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RESEARCH ARTICLE

Comparison of Oncological Outcomes After Curative Resection for Right-side Colon Cancer and Left-side Colon Cancer: a Retrospective Observational Study

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ABSTRACT

Aim: This study aims to compare clinicopathological findings and oncological outcomes after curative resection between right-side colorectal carcinoma (RCC) and left-side colorectal carcinoma (LCC).

Method: A retrospective review of 209 patients who underwent elective surgery for right and left colon cancer between January 2013 and October 2022 was conducted. After applying the exclusion criteria, 182 patients were included. The patients were grouped based on embryological development: right side (cecum, ascending colon, hepatic flexure, and proximal transverse colon) and left side (distal transverse colon, splenic flexure, descending colon, and sigmoid colon). Clinicopathological features, lymph node removal, and oncological outcomes were compared. Statistical analyses were performed using the chi-squared test, Fisher's exact test, Mann-Whitney U test, the Kaplan-Meier method, and Cox regression analysis.

Results: Among the 182 patients, 108 (59.3%) had RCC, and 74 (40.7%) had LCC. No significant differences were found between the groups regarding age, gender, body mass index, carcinoembryonic antigen value, tumor size, T/N stage, lymphovascular/perineural invasion, positive lymph nodes, and hospital stay. However, more lymph nodes were removed in RCC cases ($p<0.0001$). Oncologically, 32.4% of the patients with RCC and 29.7% of the patients with LCC died during follow-up, with no difference in mean survival. Multivariate analysis identified age and tumor size as prognostic factors for 5-year survival.

Conclusion: Despite clinical and pathological differences between RCC and LCC, no significant difference was observed in 2- and 5-year survival. Early diagnosis and personalized treatment remain crucial for both cancer types. Further large-scale studies are recommended.

Keywords: Colon cancer, curative resection, prognosis

Introduction

Colorectal cancer (CRC) is the second most common cancer worldwide and has a high mortality rate, especially in more advanced stages.[1] According to the American Joint Committee on Cancer, radical surgical resection is the standard treatment for stages I-III CRC, with postoperative adjuvant chemotherapy also being applied to patients with high-risk stages II and III colon cancer.[2]

There are embryological origin, anatomical, histological, genetic, and immunological differences between right-side colorectal carcinoma (RCC) and left-side colorectal carcinoma (LCC). During embryological development, the right-side colon (cecum, ascending colon, and proximal two-thirds of the transverse colon) develops from the midgut, whereas the left-side colon (distal third of the transverse colon, descending colon, and sigmoid colon) develops from the hindgut.[3]

In recent years, there has been increasing interest in distinguishing between RCC and LCC because these two types have different presentations, treatments, and prognoses.[4] Studies have shown that RCC and LCC have different clinical and biological characteristics and are currently considered two separate entities.[5]

This study aims to analyze the clinicopathological findings and oncological outcomes between RCC and LCC after curative resection.

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Materials and Methods

A total of 209 patients who underwent elective surgery for RCC and LCC between January 2013 and October 2022 were included in this study. Patients with rectal cancer, RCC or LCC who underwent surgery despite having metastatic disease (9 patients), patients with T1 depth of invasion (1 right-sided, 10 left-sided) (the reason for excluding T1 tumors is their expected long survival, which would not impact this study), patients with fewer than 12 lymph nodes removed (3 right-sided, 4 left-sided), and those who underwent emergency or urgent operations were excluded from the study. The evaluation was conducted on a total of 182 patients (Figure 1).

Patients with colon tumors were divided into right-sided and left-sided groups according to their embryological development sites. Right-sided colon cancers included the cecum, ascending colon, hepatic flexure, and proximal transverse colon cancers, whereas left-sided colon cancers included distal transverse colon, splenic flexure, descending colon, and sigmoid colon cancers. Proximal transverse colon cancers were included with hepatic flexure cancers, and distal transverse colon and splenic flexure cancers were included with descending colon cancers.

This study was approved by the Clinical Research Ethics Committee of University of Health Sciences Turkey, Koşuyolu Yüksek İhtisas Research and Training Hospital (approval number: 2020.4/23-325, dated: 08.05.2020), and it adhered to the ethical standards expected for medical research involving human participants.

