of bone marrow-related diseases, or a history of steroid or other medication use that could significantly affect hematological parameters. Patient demographic data, pathological characteristics, mutation status, and metastatic sites were recorded. Only patients with colon cancer were included in the study, and patients with rectal cancer were excluded. Right-sided colon cancer was defined as tumors originating from the cecum to the transverse colon, while left-sided colon cancer included tumors from the splenic flexure to the sigmoid colon. The OS was defined as the time from the diagnosis of metastatic disease to death from any cause or the last follow-up. Progression-free survival (PFS) was defined as the time from the initiation of first-line therapy to documented disease progression or death.

NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count [17]. PLR was derived by dividing the absolute platelet count by the absolute lymphocyte count [17]. SII was defined as P x N/L, where P, N, and L refer to the platelet, neutrophil, and lymphocyte counts per liter of peripheral blood, respectively [17]. All hematological parameters used for the calculation of NLR, PLR, and SII were obtained from peripheral blood samples collected at the time of metastatic disease diagnosis, before the initiation of any systemic treatment. Serum CEA and CA 19-9 levels were obtained from blood samples collected at the time of metastatic disease diagnosis, before the initiation of systemic therapy, and were evaluated as baseline prognostic markers rather than longitudinal follow-up parameters.

Statistical Analysis

Receiver operating characteristic (ROC) curve analysis was used to determine the prognostic utility of inflammatory markers and tumor antigens (Table 2, Figure 1). The area under the curve (AUC) for the neutrophil-to-lymphocyte ratio (NLR) was 0.374 (95% CI: 0.242–0.505; p = 0.067), with an optimal cut-off of 2.35 (sensitivity: 68.6%, specificity: 61.1%). The platelet-to-lymphocyte ratio (PLR) had an AUC of 0.337 (95% CI: 0.209–0.465; p = 0.018), with a cut-off of 181.55 (sensitivity: 65.7%, specificity: 69.4%). The systemic immune-inflammation index (SII) showed an AUC of 0.294 (95% CI: 0.171–0.418; p = 0.003), with a cut-off of 689.5 (sensitivity: 74.3%, specificity: 66.7%). For tumor markers, carbohydrate antigen 19-9 (CA 19-9) had an AUC of 0.435 (95% CI: 0.299–0.571; p = 0.346), with a cut-off of 26.19 (sensitivity: 60.0%, specificity: 61.1%), while carcinoembryonic antigen (CEA) had an AUC of 0.315 (95% CI: 0.191–0.440; p = 0.007), with a cut-off of 9.36 (sensitivity: 62.9%, specificity: 69.4%).

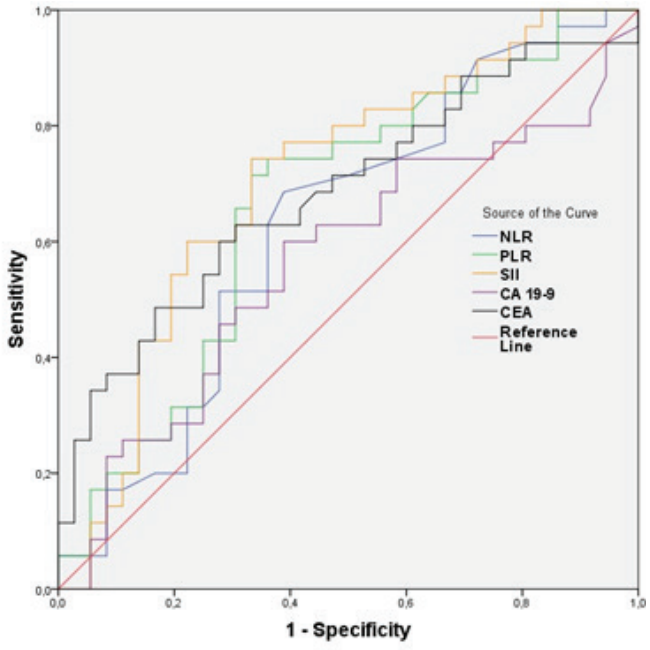

Figure 1. ROC curve analysis.

Results

A total of 71 patients were included in the study. The median follow-up duration of the study cohort was 25 months. The median age was 61 years (range: 24–83), with 59.2% (n=42) of patients being under 65 years old. The cohort consisted of 41 males (57.7%) and 30 females (42.3%). 42 patients (56.3%) presented with de novo metastatic disease, while 29 patients (40.8%) developed metastases during follow-up after an initial non-metastatic diagnosis. Clinical and pathological characteristics are presented in Table 1.

