Original Article

Evaluating factors affecting survival in colon and rectum cancer: A prospective cohort study with 161 patients

ABSTRACT

Context: Colorectal cancers are frequent among cancers of gastrointestinal system. Whether there are any differences between survival in rectum and colon cancer patients is controversial.

Aims: In this study, we aimed to compare survival in surgically treated rectum and colon cancers and determine the factors affecting survival.

Subjects and Methods: The patients with colon and rectum cancer operated between 2009 and 2013 were examined retrospectively using prospective database. Patients were categorized as colon and rectum according to the tumor's location. Survival was identified as the primary outcome. Kaplan–Meier survival analysis and log-rank tests in survival assessment were used.

Results: One hundred and sixty-one patients with a mean age of 62.8 ± 12.7 years were included in the study. Male/female ratio was 1.6. Colon and rectum patients were counted as 92 (%57.1) and 69 (%42.9), respectively. Both groups were similar in demographic data ($P > 0.05$). It was observed that in 46 months (mean) of follow-up, 39.7% (*n*: 64) died, and 60.3% (*n*: 97) survived. Median survival time was 79 months, and 5-year cumulative survival rate was 60.8%. Five-year cumulative survival rates in stages for 1, 2, 3 and 4 were 88.2%, 64.7%, 48.5%, and 37.0%, respectively. It was noted that median survival time for colon cancer was 78 months and for rectum cancer was 79 months. Five-year cumulative survival rates for colon and rectum cancers were calculated as 56.7% and 63.4%, respectively. There were no significant differences in colon and rectum cancers in the means of survival rate (P: 0.459).

Conclusions: While location of colorectal cancers shows no significant effect on survival, treatment in the early stages increases survival rate.

KEY WORDS: Colon cancer, prognostic factors, rectum cancer, survival

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INTRODUCTION

Colorectal cancers are frequent in gastrointestinal system. It is the fourth most common cancer after lung, prostate, and bladder in male population and it is the third most common after breast and thyroid cancers in female population according to the World Health Organization. It is considered to be a significant morbidity and mortality cause and estimated to develop in more than 1,000,000 individuals annually worldwide.[1,2] Colorectal cancers form 10% of all cancers in female and male population. It is the second most common cause of death among cancers in the United States of America.[2]

In studies, it is stated that risk of developing colorectal cancer in an individual is 5%–6%. Furthermore, the risk of death of an individual due to colorectal cancer was determined as 3%.[1,2] In the last 50 years, the rate of colorectal cancer mortality decreased in female population whereas it did not change in male population. Whether there is a difference in survival time between rectum and colon cancers is a controversial topic.[2-4]

With development in neoadjuvant treatment approaches, poor prognosis in the past years got better. Recent studies show that prognosis in rectum cancers is better than colon. Nevertheless,

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factors affecting prognosis other than treatment for both colon and rectum cancers are not clarified.[2,3]

In this study, we aimed to evaluate surgically treated rectum and colon cancer patients' survival and factors affecting survival time.

SUBJECTS AND METHODS

Electively operated colorectal cancer patients between 2009 and 2013 were evaluated retrospectively using prospective database. This Local Ethics Committee approved the study was prepared according to ethical standards of 1975 Helsinki Declaration's Human Experiment Committee which was revised in 2000 (www.wma.netle/policy/b3.htm).

Patients

Patients who were operated and diagnosed histopathologically as adenocarcinoma were included in the study. Inoperable and recurrent colorectal cancer patients and patients that were diagnosed with other than adenocarcinoma were excluded from the study. Demographic data, tumor specifications, treatment plan, resected lymph node count, disease stage (tumor-node-metastasis [TNM]), and survival times were recorded. Patients were divided into two groups as rectum and colon according to tumor's location. Rectosigmoid tumors were categorized as rectum. Survival time was determined as the primary outcome. Surgery methods were reviewed in two groups as open and minimally invasive. Robot-assisted laparoscopy, laparoscopy, and transanal approach were considered as minimally invasive methods. Survival analysis was performed between the two groups of surgery methods. Effect of lymph node dissection adequacy on survival was also evaluated. Twelve and more dissected nodes were accepted for adequate lymph node count. Partial mesorectal excision was performed for upper rectum tumors, and total mesorectal excision was performed for middle and distal rectum tumors.

