Epidemiological Differences between Colon Cancer and Rectum Cancer

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Abstract

Background: Clinical and epidemiological variation was seen between the colon cancer (CC) and rectum cancer (RC). So, there is not so much data available about the epidemiological and clinicopathological differences and prognostic factors regarding to CC and CR in Iran, we aimed to perform this study.

Methods: All cases of CC and RC referred to oncology and gastroenterology wards of Taleghani General Hospital, Teheran, Iran between 2002 and 2008 were retrospectively reviewed. The research group were reviewed all medical records in the study period for collecting the required data. All patients under study were followed up until end day of 2008 (closed day) from their diagnosis.

Results: There are 856 cases of CC and 427 cases of RC. Mean survival time of CC cases was relatively higher than RC cases (P <0.05). Regarding to the age at diagnosis, about 42% of CC and 42.6% of RC patients was diagnosed less than 50 years of age. Positive family history of any cancer was relatively higher in CC (40.0%) patients than RC (31.0%) patients (P<0.05). significant difference was seen between CC and RC regarding to depth of tumor invasion, pathologic stage and type of first treatment. RC patient were diagnosed in more advanced pathologic stages. Regarding to histology type of tumor 75.0% of CC cases and 79.4% of RC cases was adenocarcinoma. Abdominal pain (74.4%) and blood per rectum (89.7%) were the most prevalent symptoms mentioned by patients for CC and RC, respectively. Distant metastasis, lymph node metastasis, lower BMI and poor grading of tumor was related to increased risk of death due to CC. Regarding to RC, only pathologic stage was determine as prognostic factor.

Conclusion: Results of this study emphasis that RC has a poorer prognosis comparing to CC. Up to 42 percent of patients with CC and RC are lower than 50 years of age. Patterns of CC versus RC indicate major variations in demographic and clinicopathologic characteristics that suggest possible differences in etiology and pathogenesis. So we suggest that for the analysis of cancer data, CC and RC should be investigated as separate cancers and not to be as colorectal cancer. Abdominal pain and blood per rectum should be emphasis for detection of CC and RC, respectively.

Keywords: Colon neoplasm; Rectum neoplasm; Clinical; Epidemiology; Pathology

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Introduction

Cancers of the colon and rectum occurs in high incidence rates in Europe, North America, Australia and Japan[1], whereas the incidence of these cancers are relatively low in developing countries like Iran. Recent studies have shown that the incidence and prevalence of CC and CR is increased in Iran during the last 25 years[2-4] becoming the fourth most common among all cancers[5]. The highest CC incidence rates for males and females were in Japan and New Zealand with Age Standardized Rate (ASR) equal to 56 and 29, respectively. Also, the highest incidence rates of RC for males (ASR=27) was in Japan, Hiroshima and for females (ASR=12) in Singapore Chinese[6]. Within the USA, the incidence of CC increased by about 18% during the period 1973-1988 while the incidence of RC and mucinonous adenocarcinoma in the colon remained relatively constant in this period[7]. Overall, the average rate of CC and RC amongst males in the

less developed countries is around 20% of that of the industrialized one[8].

Previous studies reported that, age standardized incidence rate of colorectal cancer in Iran has been 9.27, 9.64 and 9.90 in 2003, 2004 and 2005 in 100,000 Iranian men and 9.12, 9.47 and 9.13 in 100000 Iranian women, respectively[9]. It is estimated that about 5,000 new cases of CC and RC are detected in Iran annually[9].

Clinical and epidemiological variation was seen between the CC and RC. Both CC and RC incidence rates are higher in males than in females[7]. While incidence rates for RC are higher amongst whites than in blacks, the incidence rates for CC are higher in blacks than in whites[7].

Approximately 60% of CC and CR in high incidence populations arise in the left colon (descending and sigmoid colon), whereas in low incidence regions there is a predominance of right-sided cases (caecum, ascending colon, hepatic flexure, transverse colon, splenic flexure) and rectum[10].

Blood loss, change in bowel habits, acute intestinal obstruction, perforation symptoms were most frequent in patients with CC[11-13], rectal bleeding while anemia, loss of body weight and abdominal pain turned out to be the predominant symptoms in patients with RC[14, 15]. Also, it showed that rectal bleeding, constipation and lower abdominal pain are the most predominant symptoms in Iranian CC and CR patients[16].

Several studies have investigated the prognostic features of the CC and CR worldwide. Dukes' stage, serum CEA level, morphology of the tumor, lymph node metastasis, depth of bowel wall invasion, was strongly associated with CC[17-20] and lymph node metastasis, depth of bowel wall invasion, differentiation of the tumor, serum CEA level, clinical stage, age at diagnosis and ethnic group were significant in RC[19, 21].

Because of, there is not so much data available about the epidemiological and clinicopathological differences and prognostic factors regarding to CC and CR in Iran, we aimed to perform this study.

