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Clinical and oncological outcomes in colon cancer: Impact of tumor location and family history in a retrospective cohort

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Abstract

Introduction: In colorectal cancer, right-sided primary tumor location is associated with a worse prognosis compared to left-sided colon cancer.

Objective: In this study, we compared clinical, pathological, oncological characteristics, and survival between cancers of the left and right colon.

Methods: Patients who underwent curative resection for colon cancer were identified and retrospectively analyzed. Clinicopathological characteristics, overall survival, postoperative complications, and postoperative liver metastasis were compared between left- and right-sided tumors using the log-rank test and multivariable Cox proportional hazards regression.

Results: A total of 108 patients with colon adenocarcinoma were included. There was no difference in overall survival (hazard ratio [HR] = 1.08, 95% confidence interval [CI]: 0.68–1.73, $p = 0.72$) between right- and left-sided primary tumors. Postoperative liver recurrence was noted in 24.1% of cases, and postoperative complications occurred in 6.5% of patients, without significant differences between groups. Higher body mass index (odds ratio [OR] = 2.31, 95% CI: 1.05–15.32, $p = 0.031$) and larger tumor size (OR = 5.32, 95% CI: 2.82–11.14, $p = 0.001$) were significantly associated with colon cancer risk. Additionally, a positive family history of cancer was significantly associated with decreased overall survival (HR = 2.44, 95% CI: 1.16–5.12, $p = 0.018$).

Conclusion: Tumor localization was not associated with overall survival among colon cancer patients who underwent curative resection. However, a positive family history of cancer was associated with overall survival.

Keywords: Colorectal cancer; Survival time; Recovery

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1. Introduction

Colorectal cancer (CRC) is the third most diagnosed cancer and the second leading cause of cancer death worldwide. More than 1.92 million people worldwide were diagnosed

in 2022.[1,2] Despite advances in diagnosis and treatment, substantial disparities in survival remain evident across regions. Five-year survival rates exceed 60% in high-income countries, yet fall below 30% in low-resource settings.[3] Mongolia currently reports the highest cancer-related mortality rate globally. Among the various cancer types, CRC represents an increasing public health burden. The incidence and mortality rates of CRC in Mongolia are 6.3 and 4.0 per 100,000 population, respectively.[4,5]

From 2018 to 2022, the national average age-standardized rate (ASR) for newly diagnosed CRC cases was 7.9 per 100,000 population. This burden is notably greater in the capital city, Ulaanbaatar, where the ASR was 8.24 per 100,000. Similarly, CRC-related mortality during the same period revealed a national ASR of 4.7 per 100,000 with Ulaanbaatar again reporting a slightly elevated rate of 4.8 per 100,000. Survival outcomes remain a major concern. Data from the 2018–2022 period indicate that while the one-year survival rate for colon cancer patients was 89.3%, the proportion of patients surviving three to five years after diagnosis dropped drastically to just 13.4%.[5]

An important development in CRC research has been the recognition of biological and clinical differences between tumors originating on the right and left sides of the colon. These distinctions were first proposed by Beart *et al.*[6] and Bufill[7] in the 1980s and 1990s, and later substantiated by O'Dwyer *et al.*[8] in studies of stage IV disease in 2001.

Colorectal cancer develops through a complex interplay of genetic susceptibility and environmental exposures. Hereditary syndromes, including Lynch syndrome and familial adenomatous polyposis, substantially increase risk. In the general population, lifetime CRC risk is approximately 4 to 5%, whereas individuals with a positive family history experience a two- to four-fold increased likelihood of developing the disease due to inherited oncogenic mutations.[9-11]

Increasing attention has been focused on the biological and clinical differences between tumors on the right and left sides of the colon. These tumors differ in embryologic origin, molecular characteristics, pathological features, and clinical behavior. CRC has traditionally been classified as right-sided colon cancer (RCC) and left-sided colon cancer (LCC), although rectal cancer is increasingly considered a distinct clinical entity.[12,13]

The right colon arises from the midgut, whereas the left colon arises from the hindgut, contributing to divergent tumor microenvironments and patterns of luminal exposure. From a histopathological standpoint, RCC is more frequently poorly differentiated and often exhibits mucinous or signet-ring cell features. LCC, in contrast, commonly demonstrates chromosomal instability.[14,15]

Distinct molecular differences also exist, with RCC showing higher rates of microsatellite instability, *BRAF* mutations, and CpG island methylation. *BRAF*-mutated tumors occur more commonly among older individuals, females, smokers, and patients with proximal colon involvement.[16,17]