Treatments were planned in oncology council as soon as the patients were diagnosed. Patients with T3-4 and/or N + rectum cancers preoperatively (neoadjuvant) received medical/radiologic oncological treatment. Adjuvant medical/radiologic oncological treatments were planned postoperatively according to patient's specifications, disease stage, and tumor histopathology. Patients were followed up in general surgery oncology control clinic once every 3 months in the first 2 years and once every 6 months in the following 3–5 years. Follow-ups were done through face-to-face meetings or phone calls. Patients' survival data were evaluated with comparison. Patients who quitted follow-ups were excluded from the study.

Statistical analysis

Number Cruncher Statistical System 2007 and Power Analysis and Sample Size 2008 Statistical Software (Utah, USA) were used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, and maximum) were used while evaluating study data. Mann–Whitney U-test was used in comparison of quantitative data with two groups and Kruskal–Wallis test for three or more groups that are not normally distributed. Fisher's Exact and Yates Continuity Correction test were used to compare qualitative data and Kaplan–Meier survival analysis and log-rank tests were used to evaluate survival. Hazard ratio was calculated using Cox regression analysis to determine parameters affecting survival. Relevance was calculated as $P < 0.05$ in the confidence interval of 95%.

RESULTS

Two hundred and five colorectal cancer patients were evaluated during the course of the study. Study was focused on 161 patients since 44 patients (recurrent cancer [$n = 10$], pathology other than adenocarcinoma [$n = 8$], and quitted follow-up [$n = 26$]) were excluded from the study [Figure 1].

Mean age was 62.8 ± 12.7 (29–105). Nearly 39.1% ($n = 63$) were female and 60.9% ($n = 98$) were male (male/female ratio: 1/6). Nearly 57.1% ($n = 92$) of the tumors were located in colon and 42.9% ($n = 69$) in rectum [Table 1]. No differences were detected in demographics, age, and sex, between colon and rectum patients [$P = 0.153$, $P = 0.053$ respectively, Table 2].

Nearly 62.7% ($n = 101$) of the patients were operated with open approach, 30.4% ($n = 49$) with robot-assisted laparoscopy, 3.7% ($n = 6$) with laparoscopy, and 3.1% ($n = 5$) with transanal approach. Operation techniques (resection/ostomy) and oncological treatments (neoadjuvant/adjuvant, chemo/radiotherapy) are shown in Table 1. Complications occurred in the 1st month after the operations are shown in Table 3. Stage 3 (44.7%) and Stage

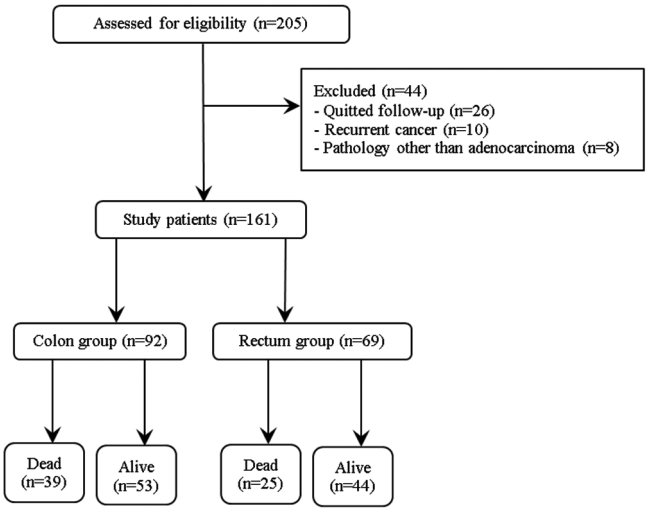

Figure 1: Flowchart of the study

2 (39.1%) were found to be the most frequent stages (TNM). There were no differences found between colon and rectum cancers in terms of stage [$P = 0.073$, Table 2].

