ORIGINAL ARTICLE

Evaluation of the left-to-right shift of colon tumors in Iran: Is the trend changing?

Seyed Mohammad Hossein Kashfi, Ehsan Nazemalhosseini Mojarad, Mohamad Amin Pourhoseingholi, Hamid Asadzadeh Aghdaei[1], Fakhrialsadat Anaraki[2], Mohammad Reza Zali

Gastroenterology and Liver Diseases Research center, Research Institute for Gastroenterology and Liver Diseases, [1]Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, [2]Colorectal Division of General Surgery Department, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background: Colorectal cancer (CRC) is the second cause of cancer-related deaths worldwide. There have been several studies reporting the proximal tumor shift, especially in Western countries. In the present study, we investigated the clinicopathologic and anatomical distributions of colorectal tumors in Iranian CRC patients. **Materials and Methods:** In this retrospective cohort study, 258 patients with CRC from 2008 to 2013 were evaluated. Comparison of variables was performed using Pearson's chi-square test and Fisher's exact test depending on the nature of the data. **Results:** A total of 258 patients including 124 (48.1%) females and 134 (51.9%) males enrolled in this study. The majority of cancers were detected in the rectosigmoid, i.e., 98 (38%) followed by the left colon, i.e., 84 (32.6%) and the right colon, i.e., 76 (29.5%). In the present study, we observed the significant association between metastases, adjuvant therapy, family history, and history of inflammatory bowel disease (IBD) with tumor, node, and metastasis (TNM) staging ($P < 0.001$). In univariate analysis, there was a strong association between overall survival (OS) and stage II CRC ($P = 0.03$). However, the predictive value was lost in multivariate analysis ($P = 0.145$). **Conclusion:** Unlike the majority of previous studies on Iranian CRC patients, we observed a considerably higher occurrence of right-sided colon cancers (84 versus 76). Although this phenomenon did not reach the statistical significance rate, based on recent studies on Iranian population including the present one, the pattern of anatomical distribution of colorectal tumors has been changed toward the proximal colon. This requires an urgent need to provide other strategies and complementary detecting approaches in order to identify proximal tumors in Iranian CRC patients.

Key words: Colorectal cancer (CRC), Iran, proximal shift, survival

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in the USA and the second cause leading to cancer deaths although intense screening programs have declined the incidence rate.[1,2] The majority of cases (90%) were above 50 years of age in both the genders.[3] It has been demonstrated that approximately 1.23 million cases are detected each year worldwide.[4] Apart from age having a first-degree relative diagnosed with CRC, physical inactivity and overweight are the other main risk factors.[5,6] Adenomatous polyps are considered to be precursors of the majority of CRCs both in the hereditary and sporadic types.[7] Diagnosis of CRC in the early stages is fundamental for further management and if the case is presented with metastasis, the survival will be lesser than 10%.[8] Colonoscopy is considered as a standard goal to identify adenomatous polyps or other suspicious legions in CRC.[9,10] However, the specificity and sensitivity of this technique for the detection of right-sided colon tumors (proximal region) is low and controversial. This requires the application of other modalities apart from colonoscopy in order to identify premalignant tumors located at the right side of the colon. Based on the National

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Address for correspondence: Dr. Hamid Asadzadeh Aghdaei, Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
E-mail: Hamid.assadzadeh@gmail.com
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Cancer Institute report, between the early 1970s and late 1990s there was a 6% increase in the rate of proximal colon cancers than left tumors.[2] The "left-to-right shift" model in CRC primary was reported in epidemiological studies in the late 1970s.[11] Several studies thereafter have indicated a proximal shift of tumors in different ethnic groups.[2,12,13] Several studies in the USA indicated that approximately 50% of proximal tumors belong to the elderly population.[14-16] Therefore, proximal tumors might also imply an aging population. In addition, it has been demonstrated that tumors in the proximal region have distinct pathologic, molecular features and different treatment outcome compared to distal lesions. So an understanding of the pattern of anatomical distribution of the tumors in every ethnic group would help in proceeding with the appropriate medical approach for each patient. In this study, we investigated the clinicopathologic features and anatomical distribution of CRC tumors in Iranian CRC patients.