The progression of CRC is frequently initiated by mutations in the adenomatous polyposis coli (*APC*) tumor suppressor gene, resulting in dysregulation of Wnt and β-catenin signaling and uncontrolled cellular proliferation. Beyond host genetic alterations, increasing evidence supports a role of the gut microbiome in CRC pathogenesis, particularly in right-sided tumors.[18]

Microbial biofilms form structured communities along the intestinal mucosa, disrupt epithelial barriers, promote chronic inflammation, and activate oncogenic signaling pathways. These biofilms are more commonly detected in proximal colon cancers and are associated with invasive tumor behavior, immune evasion, and adverse clinical outcomes.[19,20] Several biofilm-associated bacterial species, including *Fusobacterium nucleatum*, enterotoxigenic *Bacteroides fragilis*, and specific *Escherichia coli* strains, have been shown to induce DNA damage and stimulate inflammatory pathways, such as nuclear factor-κB and Signal Transducer and Activator of Transcription 3.[19]

More recently, a microbiota-driven signaling pathway involving the S100 calcium-binding protein A11 (S100A11) and the receptor for advanced glycation end-products (RAGE) has been identified in right-sided colon adenomas, where it promotes recruitment of myeloid-derived suppressor cells, suppresses antitumor immune responses, and accelerates tumor progression. Pharmacologic inhibition of this pathway has been shown to enhance responsiveness to immunotherapy, supporting its therapeutic potential. In right-sided colon adenomas, goblet cell loss allows bacteria to breach the mucus barrier. This translocation triggers the S100A11–RAGE axis, which recruits MDSCs to suppress immune activity and facilitate tumor growth.[21] These findings highlight the importance of incorporating molecular and microbial factors into contemporary models of CRC pathogenesis and management. The present study aimed to analyze the clinical, pathological, oncological characteristics, and survival between cancers of the left and right sides of the colon in a single-center cohort of patients with colon cancer who underwent surgical treatment.

2. Materials and methods

The study cohort was derived from a single-center retrospective database of CRC cases and included consecutive patients who had undergone surgery for colon adenocarcinoma with curative intent between 2012 and 2015. All data were retrospectively recorded.

All subjects included in this study were 18 years of age or older at the time of colon cancer diagnosis, and they underwent surgery with curative intent for pathologically confirmed adenocarcinoma of the colon. Exclusion criteria were as follows: rectal/rectosigmoid junction cancer, recurrent colon cancer, emergency surgery, and lack of postoperative follow-up.

The study analyzed various parameters, including patients' general characteristics (age, gender, and body mass index [BMI]), clinical symptoms, type and duration of surgery, blood and biochemistry tests, incidence of postoperative complications, postoperative liver metastasis, and duration of hospitalization. Additionally, parameters such as cancer stage, survival duration, lymph node and distant metastases, and follow-up data were included in the analysis. The patients' general characteristics and postoperative complication rates were obtained from medical records. Tumor localization, as well as the duration and type of procedure, were collected from operative records. Histopathological data were collected from our institution's internal electronic pathology system. Follow-up data were obtained from the patient's medical history from the surgical clinic and/or from hospital department records.

The cohort was divided into two subgroups based on tumor localization: RCC (cecum, ascending colon, and the proximal two-thirds of the transverse colon) and LCC (the distal third of the transverse colon, descending colon, and sigmoid colon).

2.1. Statistical analysis

Statistical analyses were performed using SPSS software (version 24.0, IBM Corp., USA). Descriptive statistics were used to analyze clinical and pathological parameters between the two groups defined by tumor location. Categorical variables were analyzed using the χ^2 or Fisher's exact test, whereas continuous variables were analyzed using the independent-samples t-test for normally distributed data or the Wilcoxon rank-sum test when normal distribution was not met. Multiple logistic regression analysis was performed to identify factors associated with colon cancer outcomes. Overall survival (OS) was analyzed using the Kaplan–Meier method, and comparisons were made using the log-rank test. Univariate and multivariate Cox regression analyses were used to determine independent predictors of OS. Post hoc power analysis was performed using G*Power software (v3.1, Heinrich Heine University, Germany). The study participants' survival time was analyzed and described as mean and median values. The mean and median survival time were 4.58 (4.42–4.73) and 4.64 (4.44–4.84) years, respectively. Additionally, we checked proportional hazard assumptions for tumor stage and colon cancer location (right, left) with time-invariant covariates. The results showed that tumor stage ($p = 0.493$) and colon cancer location ($p = 0.125$) did not change over the follow-up period. Multiple logistic regression analysis was performed, adjusting for age, BMI, smoking status, family history, hepatitis B or C virus infection, tumor size, and protein level. In the subgroup analysis, we used Cox regression to evaluate the relationship between time-to-event outcomes and predictor variables. The model was adjusted for age, protein level, tumor size, family history, smoking status, liver resection, number of chemotherapy cycles, cell differentiation, tumor stage, blood loss, and postoperative complications, and was stratified by gender. A p-value less than 0.05 was considered statistically significant.