KRAS, NRAS, and BRAF mutation analysis was performed for all patients; no mutations were detected in 30 patients (42.3%). The estimated median overall survival (mOS) for the entire cohort was 34.8 months (95% CI: 28.36–41.24).

Survival Analysis Based on Clinicopathological Features

Kaplan-Meier survival analysis revealed no statistically significant difference in OS between patients aged <65 years (32.5 months, 95% CI: 21.7–43.3) and those ≥65 years (34.8 months, 95% CI: 18.0–51.6; p = 0.091). Similarly, OS did not differ significantly by sex (males: 36.1 months, 95% CI: 29.3–42.9; females: 32.1 months, 95% CI: 28.4–35.8; p = 0.515).

However, several factors were significantly associated with survival. Patients with a body mass index (BMI) <20 kg/m^2 had

Table 1. Clinical and Pathological Characteristics.

Patient Characteristics		N	%	Median OS months (%95 CI)	P
Age	<65	42	59.2	32.5 (21.7 - 43.3)	0.091
	≥65	29	40.8	34.8 (18.0 - 51.6)	
Gender	Female	30	42.3	32.1 (28.4 - 35.8)	0.515
	Male	41	57.7	36.1 (29.3 - 42.9)	
Body Mass Index	<20	15	21.1	21.0 (2.0 - 40.0)	<0.001
	≥20	56	78.9	37.9 (29.5 - 46.3)	
ECOG PS	0-1	46	64.8	41.4 (28.7 - 54.1)	0.002
	≥2	25	35.2	24.9 (22.6 - 27.2)	
Metastasis Status	Recurrent	29	40.8	43.7 (36.5 - 51.0)	0.017
	De-Novo	42	59.2	26.4 (16.9 - 35.9)	
Tumor Grade	1	9	12.7	54.0 (24.5 - 83.5)	0.353
	≥2	62	87.3	32.5 (25.2 - 39.8)	
Tumor Location	Right	16	22.5	48.3 (24.9 - 71.7)	0.325
	Left	55	77.5	32.5 (26.8 - 38.2)	
Mutation Status	No	30	42.3	32.5 (27.1 - 37.9)	0.444
	Yes	41	57.7	37.9 (18.0 - 57.8)	
Liver Metastasis	No	19	26.8	26.3 (13.5 - 39.1)	0.994
	Yes	52	73.2	36.1 (29.7 - 42.5)	
Peritoneal Metastasis	No	60	84.5	40.7 (33.2 - 48.2)	0.001
	Yes	11	15.5	21.0 (6.9 - 35.1)	
Lung Metastasis	No	45	63.4	37.9 (27.6 - 48.2)	0.165
	Yes	26	36.6	26.2 (18.4 - 34.0)	

Abbrev.: OS: Overall Survival, Met: Metastasis, ECOG PS: Eastern Cooperative Oncology Group Performance Status, P Value obtained by Kaplan Meier.

Table 2. ROC-Curve Analysis for Determining Ideal Cut-off Values of Markers.

Test Result Variables	AUC Area	SE	p	Asymptotic 95% Confidence Interval		Ideal Cut-Off	Cut-Off Sens.	Cut-Off Spec.
				Lower Bound	Upper Bound			
NLR	0.374	0.067	0.067	0.242	0.505	2.35	68.6%	61.1%
PLR	0.337	0.065	0.018	0.209	0.465	181.55	65.7%	69.4%
SII	0.294	0.063	0.003	0.171	0.418	689.5	74.3%	66.7%
CA19-9	0.435	0.070	0.346	0.299	0.571	26.19	60.0%	61.1%
CEA	0.315	0.064	0.007	0.191	0.440	9.36	62.9%	69.4%

Abbrev.: AUC AREA: Area Under the Curve, SE: Standard Error, Sens: Sensitivity, Spec: Specificity, NLR: Neutrophil-to-Lymphocyte Ratio, PLR: Platelet-to-Lymphocyte Ratio, SII: Systemic Immune-Inflammation Index, CA 19-9: Carbohydrate Antigen 19-9; CEA: Carcinoembryonic Antigen.

a significantly shorter mOS of 21.0 months (95% CI: 2.0–40.0) compared to 37.9 months (95% CI: 29.5–46.3) in patients with a BMI ≥20 (p = 0.001). An Eastern Cooperative Oncology Group (ECOG) performance status of ≥2 was associated with poorer survival (24.9 months, 95% CI: 22.6–27.2) compared to an ECOG status of 0-1 (41.4 months, 95% CI: 28.7–54.1; p = 0.002). Patients with de novo metastases had a shorter mOS (26.4 months, 95% CI: 16.9–35.9) than those with recurrent metastases (43.7 months, 95% CI: 36.5–51.0; p = 0.017). The presence of peritoneal metastasis was a strong negative prognostic factor, with a mOS of 21.0 months (95% CI: 6.9–35.1) compared to 40.7 months (95% CI: 33.2–48.2) in patients without peritoneal involvement (p = 0.001).