Statistical Analysis

The normality of numerical data was assessed using the Kolmogorov-Smirnov test. Variables between the two groups (RCC and LCC) were analyzed using the chi-squared test, Fisher's exact test, and the Mann-Whitney U test. Kaplan-Meier analysis was used to evaluate differences between the groups in terms of 2-year, 5-year, and overall survival. Additionally, prognostic factors affecting 2-year, 5-year, and follow-up survival were assessed using Cox regression analysis with the stepwise procedure. SPSS 22 software was used for the statistical analysis, and the level of statistical significance was set at an alpha of 0.05.

Results

The average follow-up duration for the patients included in this study was 62.11±36.84 months for right-sided colon cancers and 66.45±31.95 months for left-sided colon cancers.

Clinical and Pathological Characteristics:

A total of 182 patients were included in the study, with 108 (59.3%) having RCC and 74 (40.7%) having LCC. The main clinicopathological characteristics of the patients are shown in Table 1. There were no statistical differences between the two groups in terms of age, gender, body mass index, initial carcinoembryonic antigen value, tumor size, T/N stage, lymphovascular invasion (LVI), perineural invasion (PNI), number of positive lymph nodes, Clavien-Dindo classification, and hospital stay duration. However, there was a statistical difference in the total number of lymph nodes removed ($p<0.0001$), with an average of 29±14 lymph nodes removed in right-sided colon cancers compared with 23±11 in left-sided colon cancers.

Oncological Outcomes

At the end of follow-up, 35 (32.4%) of the patients with RCC and 22 (29.7%) of the patients with LCC had died. The average survival time was 96.286±4.876 months for RCC and 99.479±5.703 months for LCC, with no difference in 2-year, 5-year, and overall survival between the groups (Table 2, Figure 2).

Univariate and Multivariate Analysis of Prognostic Factors

Potential prognostic factors for 2-year, 5-year, and overall survival, including gender, age, tumor size, tumor invasion depth, total number of lymph nodes removed, number of positive lymph nodes, PNI, and vascular invasion, were investigated using multivariate Cox regression analysis (Tables 3 and 4). Univariate and multivariate analyses did not identify any prognostic factors for 2-year follow-up. In the 5-year follow-up, univariate analysis identified age, tumor size, number of positive lymph nodes, and PNI ($p=0.001$, $p=0.028$, $p=0.030$, $p=0.034$) as prognostic factors, whereas multivariate analysis identified age and tumor size ($p=0.001$, $p=0.033$) as prognostic factors. For overall survival at the end of follow-up, univariate analysis identified age, number of positive lymph nodes, and PNI ($p=0.003$, $p=0.025$, $p=0.006$) as prognostic factors, whereas multivariate analysis identified only age ($p=0.005$) as a prognostic factor.

Discussion

CRC is one of the most common cancers worldwide. In 2018, deaths related to CRC accounted for 5.8% of all deaths.[6] It is now known that RCC and LCC differ by gender, age, and geographic region and should be considered as two distinct entities. Numerous studies have explored these differences, including pathophysiology and related genetic pathways, age and symptomatology at presentation, stage at presentation, prognosis, chemotherapy regimens, premalignant lesions, and risk factors.[7,8]

In the study by Saltzein and Behling[9] it was found that patients with RCC were more likely to be older women. Similarly, older studies also reported that RCC was more frequent in older adults and women.[10] However, in our study, men were more predominant, although this was not statistically significant.

Recent studies, in line with our findings, also report no significant difference in terms of age and gender between RCC and LCC.[11] In our cohort, the mean age for RCC was 62.14 years, whereas for LCC, it was 64.14 years.

One of the most notable distinctions between RCC and LCC is their difference in T stage at diagnosis. RCC is often diagnosed at more advanced stages, whereas LCC tends to be detected earlier. This may be due to the larger lumen of the right colon, which leads to a delayed onset of symptoms.[12] As the T stage advances, the prognosis worsens for both RCC and LCC; however, this progression tends to be more rapid in RCC. Several studies have shown that tumor penetration and peritoneal dissemination rates are higher in the T3 and T4 stages of RCC, which may contribute to higher postoperative recurrence rates.[13] These findings underscore the need for careful follow-up and tailored treatment strategies for patients with RCC.[14] In our study, however, no significant differences in the T stage between RCC and LCC were observed.