3. Results

3.1. General characteristics of the study population

A total of 108 patients with colon cancer were included, divided into two groups: RCC ($n = 52$, 48.1%) and LCC ($n = 56$, 51.9%). The mean age was 58.09 ± 12.70 years with no significant difference between groups ($p = 0.298$). The mean BMI was 23.75 ± 3.44 kg/m^2, and serum total protein levels averaged 68.61 ± 6.56 g/L across all participants. Albumin levels were significantly higher in LCC patients than in RCC patients ($p = 0.039$). No significant differences were observed between RCC and LCC groups in operation time, blood loss, hospital stay duration, or OS. Gender distribution, smoking history, family history, and viral infections showed no significant differences between the two groups (Table 1). Overall, the mean survival time was 4.58 (4.42–4.73), 80% of participants had a family history from parents, 20% from siblings (Tables S1 and S4).

3.2. Cancer stages and tumor differentiation

Tumor staging using the tumor, nodes, metastasis system revealed that the majority of patients were diagnosed at stage T3 (70.4%). No significant differences were noted in tumor staging distribution between RCC and LCC groups ($p = 0.592$). Regarding histological differentiation, most tumors were moderately differentiated (45.4%), followed by well-differentiated (33.3%) and poorly differentiated tumors (21.3%). Although a greater proportion of well-differentiated tumors was observed in LCC patients,

Table 1. General characteristics of the study population

Variables	RCC (52, 48.1%)	LCC (56, 51.9%)	Total (108)	*p*-value
Age, year	56.88 ± 13.29	59.21 ± 12.15	58.09 ± 12.70	0.298
BMI, kg/m^2	23.48 ± 3.52	24.01 ± 3.38	23.75 ± 3.44	0.342
T-protein (g/L)	68.34 ± 7.45	68.87 ± 5.67	68.61 ± 6.56	0.880
Albumin (g/L)	37.68 ± 6.11	40.51 ± 4.74	39.15 ± 5.60	0.039
Operation time, min	99.90 ± 27.94	112.95 ± 47.44	106.71 ± 39.64	0.295
Blood loss, mL	109.04 ± 34.31	113.75 ± 37.44	111.48 ± 35.88	0.664
Hospital stay, days	12.25 ± 4.74	12.07 ± 3.99	12.15 ± 4.34	0.672
Overall survival day	1,348.31 ± 562.47	1,222.61 ± 560.29	1283.13 ± 562.26	0.153
Survival months	44.33 ± 18.49	40.20 ± 18.42	42.19 ± 18.49	0.775
Tumor size, cm	6.24 ± 3.60	5.57 ± 4.37	5.89 ± 4.01	0.989
Gender				
Male	25 (48.1)	27 (48.2)	52 (48.1)	
Female	27 (51.9)	29 (51.8)	56 (51.8)	
Smoking				0.374
Yes	15 (28.8)	12 (21.4)	27 (25.0)	
No	37 (71.2)	44 (78.6)	81 (75.0)	
Family history				0.215
Yes	8 (15.4)	14 (25)	22 (20.4)	
No	44 (84.6)	42 (75)	86 (79.6)	
Virus infection				0.851
No virus	43 (82.7)	48 (85.7)	91 (84.3)	
B virus	1 (1.9)	2 (3.6)	3 (2.8)	
C virus	7 (13.5)	5 (8.9)	12 (1.1)	
Dual virus	1 (1.9)	1 (1.8)	2 (1.8)	

Notes: Mann–Whitney test was used for continuous variables; χ^2 test was used for categorical variables; Continuous variables were described as mean ± standard deviation; categorical variables were described as number (percentages).
Abbreviations: BMI: Body mass index; LCC: Left colon cancer; RCC: Right colon cancer.

the difference was not statistically significant (p = 0.123) (Tables 2 and S3).