MATERIALS AND METHODS

In this retrospective cohort study, 275 patients with pathologically documented CRC who referred to the Gastroenterology and Liver Diseases Research Center, Shahid Beheshti University of Medical Sciences from 2008 to 2013 enrolled in this study. Patients with hereditary nonpolyposis colorectal cancer (HNPCC) and polyposis syndromes including familial adenomatous polyposis were excluded from the study. Demographic data including the age at diagnosis, gender, tumor location, pathological type of tumor (grade and stage of tumor), chemotherapy history, anemia, history of inflammatory bowel diseases (IBD), family history of CRC and diabetes, metastasis status in the regional lymph node, and location of CRC metastasis in case of presentation were recorded. The TNM staging system was applied to determine the severity of disease and the local or distant extent of disease spread. The TNM staging system of the American Joint Committee on Cancer (AJCC) is the preferred and standard staging system for CRC. Written informed consent was taken from patients and the local ethics committee approved the study protocol, which was in accordance with the principles of the Helsinki Declaration. All subjects were Iranian and genetically unrelated. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 15.0 statistical package (Chicago, IL, USA). Comparison of variables was performed using Pearson's chi-square test, Fisher's exact test, or the Mann-Whitney *U* test, depending on the nature of the data. Relationships among the clinicopathologic factors were analyzed using the chi-square test. For survival analyses, the following variables were evaluated: Age, tumor location, sex, tumor-node-metastasis stage, and grade of differentiation (well/moderate versus poor), history of chemotherapy, diagnosis age, family history, and microsatellite instability (MSI). Overall survival (OS) analyses were done through a Cox proportional hazard function for both univariate and multivariate analyses, and Kaplan-Meier (log-rank test) curves were plotted. Significance for all statistics were recorded if $P < 0.05$. OS was defined as the time from histopathological diagnosis to death from any cause. Patients were followed up until September 2013. Patients who died due to reasons unrelated to CRC were censored at the time of death and were excluded from the analysis.

RESULTS

A total of 258 CRC patients including 124 (48.1%) females and 134 (51.9%) males were enrolled in this retrospective cohort study. The characteristics of the patients enrolled

Table 1: Clinical characteristics of patients with CRC

Variables	Subgroups	*N* (%)
Gender	Male	134 (51.9)
	Female	124 (48.1)
Age (years)	<50	78 (30.3)
	>50	180 (69.7)
Location	Right colon	76 (29.5)
	Left colon	84 (32.6)
	Rectosigmoid	98 (38.0)
Pathologic tumor stage	I	27 (10.5)
	II	126 (48.8)
	III	85 (33)
	IV	20 (7.7)
Tumor grade (differentiation)	Poor	51 (19.8)
	Moderate	79 (30.6)
	Well	111 (43.0)
	Unassesable	17 (6.6)
Mucinous characteristics	No	217 (84.1)
	Yes	41 (15.9)
Age of diagnosis (years)	<50	79 (30.6)
	>50	179 (69.4)
Vital status	Alive	214 (83)
	Dead	44 (17)
Chemotherapy	Yes	103 (39.9)
	No	155 (60.1)
Anemia	Present	38 (14.7)
	Absent	220 (85.3)
IBD‡	Present	49 (19.0)
	Absent	209 (81.0)
Family history	Present	73 (28.3)
	Absent	185 (71.7)
Diabetes	Present	49 (19)
	Absent	209 (81)
Metastasis	Present	50 (19.4)
	Absent	208 (80.6)
Metastasis organ	Liver	31 (62)
	Ovary	11 (22)
	Other	8 (16)

‡IBD = Inflammatory bowel disease

in this study are present in Table 1. The mean age of the participants was 56.4 ± 16 years. As it is shown in Table 1, the majority of cancers were detected in the rectosigmoid, i.e., 98 (38%) followed by the left colon, i.e., 84 (32.6%) and the right colon, i.e., 76 (29.5%). In the present study, the anatomical distribution of tumors was similar in left- and right-sided colons. However, we did not observe any significant difference between the right- and the left-sided cancers with respect to gender, age at diagnosis, stage, and grade of tumor. Among 124 women with colon cancer, the majority of the cases, i.e., 35 (28.2%) were right-sided, whereas in 134 males left-sided colon cancer was dominant in 53 (39.6) cases. In the present study, most of the cases were aged above 50 years, i.e., 180 (69.7%) and only 30.3% cases were aged under 50 years. The majority of the patients 126 (48.8%) in this study were in stage II. However, only 20 (7.7%) cases were diagnosed in stage IV. In terms of differentiation most of the tumors, i.e., 111 (43.0%) were well-differentiated and 51 (19.8%) were poorly differentiated. The most common sites of CRC metastasis were the liver, i.e., 31 (62%) followed by the ovary, i.e., 11 (22%). In eight cases, other metastatic organs were involved. According to our findings, family history of CRC was detected in 73 (28.3%) cases. The clinicopathologic features of the study population according to differentiation are presented in Table 2. Based on our findings, there was a significant association between TNM stage and the differentiation status ($P < 0.001$). In 126 stage II cases, 64 (50.8%) were well-differentiated and only 17 (13.5%) were poorly differentiated, which are present in Table 2. We also observed a significant association between the tumor location and differentiation status ($P < 0.001$). Among 98 cases in the