Materials and Methods

All cases of CC and CR referred to oncology and gastroenterology wards of Taleghani General Hospital, Teheran, Iran between 2002 and 2008 were retrospectively reviewed. The patients were referred to our center from all over the country including private/general hospitals and clinics. This medical center is a referral university hospital (affiliated to Shahid Beheshti University of Medical Sciences) for diagnosis, treatment and surveillance of CC and CR.

The research group were reviewed all medical records in the study period for collecting the required data. In a few number of CC and CR patients there is no information about the pathology reports and some other variables. Demographic factors (i.e. age, sex), medical records and diagnosis information (i.e. symptoms at diagnosis, family history, tumor metastasis, histologic grade of tumor, Depth of tumor invasion, Pathologic Stage, Tumor size etc.) were included in the study.

All patients under study were followed up until end day of 2008 (closed day) from their diagnosis. Deaths were confirmed through the different sources such as: vital and medical records, cemetery information and telephonic contact to relatives of patients. We encounter a few numbers of CC and CR patients wherein no information about the cause of death was obtained, but only the dates of their death were known, which we considered to be due to CC and RC.

Descriptive analysis was done for demographic and clinical features. We used the chi-square test for categorical variables and the Student's t-test for continuous variables. The mean survival of patients with CC and CR were calculated according to the Kaplan–Meier method and compared by the Log-rank test. Also, prognostic factors for the CC and rectum cancer were determined by the Cox proportional hazard model. Considering $P<0.05$ as statistically significant, SPSS (version13.0) software were used for data analysis.

Results

There are 856 cases of CC and 427 cases of RC. Mean survival time of CC cases was relatively higher than RC cases (Log-rank P-value<0.05). No statistical difference was seen between the diagnostic age of CC and RC patients ($P>0.05$). Regarding to the age at diagnosis, about 42% of CC and 42.6% of RC patients were diagnosed less than 50 years of age. A sex ratio equal to 1.46 and 1.77 was seen in CC and RC patients, respectively. Positive family history of any cancer was relatively higher in CC (40.0%) patients than RC (31.0%) patients ($P<0.05$) (Table1).

Table1 shown that, significant difference was seen between CC and RC regarding to depth of tumor invasion, pathologic stage and type of first treatment ($P<0.05$). Most of patients with CC and RC were detected in T3 depth of tumor invasion. RC patient were diagnosed in more advanced pathologic stages (stage III, 44.1%). Surgery as first treatment was done in higher percents of CC cases comparing to RC

Table 1. Demographic and clinical features of patients with CC and RC patients

	Colon cancer (%) (n=856)	Rectum cancer (%) (n=427)	P-value[1]
Mean survival(months)	101.91	67.19	0.024
Age (years) (n=1283)			
Mean ± SD	53.8+14.3	53.3+14.6	
<50	360(42.1)	182(42.6)	0.846
≥50	496(57.9)	245(54.7)	
Gender(n=1283)			
Male	508(59.3)	273(63.9)	0.113
Female	348(40.7)	154(36.1)	
Family history of cancer(n=1225)			
Negative	495(60.0)	276(69.0)	0.002
Positive	330(40.0)	124(31.0)	
BMI(n=828)			
≤18.5	42(7.8)	25(8.7)	0.304
18.6–24.9	274(50.8)	164(56.7)	
25–29.9	179(33.2)	80(27.7)	
≥30	44(8.2%)	20(6.9)	
Histology type(n=1283)			
Adenocarcinoma	647(75.6)	339(79.4)	0.128
Non- adenocarcinoma	209(24.4)	88(20.6)	
Depth of tumor invasion(n=894)			
T1	12(1.9)	5(1.8)	0.003
T2	61(9.8)	51(18.6)	
T3	462(74.5)	190(69.3)	
T4	85(13.7)	28(10.2)	
Grade of tumor(n=899)			
Well	346(57.5)	156(52.5)	0.149
Moderate	200(33.2)	118(39.7)	
Poor	56(9.3)	23(7.7)	
Distant metastasis(n=617)			
Absent	396(84.4)	153(85.0)	0.861
Present	68(15.6)	27(15.0)	
Regional lymph nodes metastasis(n=853)			
N0	329(54.8)	123(48.6)	0.143
N1	199(33.2)	89(33.8)	
N2	72(12.0)	41(16.2)	
Pathologic Stage(n=906)			
I	54(8.6)	42(15.1)	0.001
II	272(43.4)	86(30.8)	
III	230(36.7)	123(44.1)	
IV	71(11.3)	28(10.0)	
First treatment(n=1267)			
Surgery	701(83.2)	277(65.3)	0.001
Other	142(16.8)	147(34.7)	
Tumor size(n=818)			
<30mm	78(13.9)	48(18.8)	0.068
≥30mm	485(86.1)	207(81.2)	

[1] All P-value was calculated based on χ^2 test exclude of mean survival that calculated using Log-rank test

cases (P<0.05). In most cases tumor grading was well differentiated and there was no significant differences between CC and RC (P>0.05) (Table1).