3.3. Sites of metastasis

Regional metastasis occurred predominantly in adjacent organs (79.6%), with no significant difference between RCC and LCC groups (p = 0.098). Para-aortic lymph node metastasis was more frequent in LCC patients (12.8%) than in RCC patients (1.9%). Distant metastasis was recorded in 13.9% of cases, most commonly to the liver (10.2%), with no significant group differences (p = 0.443) (Table 3).

3.4. Surgical procedures and postoperative conditions

The type of surgery varied significantly between RCC and LCC patients (p < 0.001). Right hemicolectomy was

Table 2. Cell differentiation and the stages of cancer according to the tumor, nodes, metastasis system

Variables	RCC (52, 48.1%)	LCC (56, 51.9%)	Total (108)	*p*-value
Stages				0.592
T1	3 (5.8)	1 (1.8)	4 (3.7)	
T2	6 (11.5)	6 (10.7)	12 (11.1)	
T3	37 (71.2)	39 (69.6)	76 (70.4)	
T4	6 (11.5)	10 (17.9)	16 (14.8)	
Differentiation				0.123
Well	12 (23.1)	24 (42.9)	36 (33.3)	
Moderately	26 (50)	23 (41.1)	40 (45.4)	
Poorly	14 (25.9)	9 (16.1)	23 (21.3)	

Notes: χ^2 test was used for categorical variables; categorical variables were described as numbers (percentages)
Abbreviations: LCC: Left colon cancer; RCC: Right colon cancer.

Table 3. Sites of distant and regional metastasis in colon cancer

Variables	RCC (52, 48.1%)	LCC (56, 51.9%)	Total (108)	*p*-value
Regional metastasis				0.098
No	8 (15.4)	6 (10.7)	14 (12.9)	
Near organs	43 (82.7)	43 (76.8)	86 (79.6)	
Para-aortal	1 (1.9)	7 (12.8)	8 (7.4)	
Distant metastasis				0.443
No	47 (90.4)	46 (82.1)	93 (86.1)	
Liver	4 (7.7)	7 (12.5)	11 (10.2)	
Ovarium	–	2 (3.6)	2 (1.9)	
Other organs	1 (1.9)	1 (1.8)	2 (1.9)	

Notes: χ^2 test was used for categorical variables; categorical variables were described as numbers (percentages)
Abbreviations: LCC: Left colon cancer; RCC: Right colon cancer.

predominantly performed in RCC cases (75%), whereas left hemicolectomy, sigmoidectomy, and anterior resection were more common in LCC cases. Most surgeries were radical (87.9%), with similar rates across both groups (p = 0.557). Postoperative liver recurrence was noted in 24.1% of cases, and postoperative complications occurred in 6.5% of patients, without significant differences between groups (Table 4).

3.5. Chemotherapy and recurrence by cancer stage

Chemotherapy use was significantly associated with cancer stage (p = 0.038). Chemotherapy was more frequent in advanced stages, particularly stage IV. Recurrence rates increased significantly with advancing stages ($p < 0.001$), with the highest recurrence observed in stage IV patients (56.3%). Metastatic spread and the need for palliative care were more prominent in advanced stages. (Table 5). Furthermore, we analyzed the correlation between tumor stages and chemotherapy, controlling for tumor location and family history. The results showed a negative, statistically significant result (−0.213, p = 0.028) (Table S5).

3.6. Logistic regression analysis

In the logistic regression analysis, age (OR = 1.05, 95% CI: 1.01–1.10, p = 0.014), albumin level (OR = 1.12, 95% CI: 1.02–1.23, p = 0.015), and tumor size (OR = 5.32, 95% CI: 2.82–11.14, p = 0.001) were significantly associated with the outcome. When tumor size was analyzed as a categorical variable, tumors ≥ 5 cm were significantly associated with the outcome compared with tumors < 5 cm (OR = 0.31, 95% CI: 0.11–0.86, p = 0.024). In addition, hepatitis C virus infection was significantly associated with the outcome (OR = 0.21, 95% CI: 0.04–0.98, p = 0.047). Other variables, including BMI (p = 0.649), sex (p = 0.615), smoking status (p = 0.487), family history (p = 0.099), hepatitis B virus infection (p = 0.910), and dual viral infection (p = 0.384), were not significantly associated with the outcome (Table 6).

3.7. Survival analysis

Kaplan–Meier analysis showed survival declining from 88.9% at baseline to 57.3% at 1,700 days. Survival declined steadily over time, particularly after 1,000 days post-diagnosis (Table 7 and Figure 1).