LVI and PNI serve as important prognostic markers in colon cancer.[15] LVI, which indicates the spread of tumor cells to the lymphatic and blood vessels, is reported to be more common in RCC, suggesting a higher potential for distant dissemination and metastasis in these tumors.[16] PNI, which refers to the invasion of tumor cells around nerve sheaths, usually occurs at more advanced stages and has been shown to be more frequent in RCC compared with LCC. Both LVI and PNI are associated with a poorer prognosis and should be considered when planning postoperative treatment strategies.[17] In our study, we evaluated these factors but found no statistically significant differences between RCC and LCC.

The total number of lymph nodes removed during surgery is a critical prognostic factor in CRC. Several studies from the

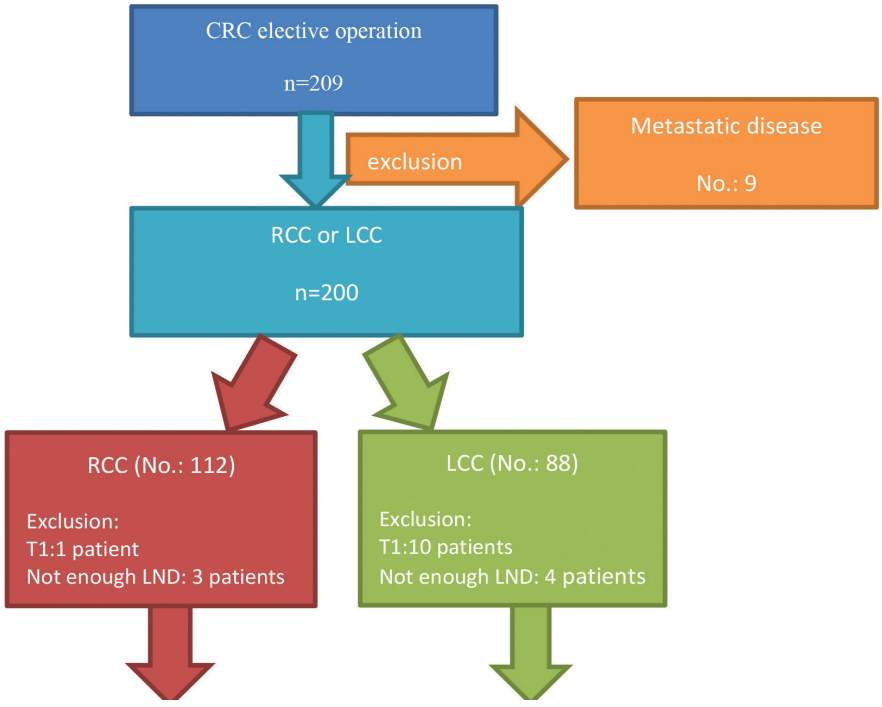

Figure 1. Flowchart of inclusion and exclusion criteria for study participants

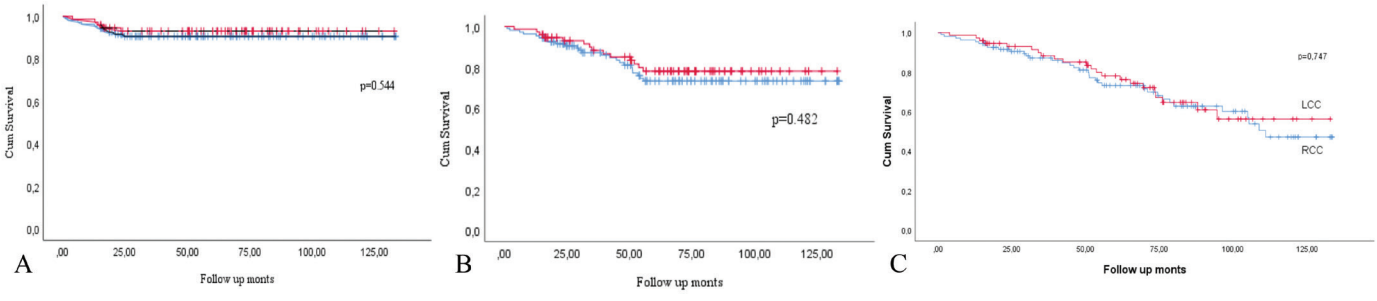

Figure 2. Comparison of survival in patients with right- or left-colon cancer. A) 2 years, B) 5 years, C) overall
RCC: Right-side colorectal carcinoma, LCC: Left-side colorectal carcinoma

Table 1. Dermographic and clinical features

	Right	Left	p
Cancer location (%)			
Ceacum			
Right colon			
Hepatic flexura	40 (37)		
Left colon	36 (33.3)	24 (67.6)	
Sigmoid colon	32 (29.6)	50 (32.4)	
Sex (%)			
Male	62 (57.4)	46 (62.2)	0.521
Female	46 (42.6)	28 (37.8)	
T stage (%)			
T2	7 (6.)	6 (8.1)	0.786
T3	85 (78.7)	55 (74.3)	
T4	16 (14.8)	13 (17.6)	
N stage (%)			
N0	65 (60.2)	47 (63.5)	0.843