Survival analysis

Mean follow-up period was 46 ± 24.4 months, 84 months being the highest. Median survival time for all the patients was 79 months, and 5-year survival rate was 60.8% [Figure 2].

Among 92 patients with colon cancer, 53 (57.6%) were found to be alive and 39 (42.4%) were dead and median survival time was 78 months. Among 69 patients with rectum cancer, 44 (63.8%) were alive and 25 (36.2%) were dead and median survival time was 79 months. Colon and rectum cancer patients' 5-year survival rate was 56.7% and 63.4%, respectively, and there were no statistically significant differences found [$P = 0.459$, Table 4 and Figure 3].

Five-year survival analysis comparison between open and minimally invasive approach surgical techniques indicated 55.8% and 70.1% of survival rates, respectively, which showed no significant difference [$P = 0.051$, Figure 4].

In regards of TNM staging, there was a substantive difference between survival rates ($P = 0.020$). Survival time of patients with Stage 1 and 2 was significantly longer than Stage 3 and 4 [Table 3 and Figure 5]. Age and stage, with 1.04 and 2.02 of hazard rates, respectively, were found to be influential on survival [$P = 0.001$, Table 5].

No significant differences were found between patients with inadequate (<12) (59.8%) and adequate lymph nodes dissection (≥12) (65.9%) in terms of 5-year survival rate ($P = 0.760$).

DISCUSSION

In this study, we evaluated tumor location's impact on survival in electively operated colorectal cancer patients. Literature shows that rectum located tumors are more frequent. The World Health Organization's statistics indicated that rectum cancer patient's survival rate was lower in earlier years, and tumor location's impact on survival is irrelevant.[2-5] Similar findings of our study show treatment approaches are consistent with the current guidelines.

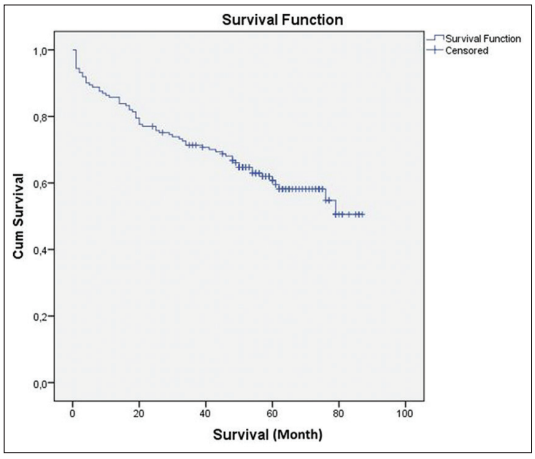

Figure 2: Colorectal cancer overall survival

Table 1: Patient's specifications

	n (%)
Cancer's location	
Colon	92 (57.1)
Sigmoid	38 (23.6)
Cecum	15 (9.3)
Descending colon	13 (8.1)
Hepatic flexure	8 (5.0)
Ascending colon	7 (4.3)
Transverse colon	7 (4.3)
Splenic flexure	4 (2.5)
Rectum	69 (42.9)
Resection	
Low anterior resection	40 (24.8)
Right hemicolectomy	35 (21.7)
Anterior resection	30 (18.6)
Left hemicolectomy	19 (11.8)
Subtotal colectomy	16 (9.9)
Abdominoperineal resection	14 (8.7)
Transanal excision	5 (3.1)
Transvers colectomy	1 (0.6)
Total colectomy	1 (0.6)
Ostomy	
Loop ileostomy	39 (24.2)
Colostomy	29 (18)
Oncologic treatments	
Neoadjuvant chemotherapy/radiotherapy	10 (6.2)
Adjuvant chemotherapy/radiotherapy	92 (57.1)