3.8. Cox proportional hazards model for overall survival

In the Cox regression analysis (Table 8), family history was significantly associated with OS (HR = 2.44, 95% CI: 1.16–5.12, p = 0.018). Blood loss ≥ 110 mL showed borderline significance (HR = 0.52, 95% CI: 0.27–1.00, p = 0.050). No significant associations were observed for other variables, including age, protein level, smoking status, tumor stage, postoperative complications, liver recurrence, and tumor laterality. After adjustment for potential confounding factors in the multivariate Cox proportional hazards model (Table S2), liver resection (HR = 0.18, 95% CI: 0.09–0.38, p < 0.001) and receiving 5–8 cycles of chemotherapy (HR = 0.09, 95% CI: 0.01–0.26, p < 0.001) were independently associated with improved OS. In contrast, RCC was independently associated with poorer OS compared with LCC (HR = 2.88, 95% CI: 1.32–6.31, p = 0.008). Notably, family history and blood loss, which were significant in the univariate analysis, were no longer significant after multivariate adjustment.

4. Discussion

4.1. Tumor laterality and overall survival

This study explored the relationship between primary tumor location and oncological outcomes in patients with colon cancer who underwent curative treatment. Our findings indicated no significant association between tumor localization and OS. These results align with previous studies conducted by Karim *et al.*[22] and Torun *et al.*,[23] which also reported no significant differences in survival by tumor laterality. A Canadian population-based cohort study concluded that tumor laterality did not independently influence long-term OS or cancer-specific survival across all stages, whether analyzed collectively or stage-by-stage.[22] Similarly, Torun *et al.*'s[23] retrospective analysis of

Table 4. Surgical procedures and post-operative conditions

Variables	RCC (52, 48.1%)	LCC (56, 51.9%)	Total (108)	*p*-value
Radical surgery				0.557
Palliative	6 (11.5)	7 (12.5)	13 (12.0)	
Radical	46 (88.5)	49 (87.5)	95 (87.9)	
Post-operative liver recurrence				0.324
Liver metastasis	11 (21.2)	15 (26.8)	26 (24.1)	
No liver metastasis	41 (78.8)	41 (73.2)	82 (75.9)	
Post-operational complication				0.541
No complication	48 (92.3)	53 (94.6)	101 (93.5)	
Ascites	2 (3.8)	–	2 (1.9)	
Ileus	–	1 (1.8)	1 (0.9)	
Peritonitis	1 (1.9)	1 (1.8)	2 (1.9)	
Wound infection	1 (1.9)	1 (1.8)	2 (1.9)	

Notes: χ^2 test was used for categorical variables; categorical variables were described as numbers (percentages)
Abbreviations: LCC: Left colon cancer; RCC: Right colon cancer.

Table 5. Chemotherapy and recurrence by cancer stages

Variables	Stage I (4, 7.4%)	Stage II (12, 11.1%)	Stage III (76, 70.4%)	Stage IV (16, 14.8%)	Total (108)	*p*-value
Chemotherapy						0.038
No	1 (25)	0	8 (10.5)	2 (12.5)	11 (10.2)	
1–4 times	2 (50)	4 (33.3)	36 (47.4)	14 (87.5)	56 (51.9)	
5–8 times	1 (25)	8 (66.7)	29 (38.2)	0	38 (35.2)	
>8	0	0	3 (3.9)	0	3 (2.8)	
Recurrence						<0.001
No	4 (100)	8 (66.7)	45 (59.2)	4 (25.0)	61 (56.5)	
Yes	0	0	4 (5.3)	9 (56.3)	27 (25.0)	
Palliative	0	3 (25.0)	21 (27.6)	3 (18.8)	13 (12.0)	
Metastasis	0	1 (8.3)	6 (7.9)	0	7 (6.4)	

Notes: χ^2 test was used for categorical variables; categorical variables were described as numbers (percentages).

Table 6. Multiple logistic regression model for odds in colon cancer

Variables	OR	95% CI	*p*-value
Age, years	1.05	1.01–1.10	0.014
BMI, kg/m^2	1.04	0.89–1.20	0.649
Albumin, g/L	1.12	1.02–1.23	0.015
Tumor size			
<5 cm	1.00	Reference	
≥5 cm	0.31	0.11–0.86	0.024
Sex			
Female	1.00	Reference	
Male	0.76	0.26–2.21	0.615
Smoking			
No	1.00	Reference	
Yes	1.51	0.47–4.84	0.487
Family history			
No	1.00	Reference	
Yes	0.36	0.11–1.22	0.099
Virus infection			
No virus	1.00	Reference	
B virus	1.19	0.06–25.55	0.910
C virus	0.21	0.04–0.98	0.047
Dual viral	3.77	0.19–74.53	0.384

Abbreviations: BMI: Body mass index; CI: Confidence interval; OR: Odds ratio.

