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Original Article

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Prognostic impact of primary tumor location in patients undergoing curative resection for colon cancer

Abstract

Aim: Tumor sidedness is a well-established prognostic and predictive factor in metastatic colon cancer. However, its prognostic significance in patients undergoing curative surgical resection remains unclear. This study aimed to evaluate the impact of primary tumor location on oncologic outcomes in patients treated with curative-intent surgery for colon cancer.
Materials and Methods: This retrospective cohort study included 179 patients who underwent curative surgical resection between 2014 and 2025. Clinicopathological characteristics and tumor location were analyzed. Progression-free survival (PFS) and overall survival (OS) were assessed using Kaplan – Meier analysis and Cox proportional hazards models.
Results: Tumor location was significantly associated with progression ($p = 0.023$). Patients with left-sided and rectosigmoid tumors demonstrated higher progression risk compared with right-sided tumors. In multivariate analysis, tumor location remained independently associated with progression risk. Tumor location was also associated with overall survival in univariate analysis; however, this finding did not remain significant after adjustment. Age was the only independent predictor of overall survival.
Conclusion: Primary tumor location may be independently associated with disease progression in patients undergoing curative-intent resection for colon cancer. Tumor location may provide additional prognostic value in non-metastatic disease.

Keywords: Colon neoplasms, tumor laterality, prognostic factors, survival

INTRODUCTION

Colon cancer remains one of the leading causes of cancer-related morbidity and mortality worldwide, with a steadily increasing global incidence and a substantial projected rise in disease burden over the coming decades (1,2). Colon cancer represents a biologically heterogeneous disease characterized by considerable variability in clinical outcomes among patients with similar tumor stages. Therefore, identifying reliable prognostic factors is essential for optimizing treatment strategies and improving survival outcomes (2,3).

Among the clinicopathological characteristics, primary tumor location has emerged as an important factor influencing disease biology and clinical outcomes in colon cancer. Right-sided colon cancer (RCC) and left-sided colon cancer (LCC) differ in embryological origin, molecular characteristics, and pathological features. RCC originates from the midgut and is more frequently associated with microsatellite instability and specific molecular alterations, whereas LCC arises from the hindgut and is typically characterized by chromosomal instability and distinct oncogenic pathways. These biological differences are believed to contribute to variations in tumor behavior, therapeutic response, and survival outcomes (2,4,5).

Several large-scale studies have reported inferior survival outcomes in RCC, particularly in advanced-stage disease (6,7), leading to the incorporation of tumor sidedness into therapeutic decision-making algorithms (8,9). However, the prognostic role of tumor location in patients undergoing curative-intent surgical resection remains less clearly defined. Emerging evidence suggests that survival disparities between right- and left-sided tumors may vary according to disease stage, patient demographics, and accompanying clinicopathological features

(7,10). These inconsistencies highlight the need for further evaluation of tumor laterality in non-metastatic disease settings.

Beyond tumor location, multiple clinicopathological variables have been identified as potential prognostic determinants in colon cancer. Tumor stage, lymph node involvement, tumor differentiation, lymphovascular invasion (LVI), perineural invasion (PNI), bowel obstruction, perforation, and surgical margin status have all been associated with recurrence risk and survival outcomes. The identification of high-risk features is particularly important in stage II disease, where the benefit of adjuvant chemotherapy remains controversial (11,12). Current clinical guidelines recommend consideration of adjuvant therapy in patients presenting with adverse prognostic features such as T4 tumors (13), inadequate lymph node sampling (14), poor tumor differentiation, or microsatellite instability (MSI) status; however, the prognostic value of these factors remains inconsistent across studies (8,9,15).

Given the ongoing uncertainty regarding the prognostic significance of tumor laterality, further comprehensive evaluation integrating clinicopathological parameters is warranted. Therefore, the present study aimed to evaluate the prognostic impact of primary tumor location on progression and survival outcomes in patients undergoing curative surgical resection for colon cancer.