N1	32 (29.6)	19 (25.7)	
N2	11 (10.2)	8 (10.8)	
Stage (%)			
I	5 (4.6)	4 (5.4)	0.972
II	66 (61.1)	45 (60.8)	
III	37 (34.3)	25 (33.8)	
Lymphovascular invasion			
No	71 (65.7)	47 (63.5)	0.757
Yes	37 (34.3)	28 (36.5)	
Perinoral invasion			
No	82 (75.9)	55 (74.3)	0.806
Yes	26 (24.1)	19 (25.7)	
Age (mean ± SD, range)	62±14 (24-88)	64±14 (31-83)	0.214
Tumor size (mean ± SD, range)	4.8±2.3 (1.8-12.5)	5±3.7 (1.1-31)	0.939
CEA	24.15±127.06 (0.2-1062)	7.94±15.93 (0.40-94)	0.861
BMI	26.92±4.46 (19-38.1)	27.06±4.36 (16.5-36.3)	0.733
Total number of lymph nodes removed	29±14 (12-90)	23±11 (12-58)	0.000
Number of positive lymph nodes	2±4 (0-21)	2±4 (0-17)	0.570
Clavian dindo			
I	21 (63.6)	12 (36.4)	0.983
II	33 (62.3)	20 (37.7)	
III	2 (66.7)	1 (33.3)	
Length of hospital stay	9±4 (4-41)	9±4 (5-22)	0.889

SD: Standard deviation, BMI: Body mass index, CEA: Carcinoembriogenic antigen

Table 2. Evaluation by Kaplan-Meier analysis according to right-sided colon cancer or left-sided colon cancer status

	2 years		5 years		Overall	
	SE	95% CI	SE	95% CI	SE	95% CI
RCC	122.094±3.467	(115.298-128.890)	106.811±4.748	(97.506-116.117)	96.286±4.876	(86.728-105.843)
LCC	124.597±3.572	(117.596-131.597)	111.347±5.138	(101.277-21.417)	99.479±5.703	(88.300-110.657)
Overall	123.382±2.528	(118.427-128.337)	108.906±3.519	(102.008-15.804)	97.274±3.744	(89.935-104.613)

RCC: Right-side colon cancer, LCC: Left-side colon cancer, SE: Estimate, CI: Confidence interval

Table 3. Univariate analysis for prognostic factor of 24 months, 60 months and overall survival after surgery for colon cancer