No significant differences in OS were observed based on tumor grade (Grade 1: 54.0 months vs. Grade ≥2: 32.5 months; p = 0.353), primary tumor location (right colon: 48.3 months vs. left colon: 32.5 months; p = 0.325), mutation status (wild-type: 32.5 months vs. mutant: 37.9 months; p = 0.444), presence of liver metastases (absent: 26.3 months vs. present: 36.1 months; p = 0.994), or presence of lung metastases (absent: 37.9 months vs. present: 26.2 months; p = 0.165).

ROC Curve and Cut-off Analysis

Receiver operating characteristic (ROC) curve analysis was used to determine the prognostic utility of inflammatory markers and tumor antigens (Table 2, Figure 1). The area under the curve (AUC) for the neutrophil-to-lymphocyte ratio (NLR)

was 0.374 (95% CI: 0.242–0.505; p = 0.067), with an optimal cut-off of 2.35 (sensitivity: 68.6%, specificity: 61.1%). The platelet-to-lymphocyte ratio (PLR) had an AUC of 0.337 (95% CI: 0.209–0.465; p = 0.018), with a cut-off of 181.55 (sensitivity: 65.7%, specificity: 69.4%). The systemic immune-inflammation index (SII) showed an AUC of 0.294 (95% CI: 0.171–0.418; p = 0.003), with a cut-off of 689.5 (sensitivity: 74.3%, specificity: 66.7%). For tumor markers, carbohydrate antigen 19-9 (CA 19-9) had an AUC of 0.435 (95% CI: 0.299–0.571; p = 0.346), with a cut-off of 26.19 (sensitivity: 60.0%, specificity: 61.1%), while carcinoembryonic antigen (CEA) had an AUC of 0.315 (95% CI: 0.191–0.440; p = 0.007), with a cut-off of 9.36 (sensitivity: 62.9%, specificity: 69.4%).

Univariate and Multivariate Cox Regression Analyses

According to univariate Cox regression analysis, overall survival (OS) was significantly shorter in patients with a body mass index (BMI) <20 compared to those with a BMI ≥20 (HR: 0.30; 95% CI: 0.15–0.62; p = 0.001) (Figure 2). Patients with an Eastern Cooperative Oncology Group (ECOG) performance status of ≥2 had poorer survival than those with a status of 0–1 (HR: 2.53; 95% CI: 1.37–4.67; p = 0.003). The presence of de novo metastasis was associated with worse survival compared to recurrent metastasis (HR: 2.05; 95% CI: 1.12–3.73; p = 0.019) (Table 3). Peritoneal metastasis was identified as a strong negative prognostic factor for OS (HR: 6.05; 95% CI: 2.55–14.32; p < 0.001). Among inflammatory markers, a high platelet-to-lymphocyte ratio (PLR) was significantly associated with poorer survival (HR: 1.81; 95% CI: 1.03–3.20; p = 0.040), as was a high systemic immune-inflammation index (SII) (HR: 2.16; 95% CI: 1.21–3.85; p = 0.009). Among tumor markers, elevated carbohydrate antigen 19-9 (CA 19-9) (HR: 1.86; 95% CI: 1.05–3.30; p = 0.033) and elevated carcinoembryonic antigen (CEA) (HR: 3.83; 95% CI: 2.09–7.00; p < 0.001) were significantly associated with reduced survival. Other variables, including age (≥65 years), sex, tumor grade, tumor location, mutation status, liver metastasis, and neutrophil-to-lymphocyte ratio (NLR), did not show a statistically significant association with OS.