MATERIALS AND METHODS

This retrospective observational study included patients aged ≥ 18 years with histopathologically confirmed colon adenocarcinoma who underwent curative-intent surgical resection at Adıyaman University Hospital between 2014 and 2025. All eligible patients meeting the inclusion criteria during the study period were consecutively included. Patients with stage IV disease who underwent curative metastasectomy and achieved no evidence of disease (NED) were included in survival analyses to reflect a curative-intent population. Patients with incomplete clinical or follow-up data, unresectable disease, or widespread metastatic disease were excluded.

Data Collection

Demographic and clinicopathological data were retrospectively collected from electronic medical records and pathology reports. Recorded variables included age, sex, comorbidity status, tumor location, histological subtype, grade, pathological T and N stages, LVI, PNI, obstruction, perforation, surgical margin status, MSI status, number of dissected and metastatic lymph nodes, and adjuvant treatment.

Tumor location was classified as right-sided (cecum to transverse colon), left-sided (splenic flexure to sigmoid colon), and rectosigmoid (tumors located at the rectosigmoid junction).

Data on LVI, PNI, and MSI were extracted from original pathology reports without central re-evaluation.

Patients were followed through hospital electronic medical records and imaging data. Disease recurrence and survival outcomes were determined based on radiological findings and documented clinical records. Disease progression was defined as radiologically or histopathologically confirmed local or distant recurrence.

Progression-free survival (PFS) was defined as the time from the date of surgery to the date of disease recurrence or last follow-up.

Overall survival (OS) was defined as the time from the date of surgery to death from any cause or last follow-up.

Statistical Analysis

Survival analyses were performed using the Kaplan – Meier method and compared with the log-rank test. Factors associated with outcomes were evaluated using Cox proportional hazards regression models. Variables with $p < 0.10$ in univariate analysis and clinically relevant factors were included in the multivariable model. Given the limited number of progression and mortality events, the number of variables included in the multivariable model was restricted to avoid overfitting. In addition, variables with potential collinearity were not simultaneously included in the model. Missing data were handled using complete-case analysis. For OS analyses, tumor location was evaluated using a binary classification (right vs left) to improve statistical stability given the limited number of mortality events. Continuous variables were presented as mean ± standard deviation or median (min – max), and categorical variables as frequency (%). A two-sided p-value < 0.05 was considered statistically significant. Analyses were conducted using IBM SPSS Statistics version 26.0.

Ethics Approval: This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Adıyaman University Clinical Research Ethics Committee (Approval number: 2026/1-15 Date: 19/1/2026).

RESULTS

A total of 179 patients with colon cancer were included in the study. The mean age was 63.6 ± 13.2 years (range, 26 – 94 years), and 56.4% of the patients were male. Comorbidities were present in 49.4% of the cohort.

Tumors were predominantly located in the right colon (51.4%), followed by the left colon (36%) and rectosigmoid region (12.6%). Adenocarcinoma was the most common histological subtype (85.8%), while mucinous and signet-ring cell carcinomas were less frequent. Most tumors were grade 2 (51.9%), and the majority of patients had stage II (46.3%) or stage III disease (39.5%). Six patients (3.4%) presented with metastatic disease at diagnosis, underwent curative metastasectomy, and achieved NED.

Pathological evaluation showed that pT3 tumors were the most frequent stage (61%), and nodal involvement was detected in approximately 43% of patients. LVI and PNI were present in 27.9% and 17.3% of patients, respectively, although data on LVI and PNI were unavailable for a subset of patients due to incomplete pathology reports. MSI status was available for 60 patients (33.5% of the cohort), of whom 42 (70%) were microsatellite stable and 18 (30%) were MSI-high.

The mean number of dissected lymph nodes was 19.3 ± 10.4, with a mean of 1.4 ± 2.7 metastatic lymph nodes. Surgical margin positivity was observed in 5.2% of patients. Obstruction and perforation were detected in 39.4% and 4% of patients, respectively. During a median follow-up period of 40.6 months, recurrence occurred in 27 patients (15%). Mortality occurred in 21 patients (11.7%). Detailed demographic and clinicopathological characteristics are summarized in Table 1.

