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ORIGINAL ARTICLE

Comparison of clinicopathological and survival features of right and left colon cancers

Kaan Helvaci[1], Emrah Eraslan[2], Fatih Yildiz[2], Gulnihal Tufan[2], Umut Demirci[2], Omur Berna Oksuzoglu[2], Ulku Yalcintas Arslan[2]

[1]Department of Medical Oncology, Hitit University Erol Olcok Training and Research Hospital, Corum, Turkey; [2]Department of Medical Oncology, Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Ankara, Turkey.

Summary

Purpose: *Right-sided colon cancers (RCCs) and left-sided colon cancers (LCCs) have different embryological, epidemiological, physiological, pathological, genetic, and clinical characteristics, which result in differences in the course, prognosis, and outcome of disease. This study aimed to compare RCCs and LCCs regarding clinicopathological and survival characteristics.*

Methods: *The present retrospective study included data of patients who were followed-up and treated for colon cancer from 2008 through 2017. Rectosigmoid, descending colon, and splenic flexure tumors were considered LCC, whereas hepatic flexure and ascending colon tumors were considered RCC. Tumors were staged according to the American Joint Committee on Cancer classification.*

Results: *The study included 1725 patients (female, 58.7%) having colon cancer with a mean age of 64±12 years. Of the patients, 83.2% (n=1436) had LCC and 16.8% (n=289) had RCC. The rate of patients aged ≥65 years and the rate of patients with a family history of colon cancer were higher in the RCC patients. The rate of metastatic patients was 29.1% in the RCC group and 23.2% in the LCC group (p=0.087). The median follow-up period was 18 months in the RCC group and 23 months in the LCC group (p=0.011). Although the median survival time was higher in the LCC group (62 vs. 43 months), no significant difference was determined between the RCC and LCC groups in terms of survival.*

Conclusions: *There are numerous clinicopathological differences between RCC and LCC and these differences are reflected in prognostic and survival differences among certain subgroups.*

Key words: *right-sided colon cancer, left-sided colon cancer, survival, RAS*

Introduction

Colorectal cancer is the third most common cancer and the fourth leading cause of cancer-related deaths worldwide [1]. Colon cancers are molecularly and morphologically quite heterogeneous neoplasms. They are grouped as right-sided (proximal) or left-sided (distal) according to the localization of the primary tumor. RCCs and LCCs have different embryological, epidemiological, physiological, pathological, genetic, and clinical characteristics, which result in differences in the course, prognosis, and outcome of disease [2]. Therefore, it seems reasonable for colon cancers to be grouped and evaluated as RCC and LCC [3]. The present study aimed to investigate the differences between RCC and LCC in terms of clinicopathological and survival characteristics

Corresponding author: Kaan Helvaci, MD. Department of Medical Oncology, Hitit University Erol Olcok Training and Research Hospital, Cepni Mahallesi, İnonu Cd. No:176, 19200 Corum, Turkey.
Tel: +90 5052428179, Email: kaanhelvaci@gmal.com
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Methods

In this study, data of all patients followed-up and treated for colon cancer in the Medical Oncology Clinic of Ankara Oncology Hospital from 2008 through 2017 were retrospectively reviewed. Demographic and clinical information of patients was retrieved from the hospital records. All patients who had been diagnosed with colorectal adenocarcinoma and had documented tumor localization and accessible data were included in the analysis.

Although transverse colon is considered in the RCC group [4], patients with transverse colon cancer were excluded as the origin and the beginning and ending of transvers colon was not clear. In total, there were 1811 patients with accessible data. Tumor localization was transverse colon in 86 patients and these patients were excluded; finally, 1725 patients were analyzed.

In the present study, rectosigmoid, descending colon, and splenic flexure tumors were considered LCC, whereas hepatic flexure and ascending colon tumors were considered RCC. Tumors were staged according to the American Joint Committee on Cancer (AJCC) classification [5].