	Univarite analysis for 24 months overall survival		Univarite analysis for 60 months overall survival		Univarite analysis overall survival	
	OR (95.0% CI)	p	OR (95.0% CI)	p	OR (95.0% CI)	p
Age	1.047 (0999-1.096)	0.054	1.056 (1.024-1.089)	0.001*	1.036 (1.012-1.060)	0.003*
Gender	0.954 (0.340-2.681)	0.929	1.168 (0.616-2.214)	0.634	1.325 (0.787-2.230)	0.288
Tumor localization (right or left)	0.724 (0.247-2.118)	0.556	0.790 (0.408-1.527)	0.483	0.908 (0.532-1.552)	0.727
Tumor size	1.048 (0.930-1.180)	0.446	1.080 (1.008-1.157)	0.028*	1.064 (0.987-1.146)	0.106
T stage (over T2 stage T3 and T4)		0.070		0.046 0.675 0.131		0.072 0.202 0.053
			1.361 (0.322-5.747) 3.190 (0.707-14.403)		2.522 (0.609-10.454) 4.293 (0.981-18.781)	
Total number of lymph nodes	0.967 (0.914-1.023)	0.239	0.987 (0.954-1.020)	0.430	0.992 (0.965-1.019)	0.548
Pozitive lymph nodes	1.057 (0.962-1.161)	0.245	1.067 (1.006-1.131)	0.030*	1.061 (1.007-1.117)	0.025*
Lenfovaskuler invasion	1.175 (0.418-3.303)	0.759	1.414 (0.746-2.681)	0.288	1.033 (0.603-1.170)	0.905
Perinoral invasion	1.579 (0.540-4.622)	0.404	2.042 (1.056-3.951)	0.034*	2.199 (1.254-3.857)	0.006*

*p<0.05 indicates statistical significance, OR: Odds ratio, CI: Confidence interval

Table 4. Multivarite analysis for prognostic factor of 24 months. Sixty months and overall survival after surgery for colon cancer

	Multivarite analysis for 24 months overall survival		Multivarite analysis for 60 months overall survival		Multivarite analysis overall survival	
	OR (95.0% CI)	p	OR (95.0% CI)	p	OR (95.0% CI)	p
Age	1.048 (0.998-1.100)	0.062	1.053 (1.022-1.085)	0.001*	1.033 (1.010-1.056)	0.005*
Gender	0.826 (0.271-2.520)	0.737	1.133 (0.568-2.259)	0.723	1.212 (0.696-2.112)	0.497
Tumor lokalization (right or left)	0.422 (0.129-1.378)	0.422	0.488 (0.231-1.029)	0.060	0.709 (0.396-1.267)	0.246
Tumor size	1.045 (0.924-1.181)	0.483	1.086 (1.007-1.172)	0.033*	1.070 (0.992-1.155)	0.079
T stage (over T2, T3 and T4)		0.043		0.098 0.800 0.353		0.096 0.486 0.122
			0.825 (0.186-3.667) 2.179 (0.422-11.256)		1.674 (0.394-7.120) 3.375 (0.722-15.772)	
Total number of	0.946 (0.884-1.012)	0.104	0.975 (0.936-1.015)	0.215	0.983 (0.953-1.014)	0.277
Pozitive lymph nodes	1.049 (0.909-1.210)	0.515	1.054 (0.967-1.148)	0.231	1.061 (0.988-1.140)	0.105
Lenfovaskuler invasion	0.575 (0.147-2.250)	0.427	0.915 (0.413-2.026)	0.826	0.629 (0.321-1.231)	0.176
Perinoral invasion	1.149 (0.293-4.512)	0.842	1.740 (0.775-3.908)	0.180	1.905 (0.972-3.734)	0.060

OR: Odds ratio, CI: Confidence interval

past 5 years have shown that removing 12 or more lymph nodes leads to better survival outcomes by providing more accurate staging and better informing postoperative treatment decisions.[18] Removing 12 or more lymph nodes provides more accurate staging and allows for better determination of treatment strategies.[19]When comparing RCC and LCC, lymph node removal was found to be equally important in both groups. This finding emphasizes that meticulous lymph node dissection during surgery can improve long-term outcomes for patients.[20] In our review, the number of lymph nodes removed was significantly higher in RCC compared with LCC, which aligned with findings from other studies suggesting that this was due to differences in surgical approaches or more advanced disease stages in RCC.