Table 1. Demographic and pathological characteristics

Characteristic variables		n / Mean ± SD	% / Median (min – max)
Age		63.56 ± 13.24	63 (26 – 94)
Gender	**Female**	78	43.6
	Male	101	56.4
Comorbidity	**No**	90	50.6
	Yes	88	49.4
Tumor location	**Right colon**	90	51.4
	Left colon	63	36
	Rectosigmoid	22	12.6
Histology	**Adenocarcinoma**	151	85.8
	Mucinous	21	11.9
	Mixed	1	0.6
	Signet-ring cell carcinoma	3	1.7
Grade	**1**	47	35.3
	2	69	51.9
	3	17	12.8
Stage	**1**	19	10.7
	2	82	46.3
	3	70	39.5
	4 (NED)	6	3.4
pT	**1**	5	2.8
	2	18	10.2
	3	108	61
	4	46	26
pN	**0**	101	57.1
	1	53	29.9
	2	23	13
LVI	**Absent**	69	38.5
	Present	50	27.9
PNI	**Absent**	81	45.2
	Present	31	17.3
Number of dissected lymph nodes		19.32 ± 10.36	17 (1 – 61)
Number of metastatic lymph nodes		1.42 ± 2.74	0 (0 – 23)
Surgical margin	**Negative**	165	94.8
	Positive	9	5.2
Obstruction		69	39.4
Perforation		7	4
MSI(n = 60)	**Stable**	42	70
	MSI-High	18	30
Second malignancy	**Synchronous**	9	5
	Metachronous	3	1.6
Recurrence		27	15
Mortality		21	11.7

Tumor location, LVI, PNI, and MSI data were not available for all patients; MSI status was available for a subset of patients (n = 60); SD: Standard deviation, min: Minimum, max: Maximum, NED: No evidence of disease, LVI: Lymphovascular invasion, PNI: Perineural invasion, pT: Pathological tumor stage, pN: Pathological nodal stage

Progression-Free Survival

Kaplan – Meier analysis revealed a significant association between tumor location and PFS (p = 0.023). Patients with right-sided tumors had longer PFS compared with left-sided or rectosigmoid tumors. Median PFS was not reached (NR) in any tumor location subgroup due to the limited number of progression events (Figure 1).

Tumor stage and nodal status were significantly associated with progression in Kaplan – Meier analyses (p < 0.001, p = 0.021, respectively). Patients with pN2 disease exhibited shorter PFS compared with those with pN0 or pN1 disease (67.4 months vs NR in the other groups). Surgical margin positivity was also associated with shorter PFS (p = 0.038).

Other clinicopathological variables, including sex, comorbidity status, histological subtype, tumor grade, LVI, PNI, obstruction, perforation and MSI status, were not significantly associated with progression (Table 2).

A supplementary binary analysis (right vs left) yielded consistent findings, further supporting the robustness of the observed association between tumor location and progression risk (p = 0.007) (Supplementary Figure S1 and Table S1).