Table 2: Analysis between groups

	Colon (*n*=92)	Rectum (*n*=69)	*P*
Age (mean±SD)	64.1±12.7	61.2±12.5	0.153
Gender (male/female)	50/42	48/21	0.053
Stages			
Stage 1	5	12	0.073
Stage 2	41	22	
Stage 3	41	31	
Stage 4	5	4	

SD=Standard deviation

Table 3: Postoperative complications during 1st month

Complication	*n* (%)
Absent	125 (77.6)
Present	36 (22.4)
Anastomose leakage	14 (8.7)
Surgical site infection	6 (3.7)
Ileus	3 (1.9)
Mechanical intestinal obstruction	2 (1.2)
Urinary tract infection	2 (1.2)
Pulmonary emboli	2 (1.2)
Enteritis	2 (1.2)
Chylous ascites	1 (0.6)
Sensational neurologic loss	1 (0.6)
Urinary incontinence	1 (0.6)
Myocardial infarction	1 (0.6)
Catheter bleeding	1 (0.6)

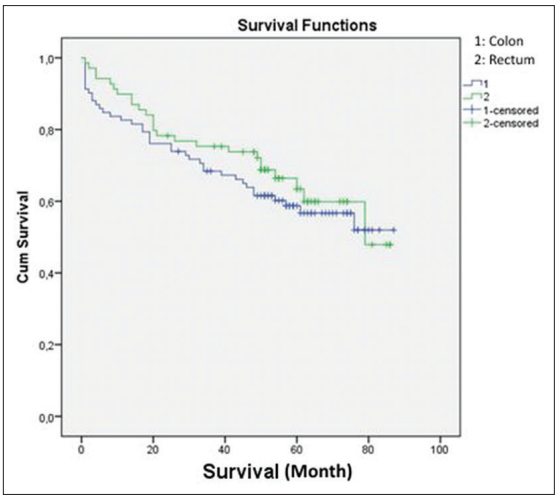

Figure 3: Tumor location-specific survival

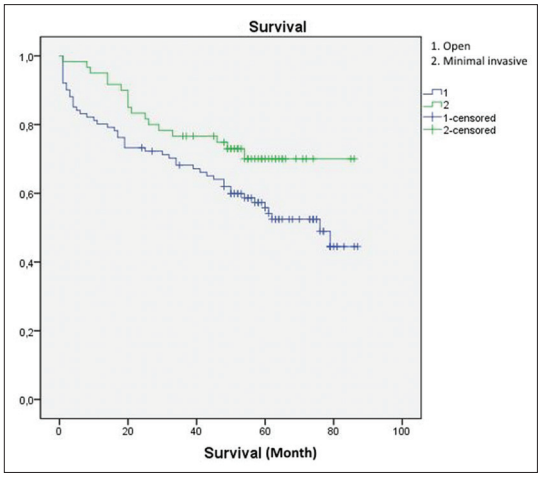

Figure 4: Surgical technique-specific survival

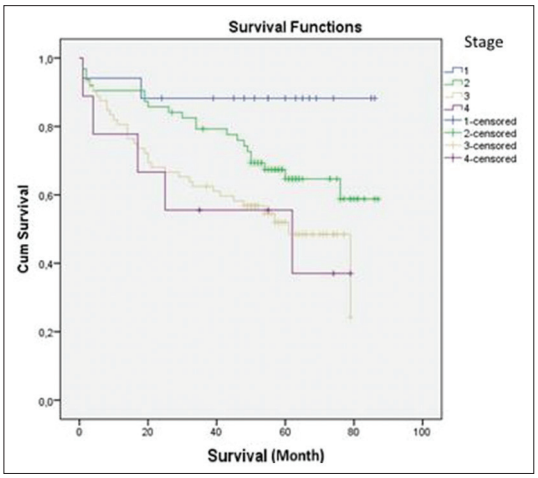

Figure 5: Tumor-node-metastasis stage-specific survival

Nearly 85.1% of patients were older than 50 years. Similar studies indicated colorectal cancers are more frequent in the male population.[6,7] According to this finding, most of the patients of the study group were male (male/female ratio 1.6). Therefore, it can be deduced that considering age and sex, study group was coherent with literature. Colorectal cancer incidence significantly rises between 40 and 50 years and more than 90% of patients are diagnosed after 50 years of age.[8] Mean age was 62.8 ± 12.7 in our study (ranging between 29 and 105).