Table 2: TNM staging in patients with CRC

Stage	*N* (%)	T	N	M	*N* (%)
0		TIS	N0	M0	
I	27 (10.5)	T1	M0	M0	9 (3.5)
		T2	M0	M0	18 (7)
II	126 (48.8)	T3	M0	M0	106 (41)
		T4	M0	M0	20 (7.4)
III	85 (33)	T1,T2	N1 or N2	M0	48 (18.6)
		T1,T2	N1 or N2	M0	37 (14.2)
IV	22 (7.7)	Any T	Any N	M1	22 (8.3)

Table 3: Clinicopathologic features of the study population according to differentiation

Variables	Total	Moderate	Poor	Well	*P* value
	N	*N* (%)	*N* (%)	*N* (%)	
Patients					
Mean age					
Years	56.39±10.756	55.19±9.903	56.55±10.655	56.35±11.070	0.161
Gender					
Female	124	40 (32.3)	26 (21.0)	54 (43.5)	0.213
Male	134	39 (29.1)	25 (18.7)	57 (42.5)	
TNM† staging					
I	27	9 (33.3)	11 (40.7)	7 (25.9)	0.001
II	126	32 (25.4)	17 (13.5)	64 (50.8)	
III	85	26 (30.6)	23 (27.1)	34 (40.0)	
IV	20	12 (60.0)	0 (0.0)	6 (30.0)	
Family history					
No	185	52 (28.1)	38 (20.5)	80 (43.2)	0.279
Yes	7	27 (37.0)	13 (17.8)	31 (42.5)	
Location					
Left	84	18 (21.4)	11 (13.1)	53 (63.1)	0.001
Right	76	23 (30.3)	22 (28.9)	21 (27.6)	
Rectosigmoid	98	38 (38.8)	18 (18.4)	37 (37.8)	
Adjuvant therapy					
No	155	46 (29.7)	30 (19.4)	68 (43.9)	0.948
Yes	103	33 (32.0)	21 (20.4)	43 (41.7)	
Age of diagnosis					
<50	79	25 (31.6)	17 (2.5)	33 (41.8)	0.883
>50	179	54 (30.2)	34 (19.0)	78 (43.6)	
Metastases					
No	208	58 (27.9)	47 (22.6)	88 (42.3)	0.052
Yes	50	21 (42.0)	4 (8.0)	23 (46.0)	
History of IBD‡					
No	209	65 (31.1)	43 (20.6)	86 (41.1)	0.589
Yes	49	14 (28.6)	8 (16.3)	25 (51.0)	

†TNM = Tumor, node, and metastasis; ‡IBD = Inflammatory bowel disease

rectosigmoid, 38 (38.8) were moderately differentiated, 18 (18.4) were poorly differentiated, and 37 (37.8) were well-differentiated [Table 3]. The clinicopathologic features of the study population according to TNM staging are presented in Table 4. The significant association was detected among the variables including metastases, adjuvant therapy, family history, and history of IBD with TNM staging $P < 0.001$. In Table 5, the clinicopathologic features of the study population according to location status are presented and in Table 6 the clinicopathologic features of the study population according to chemotherapy status are presented. According to Table 6, we found a significant association between TNM staging and chemotherapy status and among 85 patients in stage III, 77 (90.6%) received chemotherapy ($P < 0.001$). In this study, we evaluated the 5-year OS based on the clinical outcome available. According to our findings, pathologic tumor stages did not have association with survival ($P = 0.05$); similar to TNM staging; chemotherapy, family history, tumor location, and differentiation also showed no significant relationship with survival ($P > 0.05$). Based on survival curves, patients with stages II and III had poorer survival [Figure 1]. However, we observed rather a similar survival for patients with stages II and III CRC ($P = 0.05$). Kaplan-Meier curves for OS of patients according to differentiation status revealed that poorly differentiated tumors had a poorer survival rate compared with well-differentiated and moderately differentiated tumors; however, the result was did not reach a significant rate (log rank $P = 0.06$, Figure 2). We also observed that patients older than 44 years of age had a poorer OS rate than younger patients ($P = 0.02$). In patients with a younger age at diagnosis of CRC (<44), there was a better OS than older patients; however, the difference did not reach statistical significance ($P = 0.16$). All results for univariate and multivariate analyses are shown in Table 7. Multivariate analysis was performed to identify factors with independent prognostic significance and to calculate hazard ratios (HRs). The analysis included tumor location, TNM stage, differentiation, and mucinous characteristics. In