Table 2. Kaplan – Meier analysis results for progression

Characteristic variables		Mean (95% CI)	Median (95% CI)	p*
Gender	**Female**	102.72 (89.59 – 115.85)	–	0.572
	Male	138.45 (120.32 – 156.59)	–	
Comorbidity	**No**	136.52 (118.08 – 154.96)	–	0.614
	Yes	107.54 (92.91 – 122.17)	–	
Tumor location	**Right colon**	147.46 (127.8 – 167.13)	–	**0.023**
	Left colon	96.37 (81.41 – 111.33)	–	
	Rectosigmoid	88.37 (43.51 – 133.24)	–	
Histology	**Adenocarcinoma**	146.04 (133.82 – 158.26)	–	0.954
	Mucinous	104.38 (81.5 – 127.25)	–	
Grade	**1**	140.77 (111.82 – 169.73)	–	0.550
	2	115.7 (99.97 – 131.44)	–	
	3	66.93 (54.22 – 79.64)	–	
Stage	**1**	88.3 (77.81 – 98.79)	–	**< 0.001**
	2	118.78 (105.39 – 132.17)	–	
	3	140.67 (121.32 – 160.03)	–	
	4	28.67 (13.74 – 43.6)	22.43 (8.62 – 36.24)	
pT	**1**	–	–	0.863
	2	–	–	
	3	–	–	
	4	–	–	
pN	**0**	120.44 (108.58 – 132.29)	–	**0.021**
	1	142.31 (121.04 – 163.58)	–	
	2	79.93 (51.29 – 108.58)	67.4	
LVI	**Absent**	130.86 (104.39 – 157.33)	–	0.959
	Present	82 (71.55 – 92.45)	–	
PNI	**Absent**	125.48 (90.87 – 160.08)	–	0.993
	Present	83.68 (67.87 – 99.49)	–	
Surgical margin	**Negative**	141.89 (128.29 – 155.49)	–	**0.038**
	Positive	53.67 (29.67 – 77.67)	–	
Obstruction	**Absent**	151.72 (139.07 – 164.37)	–	0.367
	Present	96.58 (81.78 – 111.39)	–	
Perforation	**Absent**	142.88 (129.53 – 156.23)	–	0.769
	Present	67.89 (45.81 – 89.97)	–	
	Stable	71.11 (58.55 – 83.67)	–	
	MSI-high	100.59 (66.1 – 135.08)	–	0.439

* Log-Rank test, CI: Confidence Interval, PFS: Progression-free survival; NR: Not reached; LVI: Lymphovascular invasion; PNI: Perineural invasion; MSI: Microsatellite instability

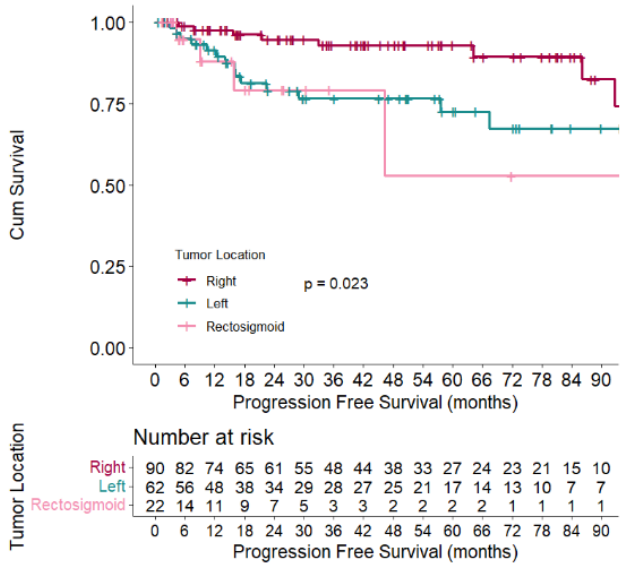

Figure 1. Progression-free survival according to primary tumor location; Kaplan-Meier overall survival curves according to primary tumor location (right-sided colon and left-sided colon tumors)

Predictors of Progression

As shown Table 3, in univariate analysis, an increased number of dissected lymph nodes was associated with reduced progression risk (HR = 0.94, p = 0.037), whereas an increased number of metastatic lymph nodes was associated with increased progression risk (HR = 1.13, p = 0.016).

Tumor location was significantly associated with progression risk. Compared with right-sided tumors, left-sided tumors were associated with increased progression risk (HR = 2.81, p = 0.020), while rectosigmoid tumors demonstrated an even higher risk (HR = 3.71, p = 0.034). Stage IV disease was also associated with markedly increased progression risk compared with stage I disease (HR = 16.15, p = 0.013). Similarly, pN2 disease was associated with increased progression risk compared with pN0 disease (HR = 3.69, p = 0.008). Surgical margin positivity showed a borderline association with progression risk (HR = 3.35, p = 0.050) and was therefore not included in the multivariable model due to the limited number of events and potential confounding.