No significant difference between open and laparoscopic approach's impact on survival was detected in literature. There are some studies which show laparoscopy's superiority in short-term survival.[9-11] In our study, 63.7% of the patients were operated through open approach, 29.7% with robot-assisted laparoscopy, 3.6% with laparoscopy, and 3% with transanal approach. Laparoscopic and transanal approach count being few, restricts surgical techniques' comparison. However, 5-year survival analysis comparison between open and minimally invasive approach groups did not achieve statistical significance ($P = 0.051$).

Some colorectal cancer patients may admit with acute symptoms such as obstruction and perforation. Colonic obstruction is seen in advanced staged tumors, and especially older patients. Complete obstruction is seen fewer than 10% of patients and this requires emergent diagnosis and surgical treatment.[12] It is anticipated that applying stent can decrease emergent operation count, like in rectum tumors. There are multiple factors for emergency surgery besides technique effecting survival. There for only electively operated patients were evaluated since this situation increases heterogeneity and disables objective evaluation.

In a study conducted in German multidisciplinary center, 5-year survival rates were informed as 76%, 65%, 42%, and 16% for Stage 1, 2, 3, and 4, respectively.[12] In our study, patient follow-up time was 87 months (7.2 years); maximum and mean follow-up time was 46 months. Five-year survival rates in Stage 1, 2, 3, and 4 patients were found 88.2%, 64.7%, 48.5%, and 37%, respectively. Rates were compatible with literature except Stage 4. High survival rate of Stage 4 was evaluated to because of low case count.

The most common complication at the early postoperative stage (in the 1st month) was anastomotic leakage with the rate of 8.7% ($n = 14$) and half of it ($n = 7$) needed surgical treatment. Second surgical treatment needed the most for the recurrent colorectal cancer patients ($n = 10$). This was coherent with literature.[13]

Total mesocolon and mesorectal dissection's positive impact on survival was mentioned in literature, and it was stated that 12 dissected lymph nodes are enough.[14-16] We could not show that the patients with more or <12 lymph nodes dissected have poor survival rate. Inability to perform standard mesocolic excision for colon cancer and a low number of patients with 12 or less dissected lymph nodes ($n = 26$) may be the explanation of this outcome.

Table 4: Kaplan–Meier survival analysis

	n	Dead	Alive	5 years survival rate (%)	Median survival (month)	Mean survival (month)	95% CI	*P**
Location								
Colon	92	39	53	56.7	78	58.7	51.59-65.75	0.459
Rectum	69	25	44	63.4	79	62.5	55.02-70.01	
Stage								
Stage 1	17	2	15	88.2	-	77.0	65.20-88.79	0.020
Stage 2	63	22	41	64.7	-	66.2	58.69-73.63	
Stage 3	72	35	37	48.5	61	50.3	42.91-57.78	
Stage 4	9	5	4	37.0	62	45.9	24.91-67.01	

*Log-rank. CI=Confidence interval

Table 5: Cox regression analysis

	B	SE	Wald	*P*	HR	95.0% CI	
						Lower	Upper
Age	0.043	0.011	14.823	0.0001	1.044	1.022	1.068
Stage	0.704	0.181	15.187	0.0001	2.022	1.419	2.882

SE=Standard error, HR=Hazard ratio, CI=Confidence interval

Colorectal cancers are common and have high mortality. It was seen in this study and some others that diagnosis at early stage can increase survival rate. It is recommended to classify the patients with a family history of colorectal cancer according to their risk groups and to include them in early scanning for diagnosis, even to perform genetic analysis if needed.[17] We think that all kinds of written, auditory, and visual conferences from expert debaters arranged to educate society about this disease would be beneficial.