Table 4: Clinicopathologic features of the study population according to TNM staging

Variables	Total	Stage I	Stage II	Stage III	Stage IV	*P* value
	N	*N* (%)	*N* (%)	*N* (%)	*N* (%)	
Patients						
Mean age						
Years	56.39±10.756	55.48±12.314	54.73±9.618	58.64±11.458	58.50±11.33	0.052
Gender						
Female	124	18 (14.5)	66 (53.2)	32 (25.8)	8 (6.5)	0.031
Male	134	9 (6.7)	60 (44.8)	53 (39.6)	12 (9.0)	
Differentiation						
Moderate	79	9 (11.4)	32 (40.5)	26 (32.9)	12 (15.2)	0.001
Poor	51	11 (21.6)	17 (33.3)	23 (45.1)	0 (0.0)	
Well	111	7 (6.3)	64 (57.7)	34 (30.6)	6 (5.4)	
Family history						
No	185	17 (9.2)	100 (54.1)	61 (33.0)	7 (3.8)	0.001
Yes	73	10 (13.7)	26 (35.6)	24 (32.9)	13 (17.8)	
Location						
Left	84	5 (6.0)	33 (39.3)	34 (40.5)	12 (14.3)	0.003
Right	76	13 (17.1)	42 (55.3)	16 (21.1)	5 (6.6)	
Rectosigmoid	98	9 (9.2)	51 (52.0)	35 (35.7)	3 (3.1)	
Adjuvant therapy						
No	155	27 (17.4)	116 (74.8)	8 (5.2)	4 (2.6)	0.001
Yes	103	0 (0.0)	10 (9.7)	77 (74.8)	16 (15.5)	
Age of diagnosis						
<50	79	9 (11.4)	42 (53.2)	25 (31.6)	3 (3.8)	0.410
>50	179	18 (10.1)	84 (46.9)	60 (33.5)	17 (9.5)	
Metastases						
No	208	25 (12.0)	109 (52.4)	74 (35.6)	0 (0.0)	0.001
Yes	50	2 (4.0)	17 (34.0)	11 (22.0)	20 (40.0)	
History of IBD‡						
No	209	19 (9.1)	117 (56.0)	58 (27.8)	15 (7.2)	0.001
Yes	49	8 (16.3)	9 (18.4)	27 (55.1)	5 (10.2)	
Mucinous						
Mucinous	41	5 (12.2)	28 (68.3)	6 (14.6)	2 (4.9)	0.024
Nonmucinous	217	22 (10.1)	98 (45.2)	79 (36.4)	18 (8.3)	

‡IBD = Inflammatory bowel disease

Table 5: Clinicopathologic features of the study population according to location status