Statistics

Data were analyzed using the PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as numbers and percentages for categorical variables and as mean, standard deviation, median, percentile 25 (Q1) and percentile 75 (Q3) for numerical variables. Chi-square analysis was used for the comparison of categorical variables between the groups. Comparison of the numerical variables between two groups was performed by the Mann-Whitney U test when the condition of normal distribution was not provided. Survival analysis was carried out using Kaplan-Meier method and differences in survival between the study groups were assessed with Log-rank test. A p value <0.05 was considered statistically significant.

Results

In this study, 1725 patients with colon cancer were included, of whom 1013 (58.7%) were male and 712 (41.3%) female. The mean age of the patients was 64±12 years (range, 24-99). Of the patients, 83.2% (n=1436) had LCC and 16.8% (n=289) RCC. General characteristics of the patients are summarized in Table 1. Both study groups were similar in terms of sex distribution. The rate of patients aged ≥65 years and the rate of patients with a family history of colon cancer were higher in the RCC patients.

Clinical and histopathological characteristics of the patients are presented in Table 2. In the RCC group, the rates of patients with the Eastern Cooperative Oncology Group (ECOG) score of 2, having diagnostic stage of II or IV, with a pathological diagnosis of signet-ring cell or mucinous adenocarcinoma, with poorly differentiated tumor, having perineural invasion, and with BRAF mutation were significantly higher than those in the LCC group. Moreover, the rate of patients with positive surgical border in the RCC group was significantly lower than that in the LCC group.

The rate of metastatic patients was 29.1% in the RCC group and 23.2% in the LCC group with no difference between the two groups in terms of the presence and location of metastasis. The rate of patients receiving adjuvant radiotherapy alone in the RCC group was significantly lower than that in the LCC group, as was expected.

The follow-up period was median (Q1-Q3) 18 months (9-35 months) in the RCC group and 23 months (10-43 months) in the LCC group (p=0.011). Mortality rate during follow-up was 36.8% (n=105)

Table 1. General patient characteristics

Characteristics	*RCC (n=289)*	*LCC (n=1436)*	*OR*	*CI*	*p*
Sex, n (%)					
Male	166 (57.4)	847 (59.0)	1 (ref.)		
Female	123 (42.6)	589 (41.0)	0.939	0.727-1.212	0.627*
Age, year, median (Q1-Q3)	67 (58-74)	65 (57-73)			0.066*
Age group, years, n (%)					
<65	123 (42.6)	709 (49.4)			
≥65	166 (57.4)	727 (50.6)	0.760	0.589-0.981	**0.035***
Family history of colon cancer, n (%)					
No	219 (82.6)	1127 (87.8)	1 (ref.)		
Yes	46 (17.4)	156 (12.2)	0.659	0.46-0.944	**0.023***

* Chi-square test; RCC: Right-sided colon cancers, LCC: Left-sided colon cancers, OR: Odds ratio, CI: Confidence interval. Bold numbers denote statistical significance.

in the RCC group and 33.1% (n=471) in the LCC group (p=0.226).

Although median survival time was higher in the LCC group (62 vs. 43 months), no significant difference was determined between the RCC and LCC groups in terms of survival (Figure 1).

Evaluating the survival rates according to the stage, no significant difference was determined between the RCC and LCC groups for stage 0/I/II (n=617), stage III (n=662), and stage IV (n=428) patients. When the patients who had undergone primary+metastasis removal (n=163) were evaluated for survival, the survival was significantly lower in the RCC than in the LCC group (Figure 2).

With regard to the patients who were KRAS-, NRAS- and BRAF-wild (n=62), survival was significantly lower in the RCC group than in the LCC group (median 14 vs 52 months, p<0.001) (Figure 3).

Considering the metastatic patients who received additional anti-epidermal growth factor receptor (EGFR) antibody in their first-line treatment (n=133), the survival was significantly lower in the RCC group than in the LCC group (median 18 vs 34 months, p=0.003) (Figure 4).