Main limitation of this study is that it used retrospective registry data that vary among hospitals. Furthermore, low patient number can be evaluated as insufficient for general assessment and accurate results. Alongside, variables of treatment such as duration differences between adjuvant chemo/radiotherapies can be considered as restrictors. However, long follow-up time, for example, 46 months, is the positive side of this study.

CONCLUSIONS

With the help of current standard treatment algorithms, we found that while the location of colorectal tumors was irrelevant on survival, age and stage were considerably affecting factors.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Inger DB. Colorectal cancer screening. Prim Care 1999;26:179-87.
2. Borum ML. Colorectal cancer screening. Prim Care 2001;28:661-74, viii.
3. Donald JJ, Burhenne HJ. Colorectal cancer. Can we lower the death rate in the 1990s? Can Fam Physician 1993;39:107-14.
4. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016;66:7-30.
5. Compton CC. Colorectal carcinoma: Diagnostic, prognostic, and molecular features. Mod Pathol 2003;16:376-88.
6. Nakagawa H, Ito H, Hosono S, Oze I, Mikami H, Hattori M, *et al.* Changes in trends in colorectal cancer incidence rate by anatomic site between 1978 and 2004 in Japan. Eur J Cancer Prev 2016 May 4. [Epub ahead of print].
7. Caldarella A, Crocetti E, Messerini L, Paci E. Trends in colorectal incidence by anatomic subsite from 1985 to 2005: A population-based study. Int J Colorectal Dis 2013;28:637-41.
8. Fante R, Benatti P, di Gregorio C, De Pietri S, Pedroni M, Tamassia MG, *et al.* Colorectal carcinoma in different age groups: A population-based investigation. Am J Gastroenterol 1997;92:1505-9.
9. Gietelink L, Wouters MW, Bemelman WA, Dekker JW, Tollenaar RA, Tanis PJ; Dutch Surgical Colorectal Cancer Audit Group. Reduced 30-day mortality after laparoscopic colorectal cancer surgery: A population based study from the Dutch surgical colorectal audit (DSCA). Ann Surg 2016;264:135-40.
10. Athanasiou CD, Markides GA, Kotb A, Jia X, Gonsalves S, Miskovic D, *et al.* Open compared with laparoscopic complete mesocolic excision with central lymphadenectomy for colon cancer: A systematic review and meta-analysis. Colorectal Dis 2016;18:O224-35.
11. Zhao D, Li Y, Wang S, Huang Z. Laparoscopic versus open surgery for rectal cancer: A meta-analysis of 3-year follow-up outcomes. Int J Colorectal Dis 2016;31:805-11.
12. Lee GH, Malietzis G, Askari A, Bernardo D, Al-Hassi HO, Clark SK. Is right-sided colon cancer different to left-sided colorectal cancer? A systematic review. Eur J Surg Oncol 2015;41:300-8.
13. Theodore RS. Anastomotic leak after colon and rectal resections. In: Fazio V, Church J, Delaney C, editors. Current Therapy in Colon and Rectal Surgery. 2nd Ed, Philadelphia, Pennsylvania: Elsevier Mosby; 2005.
14. Park EJ, Baik SH, Kang J, Hur H, Min BS, Lee KY, *et al.* The impact of postoperative complications on long-term oncologic outcomes after laparoscopic low anterior resection for rectal cancer. Medicine (Baltimore) 2016;95:e3271.
15. O'Connell JB, Maggard MA, Ko CY. Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging. J Natl Cancer Inst 2004;96:1420-5.
16. Ozawa H, Kotake K, Hosaka M, Hirata A, Sugihara K. Impact of lateral pelvic lymph node dissection on the survival of patients with T3 and T4 low rectal cancer. World J Surg 2016;40:1492-9.
17. Kinney TP, Merel N, Hart J, Joseph L, Waxman I. Microsatellite analysis of sporadic flat and depressed lesions of the colon. Dig Dis Sci 2005;50:327-30.