Variables	Total	Left	Right	Rectosigmoid	*P* value
	N	*N* (%)	*N* (%)	*N* (%)	
Patients					
Mean age					
Years	56.39±10.758	57.33±10.620	56.46±11.416	55.52±10.379	0.526
Gender					
Female	124	31 (25.0)	35 (28.2)	58 (46.8)	0.010
Male	134	53 (39.6)	41 (30.6)	40 (29.9)	
Differentiation					
Well	111	53 (47.7)	21 (18.9)	37 (33.3)	0.001
Moderately	79	18 (22.8)	23 (29.1)	38 (48.1)	
Poorly	51	11 (21.6)	22 (43.1)	18 (35.1)	
TNM† staging					
I	27	5 (18.5)	13 (48.1)	9 (33.1)	0.003
II	126	33 (26.2)	42 (33.3)	51 (40.5)	
III	85	34 (40.0)	16 (18.8)	35 (41.2)	
IV	20	12 (60.0)	5 (25.0)	3 (15.0)	
Family history					
No	185	60 (32.4)	55 (29.7)	70 (37.8)	0.988
Yes	73	24 (32.9)	21 (28.8)	28 (38.4)	
Adjuvant therapy					
Yes	103	43 (41.7)	20 (19.4)	40 (38.8)	0.006
No	155	41 (26.5)	56 (36.1)	58 (37.4)	
Age of diagnosis					
<50	79	23 (29.1)	26 (32.9)	30 (38)	0.645
>50	179	61 (34.1)	50 (27.9)	68 (38.0)	
Metastases					
No	208	60 (28.8)	67 (32.2)	81 (38.9)	0.023
Yes	50	24 (48.0)	9 (18.0)	17 (34.0)	
History of IBD‡					
No	209	62 (29.7)	65 (31.1)	82 (39.2)	0.117
Yes	49	22 (44.9)	11 (22.4)	16 (32.7)	

†TNM = Tumor, node, and metastasis; ‡IBD = Inflammatory bowel disease

univariate analysis, there was a strong association between OS and stage II CRC ($P = 0.03$). However, the predictive value was lost in multivariate analysis.

DISCUSSION

CRC is considered as the third and the fourth most common cancer in men and women, respectively, in the Iranian population.[17] It has been reported that 5,000 new cases of CRC are diagnosed each year.[17] In this regard, there have been several studies that evaluated the characteristics of CRC patients in Iran.[18-21] The detection rate of CRC via colonoscopy is approximately 85% in distal, whereas it accounts for 0% to 55% of proximal colon cancers.[22-24] It has been demonstrated that distal and proximal colorectal lesions harbor distinct molecular and clinical characteristics.[25-28] All these differences between the two sites are primarily due to embryonic tissue where they originate and the lifestyle and habits of individuals.[25,29] Previous studies revealed that in comparison to left-sided colon cancers, right-sided tumors mostly occur at an older age and in the female gender, present with advanced stages, and have increased tumor sizes with poorly differentiated features, poorer prognosis, and a larger amount of positive lymph nodes.[15,27,30,31] In the molecular pattern, tumors mostly present with MSI and CpG island methylator phenotype (CIMP).[26] The immunology of the proximal tumors is also different in comparison to the distal colon. It has been noted that intraepithelial T-cells in the proximal colon is higher than the distal colorectum in healthy individuals.[32,33] In this regard, some factors are reported to increase the risk of developing proximal tumors including the intake of high fat,[34] whereas in the distal colon, low consumption of fruits and vegetables and high meat and protein consumptions are the main contributors.[35,36] Anatomical site of tumors has a peculiar epidemiology, pathogenesis, molecular features.[37-39] Identification of the dynamic shift of CRC tumors in population would shed light on better screening and management of patients as the proximal colon cancers raise the challenge due to limitations in screening technics.[40] In the present study, the anatomical distribution of tumors was similar in left- and right-sided colons (32.6% versus 29.5%) and we did not observe any

Table 6: Clinicopathologic features of the study population according to chemotherapy status

Variables	Chemotherapy			
	Total	No	Yes	*P* value
	N	*N* (%)	*N* (%)	
Patients				
Mean age				
Years	56.39±10.756	54.97±10.223	58.52±11.227	
Gender				
Female	124	84 (67.7)	40 (32.3)	0.011
Male	134	71 (53.0)	63 (47.0)	
Differentiation				
Well	111	68 (61.3)	43 (38.7)	0.948
Moderately	79	46 (58.2)	33 (41.8)	
Poorly	51	30 (58.8)	21 (41.2)	
TNM† staging				
I	27	27 (100)	0 (0.0)	0.001
II	126	116 (92.1)	10 (7.9)	
III	85	8 (9.4)	77 (90.6)	
IV	20	4 (20.0)	16 (80.0)	
Family history				
No	185	115 (62.2)	70 (37.8)	0.172
Yes	73	40 (54.8)	33 (45.2)	
Location				
Left	84	41 (48.8)	43 (51.2)	0.006
Right	76	56 (73.7)	20 (26.3)	
Rectosigmoid	98	58 (59.2)	40 (40.8)	
Age of diagnosis				
<50	79	53 (67.1)	26 (32.9)	0.082
>50	179	102 (57.0)	77 (43.0)	
Metastases				
No	208	133 (63.9)	75 (36.1)	0.008
Yes	50	22 (44.0)	28 (56.0)	
History of IBD‡				
No	209	137 (65.6)	72 (34.4)	0.001
Yes	49	18 (36.7)	31 (63.3)	