We have also investigated the histology type of tumor. In 647 (75.0%) of CC cases and 339(79.4%) of RC cases histology of tumor was adenocarcinoma. Larger tumor (≥30mm) was seen in CC cases

Table 2. The frequency of symptoms at diagnosis in CC and RC patients

	Colon cancer (%)	Rectum cancer(%)	P-value (χ^2 test)
Sign and symptom			
Abdominal Pain(n=1070)	537(74.4)	195(56.0)	0.001
Blood per Rectum(n=1053)	407(57.9)	314(89.7)	0.001
Anemia(n=939)	254(39.1)	80(27.7)	0.001
Weight Loss(n=1054)	431(61.0)	183(52.7)	0.011
Weakness(n=1058)	380(53.7)	157(44.9)	0.007
Change in Bowel Habit(n=1035)	453(63.9)	259(74.6)	0.001
Obstructive Symptoms(n=1006)	139(20.3)	35(10.9)	0.001
Perforation Symptoms(n=987)	26(3.9)	6(1.9)	0.097
Fever of unknown origin(n=936)	64(10.0)	22(7.5)	0.222

Table 3. Prognostic factor of CC and RC of patients using Cox proportional hazard model

Prognostic factors	Hazard ratio	95% Confidence interval	P-value
Colon			
Distant metastasis(Present)	4.93	2.51-9.69	0.001
Regional lymph nodes metastasis			
N0	Ref.	-	-
N1	1.57	0.67-1.72	0.148
N2	2.64	1.27-5.48	0.005
BMI	0.85	0.79-0.91	0.001
Grade of tumor			
Well	Ref.	-	-
Moderate	0.73	0.38-1.40	0.338
Poor	3.14	1.55-6.36	0.001
Rectum			
Pathologic Stage			
I	Ref.	-	-
II	0.62	0.12-3.05	0.552
III	1.83	0.53-6.31	0.341
IV	4.64	1.08-20.02	0.040

comparing to RC, but this deference wasn't significant. Regarding to tumor metastasis, no statistical difference was seen between CC and RC patients (P>0.05).

The most three symptoms in patients at diagnosis consisted of abdominal pain (74.4%), change in bowel habit (63.9%), weight loss (61.0%) in CC and blood per rectum (89.7%), change in bowel habit (74.6%) and abdominal pain (56.0%) in RC(table 2).

The prognostic factor of CC and RC of patients under study is shown in table3. Presence of distant metastasis(HR=4.93), higher regional lymph node metastasis(HR=2.64), lower BMI(HR=0.85) and poor grading of tumor(HR=3.14) was related to increased risk of death due to CC. Regarding to RC, only pathologic stage was determine as prognostic factor. RC patients that diagnosed at stage IV, have a hazard ratio equal to 4.64 for death.

Discussion

We found that RC has a poorer prognosis comparing to CC. Up to 42 percent of patients with CC and RC are lower than 50 years of age. Positive family history of any cancer was most prevalent in CC patients. RC patient were diagnosed in higher stage (III) of disease. Surgery was the most curative procedure as the first treatment in CC patients. One Nigerian study reported that there an increasing number of CC and CR cases occurring in the young as 23% occurred below age 40 years while 12.4% occurred in patients 30 years and below in their study[22]. Other reports from other parts of the world showed that 35-42% of patients with CC and CR are below age 40 years[23-26]. High proportion of the CRC in young Iranians can be explained by this fact that Iranian population is young[27]. On the other hand, genetic factors maybe play an important

role in the development of CC and RC in young patients in our country[2].

Previous study reports that patterns of CC versus RC by sex, race, and age indicate major variations in demographic characteristics that suggest possible differences in etiology, pathogenesis, or screening of cancers at the two sites[28]. It is indicate that lower CC have demographic characteristics similar to RC rather than upper CC[29]. Other data from the literature suggest that intestinal cancers may differ in genetic characteristics related to race, sex, and location in the colon[30]. Thus, the demographic characteristics of these cancers together with basic biologic evidence suggest that investigators should be looking for a different set of risk factors for cancers of the upper colon when compared with that of the rectum and sites within the lower colon.

Cheng et al. reported that rates are higher in males than females for every site, but the male/female ratio increases from the cecum through the rectum[31]. While the RC shows gradual increase in men, the tendency for peaking and stabilization could be seen in women[32]. In our study a male predominance were seen in the both of CC (m/f ratio=1.46) and RC (m/f ratio=1.77) patients.