Table 3. Evaluation of factors affecting progression

Characteristic	Univariate		Multivariate	
	HR (95% CI)	p	HR (95% CI)	p
Age	1.02 (0.99 – 1.05)	0.199		
Number of dissected lymph nodes	0.94 (0.89 – 1)	**0.037**	0.94 (0.89 – 1)	0.054
Number of metastatic lymph nodes	1.13 (1.02 – 1.25)	**0.016**	1 (0.74 – 1.34)	0.981
Tumor location (Ref: Right colon)				
Left	2.81 (1.18 – 6.7)	**0.020**	3.04 (1.1 – 8.35)	**0.031**
Rectosigmoid	3.71 (1.11 – 12.41)	**0.034**	6.35 (1.45 – 27.9)	**0.014**
Stage (Ref.: 1)				
2	1.82 (0.23 – 14.35)	0.572		
3	2.99 (0.39 – 23.23)	0.294		
4	16.15 (1.79 – 146.04)	**0.013**		
pN (Ref.: 0)				
1	1.7 (0.67 – 4.31)	0.266	0.84 (0.25 – 2.82)	0.776
2	3.69 (1.4 – 9.74)	**0.008**	3 (0.34 – 26.74)	0.325
Surgical margin (Ref.: Negative)	3.35 (1 – 11.25)	**0.050**		

HR: hazard ratio, CI: confidence interval, Ref: reference category; Overall model fit was $\chi^2 = 21.025$, p = 0.002

In multivariate analysis, tumor location remained independently associated with progression risk. Compared with RCC, LCC (HR = 3.04, p = 0.031) and rectosigmoid tumors (HR = 6.35, p = 0.014) were associated with increased progression risk. The number of dissected and metastatic lymph nodes did not retain statistical significance in the multivariate model.

Overall Survival

Kaplan – Meier analysis demonstrated a difference in OS between tumor locations when analyzed using a binary classification (right vs left) (Figure 2). Perforation status was also associated with survival, with patients without perforation showing longer OS compared to those with perforation (p = 0.049).

Given the limited number of mortality events, two multivariable models were constructed with different variable selections to minimize overfitting; the results were consistent across both models (Table 4).

In univariate Cox regression analysis, tumor location was significantly associated with mortality, with LCC conferring

a higher risk of death compared to RCC (HR = 2.82, 95% CI: 1.08 – 7.34, p = 0.034). However, this association did not remain statistically significant in multivariable analysis after adjustment for clinically relevant factors (HR = 1.94, 95% CI: 0.71 – 5.26, p = 0.195).

Increasing age emerged as the only independent predictor of OS (HR = 1.07, 95% CI: 1.03 – 1.11, p < 0.001). Perforation showed a borderline association with mortality in univariate analysis (HR = 3.95, 95% CI: 0.9 – 17.27, p = 0.068), but did not retain statistical significance in multivariable analysis.

Table 4. Evaluation of factors affecting overall survival

Characteristic	Univariate		Multivariate 1		Multivariate 2	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Age	1.08 (1.04 – 1.13)	**< 0.001**	1.07 (1.03 – 1.11)	**< 0.001**	1.07 (1.03 – 1.11)	**< 0.001**
Number of dissected lymph nodes	0.98 (0.93 – 1.02)	0.297				
Number of metastatic lymph nodes	1.12 (1 – 1.27)	0.056	1.11 (0.96 – 1.28)	0.148		
Perforation (Ref.: Absent)	3.95 (0.9 – 17.27)	0.068	2.23 (0.48 – 10.26)	0.305		
Tumor location (Ref: Right colon)	2.82 (1.08 – 7.34)	**0.034**			1.94 (0.71 – 5.26)	0.195

HR: hazard ratio, CI: confidence interval, Ref: reference category; Overall model fit was $\chi^2 = 19.745$, p < 0.001