Two- and 5-year overall survival rates are critical metrics in assessing the success of colon cancer treatment. Studies comparing survival rates between RCC and LCC have yielded

mixed results.[21] Some research suggests that patients with LCC have higher survival rates, with 2-year survival rates ranging from 70-75% in patients with RCC and up to 75-80% in patients with LCC. These differences can be attributed to the fact that RCC is generally diagnosed at more advanced stages and is associated with a worse prognosis.[3] However, in our study, no significant difference in 2-year survival rates between RCC and LCC was observed. Similarly, 5-year overall survival rates have been reported with variation in the literature. Some studies suggest that 5-year survival rates are approximately 55-60% for RCC and 60-65% for LCC.[22] The lower survival rates in RCC can be explained by its tendency to be diagnosed at later stages and its more aggressive biological behavior. However, in our study, no significant difference in 5-year survival rates between RCC and LCC was found. These findings suggest that despite the distinct clinical and pathological characteristics of right- and left-sided colon cancers, survival rates may be similar between the two.[23] This highlights the importance of early diagnosis and personalized treatment strategies in both cancer types.[16]

Some studies in the literature have proposed that RCC may have a more aggressive course and that patients with RCC may require closer monitoring and more aggressive treatment.[11] However, the lack of such a distinction in our study suggests that larger-scale prospective studies are necessary. Particularly in RCC, factors such as peritoneal dissemination and advanced tumor penetration may significantly impact survival outcomes. Therefore, follow-up and additional treatment strategies should be carefully planned for patients with advanced-stage RCC. In conclusion, despite the clinical and pathological differences between RCC and LCC, the similar survival outcomes observed in our study emphasize the importance of multidisciplinary approaches and individualized treatment for both cancer types.

Study Limitations

This study has several limitations. Its retrospective design and single-center nature may limit the generalizability of the findings. While the sample size is substantial, a larger cohort would allow for more robust analyses and stronger statistical power. Additionally, variability in follow-up duration and missing clinical and pathological data may influence the accuracy of the results. The study lacked molecular and genetic data, which are crucial for a more comprehensive understanding of CRC subtypes, particularly regarding microsatellite instability-high (MSI-H) and BRAF mutations. These mutations are known to have a negative impact on prognosis, and their absence from the analysis limits the study's ability to fully evaluate their roles in RCC and LCC outcomes. Treatment variability across patients and the absence of quality-of-life assessments also represent limitations. Furthermore, the evolving nature of treatment guidelines may affect the current applicability of the results. External validation through multicenter studies is necessary to strengthen the findings. Future research should aim to address these limitations by conducting prospective, multicenter studies with larger patient cohorts and incorporating comprehensive molecular profiling, including MSI-H and BRAF mutation analysis.

Conclusion

In conclusion, despite the well-documented clinical and pathological differences between RCC and LCC, our study found no significant difference in 2- and 5-year survival rates between the groups. This suggests that both RCC and LCC, though distinct entities in terms of presentation and pathophysiology, may have comparable oncological outcomes. These findings emphasize the importance of early diagnosis and individualized treatment strategies, regardless of tumor location. Additionally, the higher number of lymph nodes removed in RCC and its potential for more advanced tumor stages highlight the need for meticulous surgical techniques and close postoperative monitoring, particularly in patients with RCC. Future large-scale studies are warranted to further explore the role of factors such as peritoneal dissemination and tumor penetration in influencing survival outcomes in RCC, ensuring that tailored follow-up and treatment strategies are effectively implemented. Ultimately, a multidisciplinary approach remains crucial in optimizing care and improving long-term outcomes for all patients with CRC.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of University of Health Sciences Turkey, Koşuyolu Yüksek İhtisas Research and Training Hospital (approval number: 2020.4/23-325, dated: 08.05.2020).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: O.U., M.D., S.G., A.O.S., Concept: M.T., E.P., A.S.S., A.O.S., Design: M.T., O.U., E.P., A.S.S., Ö.Ö., Data Collection or Processing: M.D., M.Di., Ö.Ö., Analysis or Interpretation: E.P., A.S.S., Literature Search: E.P., M.Di., A.O.S., Writing: M.T., S.G.

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