†TNM = Tumor, node, and metastasis; ‡IBD = Inflammatory bowel disease

significant difference between the right- and the left-sided cancers with respect to gender, age at diagnosis, stage, and grade of tumor in the Iranian population. In consistennce with our study, several other studies in Asia have observed no significant anatomical distribution.[41-43] In line with our study in the Iranian population, Bafandeh *et al*. also revealed no difference in the age of diagnosis and right-sided or left-sided tumors.[44] Several studies on Iranian CRC cases revealed that the majority of tumors are located on the left side of the colon.[42,45,46] Omranipour *et al*. study on 442 CRC patients including 157 (35.5%) colon cancers and 285 (64.5%) rectal cancers demonstrated that 43.3% of the colon cancers were located on the right side and 56.7% were left-sided. However, Omranipour *et al*. did not find any statistically significant increase rate in right-sided cancer during the period of 15 years.[47] In contrast, Mahmodlou *et al*. reported a significant number of tumors located in the right colon, i.e., 192 (35%) followed by the left colon, i.e., 110 (20%).[48] In other ethnic groups Weiss *et al*. found that within stage II, CRC patients with proximal tumors had lower mortality; however, patients with stage III distal tumors had a higher mortality rate.[27] Proximal tumors have gender specific features, which seem to be related to the age of patients. In a study by Yuuki Iida *et al*., they reported that female CRC patients presented with a higher number of proximal tumors than distal tumors. They revealed that the right-sided shift elevated with increasing age ($P < .0001$).[49] In the present study, we also evaluated the characteristics of CRC patients and the association of these clinicopathologic variables with the survival status. We observed that most of the cases were in stage II, i.e., 126 (48.8%). This is in contrast to a previous study by Mahmodlou *et al*. who reported that the most Iranian CRC patients were in stages III and IV (57%).[48] Based on survival curves, patients with stages II and III had poorer survival. However, we observed rather the similar survival curves for patients with stages II and III

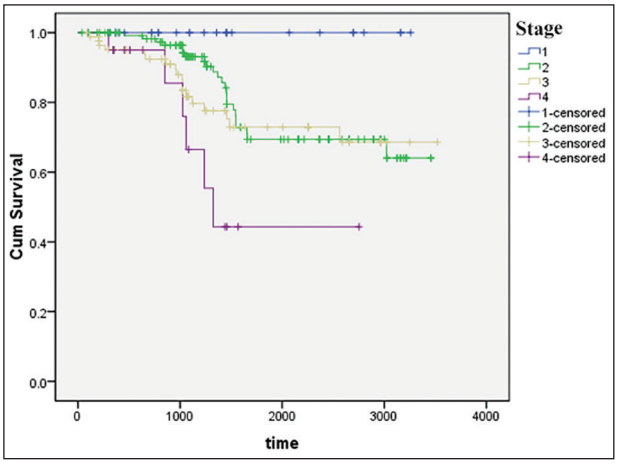

Figure 1: Kaplan-Meier curves of overall survival in colorectal cancer patients according to the stages ($n = 258$). The survival curves showed that patients with stages II and III had poorer survival. However, we observed rather the similar survival curves for patients with stages II and III CRC. Log-rank $P = 0.05$

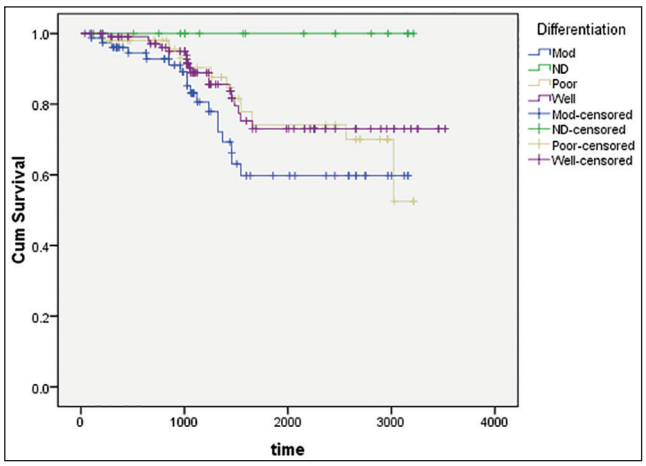

Figure 2: Kaplan-Meier curves of overall survival of patients according to differentiation status. While the poorly differentiated tumors had a poorer survival rate compared with well-differentiated and moderately differentiated tumors, the result was not reach a significant rate. Log-rank $P = 0.06$