Table 7. Effect measures for time-to-event (survival) outcomes

Time (day)	Risk	Event	Survival %	SE	95% CI
0	108	12	88.9	0.030	83.2–95.0
60	96	1	88.0	0.031	82.0–94.3
200	95	1	87.0	0.032	80.9–93.6
300	94	1	86.1	0.333	79.8–92.9
330	93	1	85.2	0.034	78.7–92.2
365	92	1	84.3	0.035	77.7–91.4
395	91	1	83.3	0.036	76.6–90.7
404	90	1	83.3	0.037	75.5–89.9
425	88	1	81.5	0.037	74.5–89.1
485	87	2	79.6	0.039	72.3–87.6
600	85	1	78.7	0.040	71.3–86.8
605	84	2	76.8	0.041	69.2–85.2
635	82	1	75.9	0.041	68.2–84.4
730	81	1	74.9	0.042	67.2–83.6
760	79	2	73.0	0.043	65.1–81.9
790	77	1	72.1	0.043	64.1–81.1
820	76	1	71.1	0.044	63.0–80.2
910	75	2	69.2	0.045	61.0–78.5
1,030	73	2	67.3	0.045	59.0–76.8
1,095	71	2	65.4	0.046	57.0–75.1
1,110	69	1	64.5	0.046	56.0–74.2
1,155	68	2	62.6	0.047	54.0–72.5
1,245	65	1	61.6	0.047	53.0–71.6
1,365	57	1	60.5	0.048	51.9–70.6
1,460	45	1	59.2	0.048	50.4–69.5
1,700	31	1	57.3	0.050	48.2–68.1

Abbreviations: CI: Confidence interval; SE: Standard error.

182 patients revealed no significant differences in 2- and 5-year survival rates between RCC and LCC. However, the literature presents mixed findings regarding the prognostic significance of tumor sidedness. Several studies suggest that RCC is associated with poorer outcomes. For example, Meguid *et al.*[24] analyzed 77,978 patients and reported a worse prognosis in RCC compared to LCC. Similarly, Suttie *et al.*,[25] utilizing Surveillance, Epidemiology, and End Results data encompassing 841 patients, found that RCC conferred a reduced survival advantage. Jung *et al.*[26] observed that among 974 nonmetastatic cases, RCC was associated with a significantly higher hazard ratio for mortality (adjusted HR = 1.49, 95% CI: 1.11–2.00, $p = 0.009$). In stage III patients, Zenger *et al.*[27] reported significantly lower 5-year survival rates in RCC—66.9% versus 81.8% in LCC—with both overall and disease-free survival metrics favoring LCC. Furthermore, Diez-Alonso *et al.*[28] demonstrated that patients with stage III RCC had inferior overall and cancer-related survival rates at five years compared to their LCC counterparts.

Several meta-analyses have evaluated the prognostic impact of tumor laterality. Petrelli *et al.*,[29] encompassing 66 studies, concluded that LCC portends a better prognosis (HR = 0.82, 95% CI: 0.79–0.84, $p < 0.001$). Similarly, Yahagi *et al.*[30] analyzed 15 studies and reinforced the survival advantage of LCC (HR = 1.14, 95% CI: 1.06–1.22, $p < 0.01$).

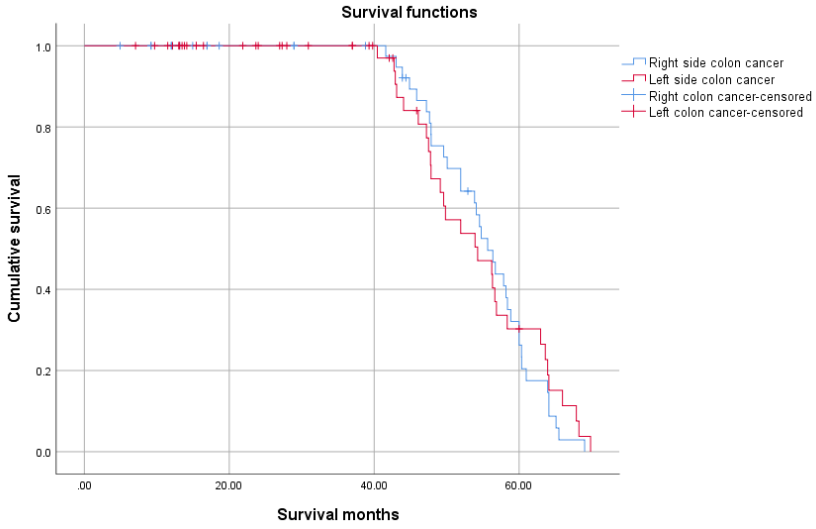


Figure 1. Overall survival by tumor location/family history

Table 8. Multivariable Cox proportional hazards model for overall survival duration