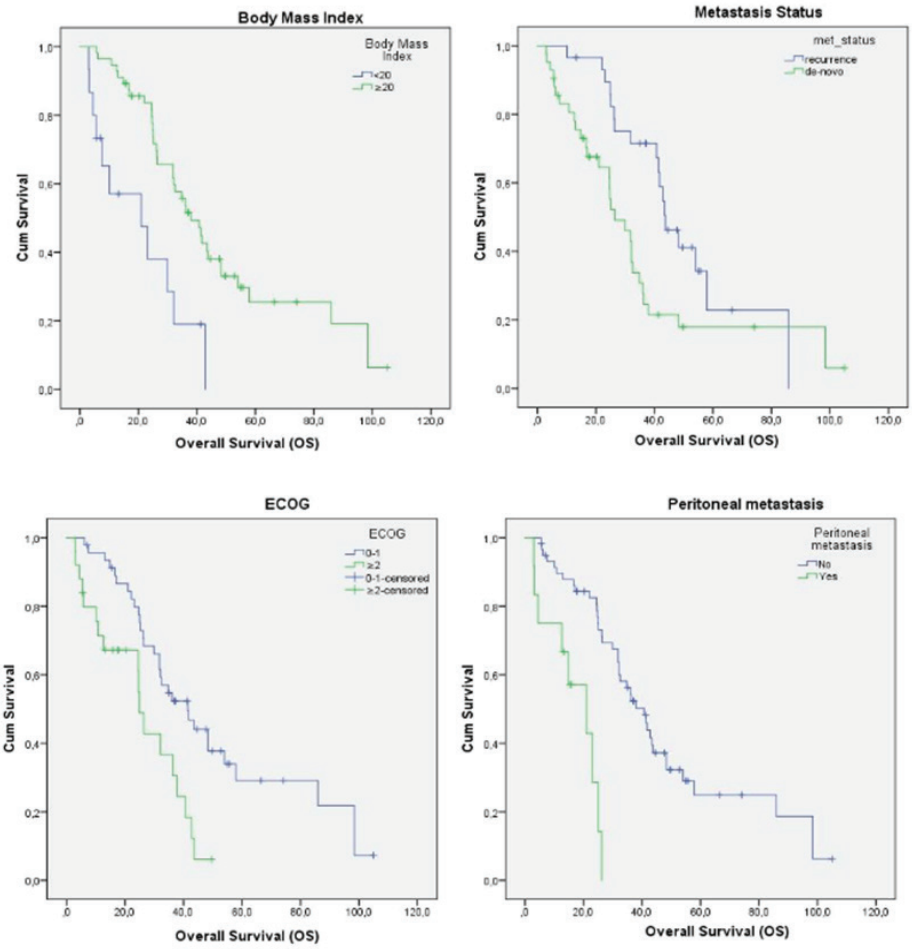

Figure 2. Survival plots.

Table 3. Cox Regression Analysis for Overall Survival Values.

Variable	Category	Univariate Analysis		Multivariate Analysis	
		HR (95% CI)	p	HR (95% CI)	p
Age	<65 / ≥65	1.64 (0.92 - 2.93)	0.095		
Gender	Male / Female	0.82 (0.46 - 1.48)	0.516		
BMI	<20 / ≥20	0.30 (0.15 - 0.62)	0.001		
ECOG PS	0-1 / ≥2	2.53 (1.37 - 4.67)	0.003	3.71 (1.93 - 7.14)	<0.001
Metastasis Status	Recurrent / De Novo	2.05 (1.12 - 3.73)	0.019		
Grade	<2 / ≥2	1.46 (0.65 - 3.30)	0.365		
Tumor Location	Right / Left	1.44 (0.69 - 3.00)	0.329		
Mutation Status	No / Yes	1.26 (0.70 - 2.27)	0.446		
Liver Metastasis	No / Yes	1.00 (0.53 - 1.89)	0.994		
Peritoneal Metastasis	No / Yes	6.05 (2.55 - 14.32)	<0.001	4.20 (1.69 - 10.42)	0.002
Lung Metastasis	No / Yes	1.53 (0.83 - 2.81)	0.169		
NLR	Low / High	1.09 (0.59 - 2.00)	0.791		
PLR	Low / High	1.81 (1.03 - 3.20)	0.040		
SII	Low / High	2.16 (1.21 - 3.85)	0.009	2.42 (1.28 - 4.58)	0.006
CA19-9	Low / High	1.86 (1.05 - 3.30)	0.033		
CEA	Low / High	3.83 (2.09 - 7.00)	<0.001	4.51 (2.36 - 8.60)	<0.001

Abbrev.: BMI: Body Mass Index, ECOG PS: Eastern Cooperative Oncology Group Performance Status, NLR: Neutrophil-to-Lymphocyte Ratio, PLR: Platelet-to-Lymphocyte Ratio, SII: Systemic Immune-Inflammation Index, CA19-9: Carbohydrate Antigen 19-9, CEA: Carcinoembryonic Antigen.

Multivariate analysis was performed using the forward-lr stepwise method. Eight parameters that were significant in the univariate analysis (BMI, ECOG PS, Metastasis Status, Peritoneal Metastasis, PLR, SII, CA19-9, CEA) were included in the multivariate analysis.