Table 2. Clinical and histopathological patient characteristics

Characteristics	*RCC n (%)*	*LCC n (%)*	*OR*	*CI*	*p*
ECOG performance score					
0	24 (8.3)	168 (11.7)	1 (ref.)		
1	211 (73.0)	1050 (73.1)	0.711	0.452-1.118	0.139*
2	44 (15.2)	167 (11.6)	0.542	0.315-0.932	**0.027***
3	10 (3.5)	51 (3.6)	0.729	0.327-1.624	0.439*
Pathological diagnosis					
Adenocarcinoma	238 (82.4)	1323 (92.1)	1 (ref.)		
Signet-ring cell	7 (2.4)	8 (0.6)	0.206	0.074-0.572	**0.002***
Mucinous adenocarcinoma	44 (15.2)	105 (7.3)	0.429	0.294-0.627	**<0.001***
Diagnostic stage					
0	0 (0.0)	3 (0.2)	-		
I	14 (4.8)	143 (10.0)	1 (ref.)		
II	107 (37.0)	362 (25.2)	0.331	0.184-0.597	**<0.001***
III	83 (28.7)	584 (40.7)	0.689	0.38-1.249	0.220*
IV	85 (29.4)	344 (24.0)	0.396	0.218-0.721	**0.002***
Lymphovascular invasion	34 (16.0)	119 (12.1)	0.723	0.478-1.093	0.124*
Perineural invasion	46 (21.7)	157 (16.0)	0.688	0.476-0.994	**0.046***
Grade of differentiation					
Well differentiated	41 (23.0)	262 (32.8)	1 (ref.)		
Moderately differentiated	113 (63.5)	494 (61.8)	0.684	0.464-1.008	0.055*
Poorly differentiated	24 (13.5)	43 (5.4)	0.280	0.154-0.510	**<0.001***
Cancer cell in the surgical border					
Negative	274 (99.6)	1298 (96.9)	1 (ref.)		
Positive	1 (0.4)	41 (3.1)	8.655	1.185-63.188	**0.033***
KRAS					
Wild	47 (56.0)	231 (55.5)	1 (ref.)		
Mutant	37 (44.0)	185 (44.5)	1.017	0.634-1.631	0.943*
NRAS					
Wild	27 (87.1)	122 (80.8)	1 (ref.)		
Mutant	4 (12.9)	29 (19.2)	1.605	0.521-4.944	0.410*
BRAF					
Wild	14 (70.0)	70 (94.6)	1 (ref.)		
Mutant	6 (30.0)	4 (5.4)	0.133	0.033-0.535	**0.004***

* Chi-square test; RCC: Right-sided colon cancer, LCC: Left-sided colon cancer, OR: Odds ratio, CI: Confidence interval, ECOG: Eastern Cooperative Oncology Group. Bold numbers denote statistical significance

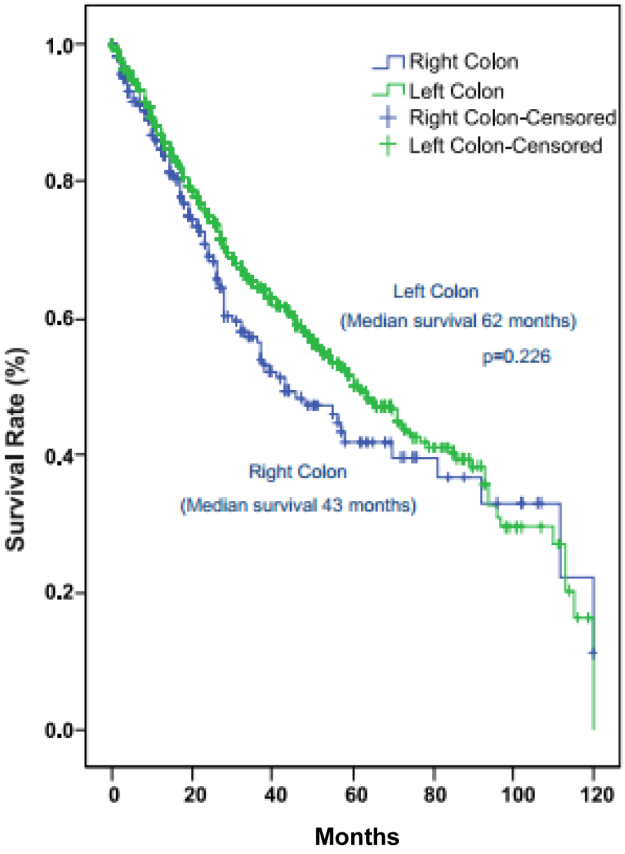

Figure 1. Survival curve of all study patients.