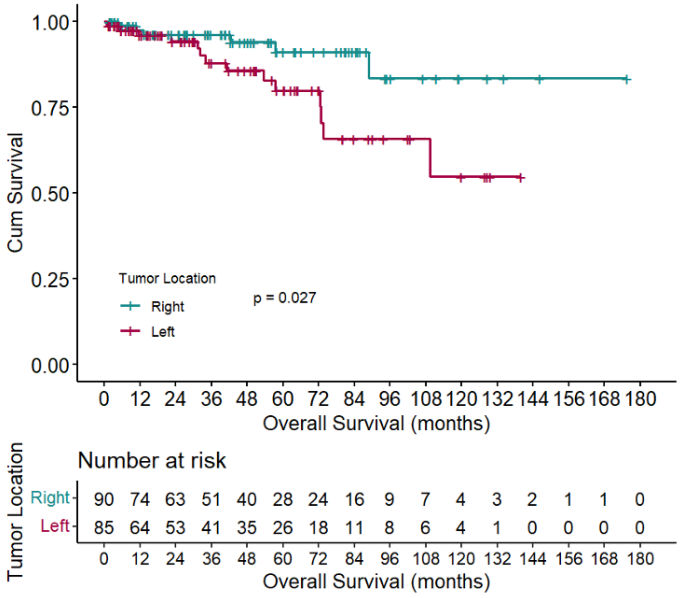

Figure 2. Overall survival according to primary tumor location; Legend: Kaplan-Meier overall survival curves according to primary tumor location (right-sided colon and left-sided colon tumors)

DISCUSSION

In the present study, we investigated the prognostic significance of primary tumor location and clinicopathological characteristics in patients undergoing curative-intent surgical resection for colon cancer. Our findings suggest that tumor location may be independently associated with progression risk, but not with OS.

The prognostic and predictive importance of tumor sidedness has been well established in metastatic colon cancer. Several large-scale studies have demonstrated differences in treatment response and survival outcomes between right- and left-sided tumors, leading to the incorporation of tumor location into therapeutic decision-making algorithms (6-9,16). However, the prognostic role of tumor laterality in patients undergoing curative surgical resection remains less clearly defined. Emerging evidence suggests that survival differences between tumor locations may vary according to disease stage, patient characteristics, and treatment strategies (7,10,17,18). Recent analyses focusing on stage II – III disease have reported heterogeneous results, highlighting the complexity of tumor biology in localized colon cancer (3,10,11). Our findings contribute to this evolving evidence by demonstrating that tumor location may also have clinically relevant prognostic implications in non-metastatic disease.

Interestingly, our study demonstrated a higher progression risk in LCC and rectosigmoid tumors compared with RCC. This finding contrasts with several previous reports suggesting poorer outcomes in RCC, particularly in advanced disease stages (6,7). This discrepancy may be explained by several factors. First, our cohort predominantly consisted of non-metastatic patients undergoing curative-intent resection, whereas many prior studies focused on metastatic or heterogeneous populations. Second, the relatively limited number of progression events and the moderate follow-up duration may have affected the stability of risk estimates and the ability to detect long-term survival differences. Third, potential imbalances in stage distribution, nodal status, and other clinicopathological factors across tumor locations may have contributed to the observed differences. Moreover, the retrospective design may have introduced variability in outcome assessment. Finally, limited molecular characterization, particularly the incomplete availability of MSI data, may have further influenced the findings. Therefore, these results should be interpreted with caution and considered hypothesis-generating rather than definitive.

From a biological perspective, right-sided tumors are typically associated with microsatellite instability, BRAF mutations, and distinct tumor microenvironment characteristics, which may influence tumor behavior and treatment responsiveness (4,18,19). In contrast, LCC are more frequently characterized

by chromosomal instability and alternative oncogenic pathways, which may contribute to different progression dynamics (4,5). The higher prevalence of microsatellite instability in early-stage RCC may partially explain the relatively favorable progression outcomes observed in this subgroup. The consistency of findings across subgroup and binary analyses (right vs left) further supports the robustness of the observed association between tumor location and progression risk.