In the multivariate Cox regression analysis performed using the Forward: LR method, ECOG performance status ≥2 (HR: 3.71; 95% CI: 1.93–7.14; $p < 0.001$), presence of peritoneal metastasis (HR: 4.20; 95% CI: 1.69–10.42; $p = 0.002$), elevated systemic immune-inflammation index (SII) (HR: 2.42; 95% CI: 1.28–4.58; $p = 0.006$), and elevated carcinoembryonic antigen (CEA) (HR: 4.51; 95% CI: 2.36–8.60; $p < 0.001$) were identified as independent prognostic factors for overall survival.

Discussion

According to our results, clinical factors (ECOG performance status and BMI), metastasis characteristics (peritoneal metastasis and de novo metastasis), inflammatory markers (PLR and SII), and tumor markers particularly carcinoembryonic antigen (CEA) were important in predicting survival in metastatic colon cancer.

Chen et al. reported that overall survival (OS) and disease-free survival (DFS) were better in patients with low NLR, PLR, and SII [10]. Similarly, Young et al., in their study of patients undergoing transarterial radioembolization (TARE) for metastatic colorectal cancer, concluded that inflammatory markers may be associated with OS and progression-free survival (PFS) [18]. Kim et al. also demonstrated that high NLR and PLR were useful prognostic factors for predicting long-term outcomes in patients with stage III and IV colorectal cancer [19]. These findings have been attributed to the activation of transcription factors such as nuclear factor-kappa B (NF-κB), signal transducer and activator of transcription 3 (STAT3), and hypoxia-inducible factor 1α (HIF-1α) in tumor cells during inflammatory processes [19]. Furthermore, chronic inflammation is thought to influence both cancer development and prognosis through DNA damage–induced mutations and aberrant DNA methylation [20].

Peripheral blood counts of lymphocytes, neutrophils, and platelets reflect the interaction between immune and inflammatory responses within the tumor microenvironment [21]. Tumor-infiltrating lymphocytes exert antitumor effects by recognizing malignant cells and inducing apoptotic cell death [21]. In contrast, neutrophils may promote tumor progression by producing reactive oxygen species (ROS), leading to genetic instability and DNA damage [21]. Platelets have also been recognized as reliable predictors of tumor prognosis [21]. Accordingly, inflammation-based indices that reflect both systemic inflammation and the tumor microenvironment represent cost-effective and easily accessible prognostic markers [16]. In line with previous studies, our findings demonstrated that elevated PLR and SII were associated with poorer survival outcomes.

Several studies have explored optimal cut-off values for systemic inflammatory markers such as NLR and PLR in colorectal cancer [22,23]. Reported NLR cut-off values typically range from 2 to 5, while PLR values generally range from approximately 150 to 225, with higher levels associated with worse survival

outcomes [22]. Although sensitivity and specificity values vary across studies, ROC curve–based analyses support the role of these indices in risk stratification [23].

Patients presenting with de novo metastatic disease have consistently been shown to have poorer survival compared with those who develop metachronous metastases, and peritoneal metastasis is a well-established adverse prognostic factor [24,25]. Our findings are consistent with these reports. Carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) are commonly used tumor markers in colorectal cancer, although reported prognostic cut-off values vary. Previous studies have suggested thresholds of approximately 5–10 ng/mL for CEA and 30–40 U/mL for CA 19-9, with higher baseline levels associated with reduced survival [26,27]. In our study, ROC-derived cut-off values demonstrated modest sensitivity and specificity, supporting their use as prognostic rather than diagnostic markers, particularly when interpreted alongside clinical and pathological features [26,28].

Limitations Of The Study

The primary limitation of this study is its retrospective design, which may have resulted in unrecognized factors influencing laboratory parameters. Nevertheless, a key strength of this study lies in the use of homogeneous, single-center survival data to evaluate multiple reproducible, inexpensive, and readily available clinical and laboratory parameters applicable to both clinical practice and clinical trial settings.

In conclusion, clinical factors (ECOG performance status and BMI), metastasis characteristics (peritoneal and de novo metastasis), inflammatory markers (PLR and SII), and tumor markers particularly CEA were significant predictors of survival in patients with metastatic colorectal cancer.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

This study was approved by the Balikesir Ataturk City Hospital's Non-Invasive Clinical Research Ethics Committee (Approval No: E-30041352-514.19.99-281272412 2025/06/62 Date: 19.06.2025).

Authors' contribution

S.S.: Surgical and Medical Practices, Concept, Design, Data Collection or Processing, Analysis or Interpretation, Literature Search, Writing, Critical Review. Y.İ.: Surgical and Medical Practices, Concept, Design, Data Collection or Processing, Analysis or Interpretation, Critical Review. All authors have read and approved the final manuscript.

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