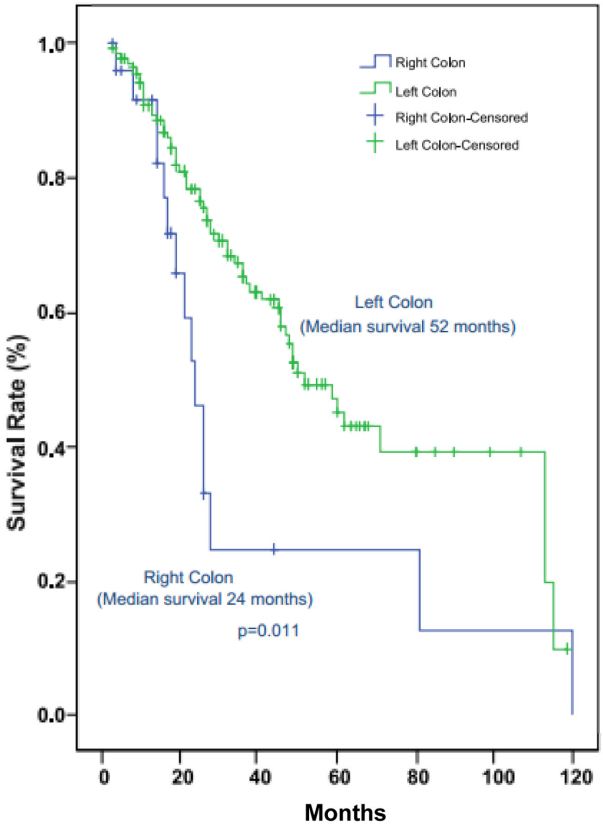

Figure 2. Survival curve in the patients who had undergone primary + metastasis removal.

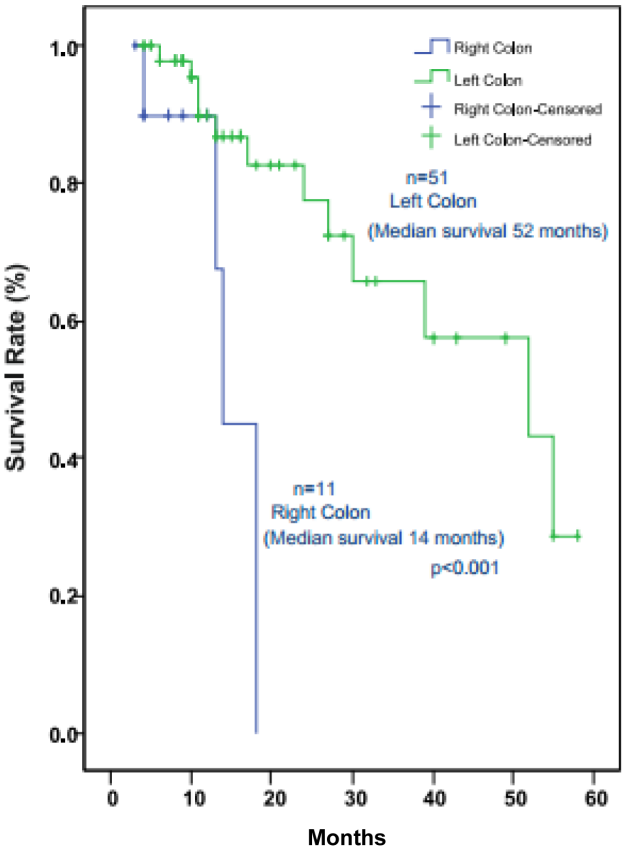

Figure 3. Survival curve in the patients who were KRAS-, NRAS-, and BRAF-wild.