Rectosigmoid tumors represent a particularly heterogeneous subgroup that may share biological and clinical characteristics with both colon and rectal cancers. Differences in vascular and lymphatic drainage patterns, as well as variations in surgical management, may contribute to unique recurrence patterns in this anatomical region (4,20). Our findings support the concept that tumor location should be considered as a biological continuum rather than a simple binary classification of right- versus left-sided disease (20), potentially allowing for a more comprehensive understanding of tumor behavior and improved risk stratification. However, in our study, the relatively small number of patients in the rectosigmoid subgroup may have limited the precision of the estimates, as reflected by the wide confidence intervals.

Consistent with previous studies, tumor stage and nodal involvement were associated with progression risk in univariate analyses. Nodal metastasis is widely recognized as a key determinant of tumor dissemination and adverse oncologic outcomes, reflecting both tumor aggressiveness and metastatic potential (8,14,17). Similarly, we observed that a higher number of dissected lymph nodes was associated with reduced progression risk, highlighting the clinical importance of adequate surgical staging and lymph node evaluation. Adequate lymphadenectomy improves staging accuracy and may facilitate appropriate selection of adjuvant therapy, thereby contributing to improved oncologic outcomes (8,14,15). However, these variables did not retain independent significance in multivariate analysis, which may be related to limited number of progression events in our cohort.

Surgical margin positivity showed a borderline association with PFS in survival analyses. Positive margins have consistently been reported as adverse prognostic factors due to their association with residual tumor burden and increased recurrence risk. Previous studies have also demonstrated that incomplete tumor resection and inadequate lymph node sampling are associated with poorer outcomes, particularly in patients with high-risk stage II disease (8,11,12).

Regarding OS, age was identified as the only independent prognostic factor. Increasing age has been consistently associated with poorer survival outcomes in colon cancer and may reflect a combination of increased comorbidity burden, reduced tolerance to systemic therapies, and age-related decline in physiological and immune reserve (3,4,17). Although tumor location showed a significant association with OS in univariate analysis, this finding was not confirmed in multivariable modeling. This discrepancy may be related to the limited number of mortality events and potential confounding factors. Therefore, the impact of tumor location on OS should be considered exploratory and requires validation in larger cohorts.

Limitations

Several limitations of this study should be acknowledged. First, the retrospective single-center design may introduce selection bias and limit the generalizability of the findings. Second, the relatively limited number of progression and mortality events may have reduced the statistical power of the analyses and increased the risk of model instability. Therefore, the number of variables included in the multivariable model was restricted, and the findings should be interpreted with caution and considered hypothesis-generating. Third, although key clinicopathological variables were included, missing data for certain parameters and the use of complete-case analysis may have introduced bias. In addition, comprehensive molecular profiling, including detailed MSI and mutational analyses, was not available for all patients. Given the known biological association between MSI status and tumor sidedness, incomplete MSI data represents an important limitation and may have limited the ability to fully evaluate its potential confounding effect on the relationship between tumor location and outcomes. Furthermore, the retrospective nature of the study may have led to variability in data collection, outcome assessment, and measurement of clinicopathological variables. Finally, although sensitivity analysis excluding stage IV (NED) patients did not materially change the results, the inclusion of this subgroup may still have introduced a degree of biological heterogeneity.

CONCLUSION

In conclusion, our findings suggest that primary tumor location may be associated with disease progression in patients undergoing curative resection for colon cancer. Tumor laterality may provide additional prognostic information beyond conventional clinicopathological factors and could be considered in risk stratification of non-metastatic disease. Future prospective studies incorporating molecular profiling are warranted to further clarify the biological mechanisms underlying tumor location-associated differences.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that there is no financial support.

Ethical Approval
This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Adiyaman University Clinical Research Ethics Committee (Approval number: 2026/1-15 Date: 19/1/2026).

Informed Consent
Due to the retrospective design of the study, informed consent was waived by the ethics committee.

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