Variable	HR	95% CI	*p*-value
Age, years	1.01	0.99–1.03	0.394
T protein, g/L	1.01	0.97–1.06	0.559
Family history			
No	1.00	Reference	
Yes	2.44	1.16–5.12	0.018
Smoking			
No	1.00	Reference	
Yes	1.08	0.53–2.23	0.828
TMN stages			
≤Stage II	1.00	Reference	
≥Stage III	0.95	0.46–1.95	0.878
Blood loss			
≤110 mL	1.00	Reference	
≥110 mL	0.52	0.27–1.00	0.050
Post-operative complication			
No	1.00	Reference	
Yes	2.52	0.70–9.12	0.160
Post-operative liver occurrence			
No	1.00	Reference	
Yes	0.77	0.18–3.33	0.726
Colon cancer			
RCC	1.00	Reference	
LCC	1.11	0.61–2.02	0.742

Note: The Cox proportional regression test was analyzed
Abbreviations: CI: Confidence interval; HR: Hazard ratio; LCC: Left colon cancer; RCC: Right colon cancer; TMN: Tumor, nodes, metastasis.

Conversely, several studies have reported favorable outcomes in RCC across certain disease stages. Weiss *et al.*[31] evaluated 53,801 patients with stage I–III CRC and found negligible differences in overall prognosis when all stages were aggregated. However, subgroup analysis revealed better survival in stage II RCC patients (HR = 0.92, 95% CI: 0.87–0.97, $p = 0.001$), while stage III RCC was associated with poorer prognosis (HR = 1.12, 95% CI: 1.06–1.18, $p = 0.001$). Warschkow *et al.*,[32] analyzing data from nearly 92,000 patients, reported improved five-year overall and cancer-specific survival in early-stage (I and II) RCC. Similarly, Yang *et al.*[33] found that RCC conferred better disease-specific survival in stages I and II but worse outcomes in stage III. Conversely, He *et al.*[34] observed that although LCC had higher rates of liver and lung metastases, the prognosis was better than that of RCC. Overall, published findings remain inconsistent, with some studies emphasizing worse prognoses for RCC, while others suggest stage-dependent differences or no significant prognostic impact. The heterogeneity among study populations, disease stages, and methodologies underscores the complexity of tumor laterality as a prognostic factor.

4.2. Family history and overall survival

Notably, multivariable Cox regression analysis identified a positive family history of cancer as an independent predictor of poorer OS in this Mongolian cohort. While family history is widely recognized as a significant risk factor for CRC, its impact on prognosis remains inconsistent across studies.[35] Most large-scale investigations have been conducted in Western populations, whereas available data from Asian cohorts are more limited and reflect distinct genetic backgrounds, environmental exposures, and healthcare practices.[26,36] Several reports have suggested improved survival among patients with a familial history of CRC, potentially attributable to earlier diagnosis through increased screening and heightened disease awareness. In contrast, meta-analyses of Asian populations and large cohort studies from Korea have consistently demonstrated elevated CRC incidence among individuals with affected relatives.[26,35] Variability in genetic susceptibility, lifestyle factors, access to screening programs, and duration of follow-up likely contributes to differences in observed outcomes. The molecular tumor subtype further modifies the prognostic implications of familial risk. Jansson-Knodell *et al.*[37] reported a significant interaction between deficient mismatch repair status and family history of CRC in first-degree relatives, with an increasing number of affected relatives associated with improved OS.

In addition, disease stage at diagnosis, tumor location, and the number of affected relatives are known to influence prognosis and may vary substantially between populations. These findings suggest that family history should not only guide CRC screening strategies but should also be incorporated into prognostic assessment and individualized follow-up planning, particularly in Mongolia, where survival outcomes remain poor.