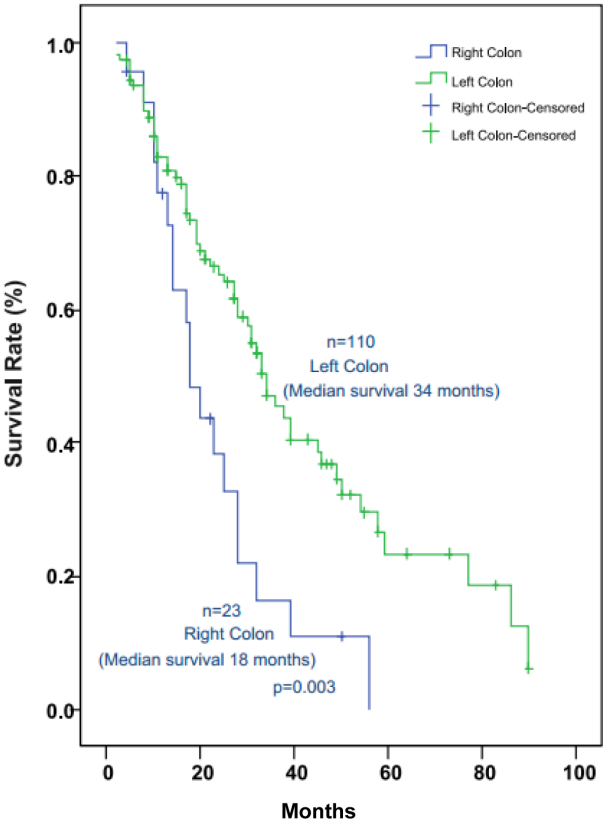

Figure 4. Survival curve in the patients who were metastatic and received additional anti-epidermal growth factor receptor in the first-line treatment.

Discussion

Colon cancers display diverse clinicopathological characteristics according to their localizations. Many earlier studies have reported that RCC patients are older [6-13] and are more likely to be female [7,9-13]. Besides, there are studies reporting no difference between RCC and LCC patients in terms of age and sex [14-16]. In the present study, RCC and LCC groups were similar in terms of sex; however, the rate of patients aged ≥65 years was higher in the RCC group than that in the LCC group.

In several studies, it has been reported that the tumor size is larger [12,15,16], the rate of advanced-stage patients is higher [6-8,15,16], and the rate of patients with poorly differentiated tumor is higher [6-8,10,12,15,16] among RCC patients as compared to LCC patients. In the present study, likewise, the rate of stage-IV patients and the rate of patients with poorly differentiated tumors were higher in the RCC group than in the LCC group.

Perineural invasion has been reported to be one of the independent risk factors for locoregional recurrence of colon cancers [17]. While some studies have reported no difference between RCC and LCC patients in terms of perineural invasion [13,15,16], some others have reported higher perineural invasion in those with RCC [8]. Similarly, in the present study, perineural invasion was more prevalent in the RCC group.

Lymphovascular invasion has been found to be higher in RCC patients in some studies [6,8,16], whereas some other studies have reported no difference between RCC and LCC patients in terms of lymphovascular invasion [13,15]. In the present study, there was also no difference between the RCC and LCC groups in terms of lymphovascular invasion.