Table 7: Univariate and multivariate analysis for clinical variables in this study

Variables	Univariate analysis		Multivariate analysis	
	Hazard ratio for death (95% confidence interval)	*P* value	Hazard ratio for death (95% confidence interval)	*P* value
Gender				
Female	1 ref.		1 ref.	
Male	0.735 (0.413-1.306)	0.294	0.707 (0.371-1.345)	0.291
Location of tumor				
Left colon	1 ref.		1 ref.	
Right colon	1.128 (0.745-1.707)	0.569	1.751 (0.371-1.728)	0.523
Rectosigmoid	0.884 (0.570-1.370)	0.580	0.801 (0.371-1.728)	0.572
Differentiation				
Well	1 ref.		1 ref.	
Moderately	0.700 (0.234-2.091)	0.523	0.756 (0.221-2.587)	0.656
Poorly	0.546 (0.147-2.031)	0.367	0.375 (0.076-1.840)	0.227
Mucinous characteristics				
No	1 ref.		1 ref.	
Yes	0.896 (0.599-1.339)	0.591	0.756 (0.451-1.267)	0.288
TNM† staging				
I	1 ref.		1 ref.	
II	0.392 (0.161-0.952)	0.039	0.459 (0.161-1.307)	0.145
III	0.831 (0.508-1.359)	0.460	0.641 (0.347-1.185)	0.156
IV	1.114 (0.673-1.843)	0.674	0.921 (0.463-1.832)	0.815

†TNM = Tumor, node, and metastasis

CRC ($P = 0.05$). In our study, most of the cases were aged above 50 years, i.e., 180 (69.7%) and only 78 (30.3) cases were younger than 50 years. We observed that patients aged older than 44 years had poorer OS rate than younger patients ($P = 0.02$). When we evaluated the 5-year OS based on the clinical outcome available, we did not observe a significant association between tumor stages and survival ($P = 0.05$); in addition, other factors including chemotherapy, family history, tumor location, and differentiation showed no significant relationship with survival as well ($P > 0.05$). In univariate analysis, there was a strong association between OS and stage II CRC ($P = 0.03$). However, the predictive value was lost in multivariate analysis. In line with our study, Hermann Brenner in 2012 evaluated the 5-year relative survival for European CRC patients with regard to age, stage at diagnosis, and location. They reported that the survival rate increased in all European regions over time and this rate was more remarkable in younger cases than in older patients, for earlier than for more advanced cancer stages, and also for rectum cancer than for colon cancer.[50] In another study on the Iranian population, Moradi *et al*. reported that the worst survival rate was detected in young patients (aged less than 20 years) and in patients aged more than 80 years. They revealed that the 5-year OS in Iranian CRC patients was 41% (45% for female and 39% for men).[20] Another valuable paper by Zuli Yang *et al*. evaluated demographic data and prognosis in a series of CRC patients aged 44 years and below.[51] They found that in comparison to older patients, this group of patients had larger tumors, poorly differentiated, infiltrative growth type, mucinous, and signet-ring cell adenocarcinoma, and they mostly had advanced TNM stages. They reported that histological grade, TNM stage, and recurrence were considered as independent factors related to survival in the younger group.

CONCLUSION

Unlike the majority of previous studies on Iranian CRC patients, which indicated the left-sided predominance of colorectal tumors, in this study we observed the higher occurrence of right-sided colon cancers. However, this phenomenon did not reach the statistical significance rate. According to recent cohort studies on the Iranian population including the present one, the pattern of anatomical distribution of colorectal tumors has been following the Western populations. This might have been due to several environmental and lifestyle factors, which contributed to this anatomical shift. The differences in genetic and molecular pathologic profiles in each side of the colon and the fact that colonoscopy alone fails to identify all the proximal lesions calls for an urgent need to provide other strategies and complementary detecting approaches in order to identify proximal tumors in Iranian CRC patients.

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Conflicts of interest
There are no conflicts of interest.

AUTHOR'S CONTRIBUTION

All authors contributed in the conception of the work, conducting the study, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work.

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