4.3. Molecular and clinical heterogeneity by tumor sidedness

The molecular landscape of CRC shows distinct differences across tumor locations. RCC is characterized by the "serrated" pathway phenotype, with high concordance among high microsatellite instability (MSI-H), high CpG island methylator phenotype, and *BRAF* V600E mutations.[38,39] These features are clinically associated with elderly female patients and, despite the early-stage survival benefit of MSI-H, contribute to the poor prognosis observed in metastatic RCC.[40] Conversely, LCC, predominantly involving the sigmoid colon and rectum, is driven primarily by the Kirsten rat sarcoma viral oncogene homolog (KRAS) pathway and chromosomal instability, and generally results in superior survival outcomes in metastatic settings compared with RCC.[41]

Geographic variability further nuances these profiles. While the fundamental molecular drivers are globally consistent, the frequency of specific mutations varies; notably, *BRAF* mutations are significantly less common in Asian cohorts than in Western populations.[42-44] However, KRAS mutations remain a dominant driver of metastasis globally, particularly in liver metastases.[45] The association of proximal colon tumors with high-degree methylation (CIMP-H) and *BRAF* mutations underscores the need for location-specific molecular profiling to guide prognosis and therapeutic strategy.

4.4. Prospective advances and future directions in colorectal cancer treatment

Advances in omics-based technologies have improved the understanding of CRC biology by revealing molecular mechanisms underlying tumor initiation and progression. Integrated analyses across genomic, transcriptomic, proteomic, and metabolomic platforms have identified key driver mutations, regulatory non-coding RNAs, and clinically relevant molecular subtypes associated with prognosis and therapeutic response.[46-48] Several biomarkers, including miR-21, miR-92a, and specific long non-coding RNAs, have shown promise for early detection and risk stratification.[46] In parallel, metabolic reprogramming and interactions between tumor cells and the gut microbiota have emerged as factors associated with disease progression.[49,50]

Despite improvements in surgical techniques and systemic therapies, therapeutic resistance and disease recurrence remain ongoing challenges in CRC management. Nearly half of patients ultimately develop recurrent or treatment-resistant disease, highlighting the need for additional therapeutic strategies. Emerging approaches such as immune modulation, RNA-based therapies, probiotic interventions, and biomarker-guided treatments are increasingly being explored.[51-53] Plant-derived bioactive compounds have been investigated for their anticancer activity and relatively favorable toxicity profiles.[54-56] Drimenol, a sesquiterpene alcohol, has demonstrated antiproliferative effects in colon cancer cells by inhibiting topoisomerase I and suppressing β-catenin signaling.[57] Similarly, extracts from *Polygonum minus* have exhibited cytotoxic activity across several CRC cell lines.[2,54,58]

In addition, combinatorial phytochemical strategies involving compounds such as isothiocyanates, carotenoids, quinones, and alkaloids have demonstrated synergistic tumor suppression and reduced chemoresistance by modulating key oncogenic signaling pathways.[55]

Nanotechnology-based therapies represent another rapidly advancing area. Metal nanoparticles, particularly gold and silver nanoparticles, have shown potential for targeted drug delivery, enhanced imaging, and increased cytotoxicity against tumor cells.[59]

Recent developments in nanoparticle drug delivery systems have further improved therapeutic precision. Calcium carbonate nanoparticles have emerged as promising carriers due to their biocompatibility, pH-responsive drug release, and targeted delivery capacity within the acidic tumor microenvironment.[60-62] Drug-loaded nanoparticle formulations have demonstrated enhanced anticancer efficacy, reduced toxicity to normal tissues, and suppression of tumor proliferation and migration by modulating critical molecular targets.[54,63]

These advances reflect increasing interest in personalized, multi-targeted therapeutic strategies for CRC. Further translational research is needed to validate these approaches and facilitate their integration into clinical practice.

Our study is limited by its small sample size, which constrains statistical power and may affect the robustness and generalizability of the findings. Larger, prospective studies are needed to definitively elucidate the prognostic significance of tumor location.

5. Conclusion

In this cohort, tumor localization was not associated with OS among patients undergoing curative resection for colon cancer. Notably, a positive family history of cancer emerged as an independent predictor of survival, underscoring the importance of genetic and familial factors in prognosis. Further large-scale investigations are warranted to clarify the prognostic implications of tumor sidedness and familial predispositions.

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Conflict of interest

The authors declare no conflict of interest.

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Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of the Mongolian National University of Medical Sciences (Ulaanbaatar, Mongolia) approved the study (9 March 2020: No 20/03-D02). All methods were carried out in accordance with relevant guidelines and regulations. The requirement for informed consent to participate was waived by the Institutional Review Board due to the retrospective nature of the study and the use of anonymized patient data.

Consent for publication

Informed consent to participate was not obtained because this study was a retrospective analysis of anonymized data.

Availability of data

Data are available from the corresponding author upon reasonable request.

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