It has been reported that 5-year survival rate in colorectal cancers shows increasing tendency in the developed countries [18]. While 5-year relative survival rate in colorectal cancers reaches up to 65% in the developed countries, it remains below 50% in the low-income countries [19]. The primary tumor localization, being either right-sided or left-sided, has an impact on prognosis and survival. The risk of recurrence is higher in patients with RCC than in those with LCC [14,17]. Although studies comparing RCC with LCC have reported different outcomes, reviews and meta-analyses that reviewed many studies have revealed that RCC is associated with poorer prognosis and lower survival rate as compared to LCC [20-22]. Gervaz et al [7] reported that 5-year survival rate was similar between RCC and LCC patients (47% and 49%, respectively) in the early 1980s; however, LCC was reported to be associated with better outcomes compared with RCC nearly three decades later (75% vs. 60%). Brungs et al [9] reported 5-year overall survival rate 70% in LCC and 66% in RCC; while the difference was significant in the univariate analysis, it was not significant in the multivariate analysis. Lim et al [16] found 5-year overall survival significantly better in LCC than in RCC (88.7% and 82.1%, respectively). Cienfuegos et al [13] determined no difference between LCC and RCC patients in terms of 5-year overall survival rate (90.8% and 90.6%, respectively). In the present study, 5-year survival rate was 42% in the RCC group and 51.6% in the LCC group. The median survival time was 43 months in the RCC group and 62 months in the LCC group. No statistically significant difference was determined between the RCC and LCC groups in terms of survival rate (p=0.060).

It has been reported that the stage of cancer is correlated with survival and that 5-year cause-specific survival rates for stage I to stage IV patients are 93.6%, 84.8%, 68.3%, and 13.1%, respectively [12]. Hu et al [6] reported the median overall survival to be 67 months for RCC patients and 68 months for LCC patients. While there was no difference between RCC and LCC patients in terms of 5-year overall survival rate for those with stage I/II (91.4% and 88.6%, respectively; p=0.819), survival was poorer in RCC patients for those with stage III (66.1% vs 75.4%; p=0.010) and stage IV (27.8% and 38.5%; p=0.020). Qin et al [14] found no significant difference between RCC and LCC patients in terms of 5-year overall survival, whereas they reported poorer prognosis in RCC patients for those with stage III. In the study by Karim et al [11], the stage I, II and III patients were evaluated and no significant difference was determined between RCC and LCC in terms of long-term survival rate. In the present study, evaluation of survival according to the stage revealed no statistically significant difference between the RCC and LCC groups for stage 0/I/II, stage III, and stage IV.

Distant metastasis is present in nearly 20% of newly diagnosed colorectal cancer patients, the majority of which is localized in the liver [19]. In the present study, 29.1% of the RCC patients and 23.2% of the LCC patients were metastatic. There was no difference between the two groups in terms of the presence or location of metastasis. Evaluating the patients treated by the removal of primary+metastasis (n=163) in terms of survival, survival was found to be significantly lower in the RCC group than that in the LCC group. The median survival time was 24 months for the RCC group and 52 months for the LCC group.

The same treatment can provide different benefits in RCCs and LCCs [23]. Studies have investigated the benefit of EGFR-targeted therapies (anti-EGFR therapy) in metastatic colon cancers [23,24]. In the present study, evaluation of the metastatic patients receiving additional anti-EGFR therapy in their first-line treatment (n=133) demonstrated significantly lower survival rate in the RCC group compared with the LCC group. The median survival was 18 months for the RCC group and 34 months for the LCC group.

Potential prognostic effects of KRAS, NRAS, and BRAF mutations have been reported in patients with advanced-stage colon cancer [23,25,26]. Presence of genetic mutations in patients with colorectal cancer plays an important role also in the choice of treatment [24]. Ulivi et al [27] determined no difference between the RCC and LCC patients in terms of the frequency of KRAS and NRAS mutations. Nevertheless, the rate of patients BRAF mutations was significantly higher in RCC as compared to LCC (15.7% and 2.8%, respectively; p=0.017). Likewise, in the present study, no difference was determined between the RCC and LCC groups in terms of KRAS and NRAS mutations; however, the rate of patients with BRAF mutation was significantly higher in the RCC group than in the LCC group (30% and 5.4%, respectively; p=0.004). With regard to the patients who were KRAS-, NRAS-, and BRAF-wild (n=62), the survival was significantly lower in the RCC group than that in the LCC group. The median survival was 14 months for the RCC group and 52 months for the LCC group.

In conclusion, there are numerous clinicopathological differences between RCC and LCC and these differences are reflected in prognostic and survival differences among certain subgroups.

Conflict of interests

The authors declare no conflict of interests.

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