Family history of CC and CR consistently has been shown to increase risk of CC[33-38]. It has been estimated that having a history of CC and CR in first-degree relatives results in about a twofold increase in risk of developing the disease. Few studies have evaluated the risk of having a family history of CC and CR on developing cancer of the rectum[20, 39], although it could be hypothesized that more distal tumors are less strongly associated with family history. Our study showed that CC and CR patients have a higher proportion of family history of cancer comparing to RC patients ($P<0.005$). It has been suggested that risk associated with family history of CC and CR can be altered by diet and lifestyle factors[40, 41].

Regarding to depth of tumor invasion, CC patients were detected with more invasive tumors comparing to RC cases ($P<0.05$). Statistical difference was seen among CC (stage II) and RC (stage III) cases regarding stage at diagnosis. Other results of our study show that, CC and RC patients were similar regarding to variables such as: age at diagnosis, gender, BMI, histology type, grade of tumor, distant metastasis, and regional lymph node metastasis.

Our Finding showed adenocarcinoma to be the most common cancer type in our study which is compatible to other studies conducted other part of Iran[42-45] and china[46]. Sheidan et al., reported that colorectal adenocarcinoma has been the third most frequent cancer in Luxembourg[47].

In a Jamaican study on CC and CR, most of the tumors were well or moderately differentiated adenocarcinoma[15]. Our results are in agreement with two other reports from Iran[48, 49].

In present study, the most reported symptom was abdominal pain for CC and blood per rectum for RC. Kalavi reported that abdominal pain and rectal bleeding were the most common symptoms seen in right or left CC (99%) and RCs (94.1%) and anemia was more common in right CC cases[50]. In contrast to our results; Sarmast et al. reported that most significant signs include rectal bleeding (34%) and obstruction (26%) in their study[51]. Other study showed that Common presenting features in right CC were abdominal pain, pallor, and palpable mass; in left CC were symptoms of obstruction, and in RC predominated bleeding[52].

Most reports suggest that RC has a poorer prognosis than CC[53-55]. Base on univariate analyses of our data, RC have a poorer outcome comparing to CC (mean survival: 102 v.s 67 month, $P<0.05$). Distant metastasis, regional lymph node metastasis, lowers BMI and poor differentiation were related to poorer prognosis for CC patients. So, for RC only higher stages of tumor was leading to bad outcome in patients under study. Tominaga et al., reported that for CC, only Dukes stage was significant, whereas for RC, Dukes stage, age, location of the tumor, and serosal and venous invasion by cancer cells were prognostic factors[56]. Another study carried out by He et al., the three tumor variables identified in multivariate analysis as bearing the strongest independent effect on the 5-year survival in low and middle RC were (in order to decrease prognostic impact) venous invasion, tumor size, and TNM stages[57]. Also, Hojo et al., showed that factors greatly influencing prognosis were the presence of lymph node metastasis, the degree of invasion of the intestinal wall and the site of the primary lesion. Lymph node metastasis was an especially important prognostic factor[58]. The results of Deans et al. study, confirms that Duke's stage, patient age and tumor differentiation are still the most important clinicopathological variables in CC and CR [59].

In another study conducted in China, Xu et al., have been used univariate and multivariate analysis to determine the prognostic factors that affect on survival of CC and CR patients. By using univariate analysis, they identified that lymph node metastasis and distant metastasis were the common prognostic factors for both CC and RC. Smoking, deep

infiltration, chemotherapy and serum albumin concentration were the uncertain prognostic factors for CC. Signet-ring cell carcinoma, larger tumor size (>6 cm), deep infiltration, lack of radical surgery, and advanced TNM stage were the exclusive adverse prognostic factors for RC. Also, by using multivariate analysis based on a Cox regression model, it was identified that smoking, lymph node metastasis and serum albumin concentration were independent prognostic factors for CC; advanced TNM stage, distant metastasis and palliative surgery for RC; and vessel invasion, lymph node metastasis and urine glucose for RC under curative resections[60].

This study have some limitations for example, we didn't access to part of important data. Also, in some cases the patient's medical records were Imperfect. Generally we encounter to defective data for the reason that registration of data on cancer in our centre was incomplete.

Conclusion

In conclusion, this study emphasis that RC has a poorer prognosis comparing to CC. Up to 42 percent of patients with CC and RC are lower than 50 years of age. Patterns of CC versus RC indicate major variations in demographic and clinicopathologic characteristics that suggest possible differences in etiology and pathogenesis. So we suggest that for the analysis of cancer data, CC and RC should be investigated as separate cancers and not to be as colorectal cancer. Abdominal pain and blood per rectum should be emphasis for detection of CC and RC, respectively.

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Conflict of Interest

None to declare

Authors' Contribution

AS conceived and designed this study and interpreted the results and drafted the manuscript. BMD designed and carried out the analysis and participated in writing and revise the manuscript. SRF revised and approved the final manuscript. MRZ supervised the project. All authors read and improved the final manuscript.

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