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Original Article

Comparison of young and elderly patients with rectal cancer in terms of prognostic factors and clinical features: A retrospective analysis

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Abstract

Aim: Rectal Carsinoma (RC) has considerable morbidity, mortality, and highly operational costs. RC is generally known as a disease of the elderly especially beyond the age of 50 years. Nevertheless, the incidence of RC in younger adults (aged ≤50 years) has been increasing widely. Our aim is to evaluate the clinical and histopathological features of the patients under and over 50 years with RC and their contribution to prognosis.

Material and Methods: Patients with RC who were treated in our clinic included in the current retrospective designed study, and their data collected including demographics, clinical presentations, histopathological features, disease characteristics, treatment received or not, survival and outcomes. Their variables were compared statistically.

Results: This study included 187 RC patients from our General Surgery Clinic. Median age at diagnosis was 62 years (min:26-max:88). Lack of perineural invasion significantly affected disease-free survival and overall survival in general (p <0.035-p <0.001). High grade of tumor variable was statistically significant in favor of ≤ 50 years group (p: 0.0082).

Conclusion: RC in young-onset is related with poor prognostic factors such as aggressive histological features, high grade and stage tumors. Clinicians should pay more attention and interest to the symptoms and sings of the bowel in younger patients and should not hesitate to perform screening tests such as blood test, or especially rectosigmoidoscopy, etc to be initiate early diagnosis and further treatment.

Keywords: Prognosis; rectal cancer; young-onset colorectal cancer

INTRODUCTION

Colorectal carcinoma (CRC) is one of the most seen tumors especially in developed countries with more than 500,000 deaths worldwide per year (1). Rectal Carsinoma (RC) is such a disease that carries considerable morbidity, mortality, and highly operational costs. RC is generally known as a disease of the elderly especially beyond the age of 50 years. Unfortunately, the screening studies usually initiates after the fifth decade (2). RC can be diagnosed in an early stage even if there is no clinical finding thanks to the improvement of diagnostic techniques. Screening programs for RC in young adults are not initiated without a familial history or any major complaint. Although there is no consensus about in the literature, the agreed cut off age is generally 50 years, and, the incidence of RC in younger adults (aged <50 years) has been increasing widely (3). In addition, these individuals often represent the most productive population in any society (4). Some series with large sample size have shown that the ratio of the individuals under 50 years with RC as 3 to 31 % (5). Unfortunately, there is no information about the incidence of RC in young individuals in our country. Overall, the presentation and prognosis of the disease in young-onset are generally less well defined in the literature.

In this retrospective clinical study, our aim is to evaluate the clinical and histopathological features of the patients under and over 50 years with RC and their contribution to prognosis.

MATERIAL and METHODS

After approving by Diskapi Yildirim Beyazit University Local Ethics Committee with number of 78-06/2019, the retrospective observational study of RC patients where were evaluated and treated at Diskapi Yildirim Beyazit Training and Research Hospital General Surgery Clinic from 2012 to 2019 were conducted. Data collected included demographics, clinical presentations, histopathological

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features, disease characteristics, treatment received or not, survival and outcomes. Inclusion criteria were patients with curative surgery for stage 1-3 rectal cancers, and histopatholigically negative distal, proximal, and radial surgical margins. Patients who had mortality within the first 30 days postoperatively were not included in the study. Subgroup analysis was performed based on their age group (≤50 vs >50 years) to further analyze their impact on outcome. In survival analysis; progression-free survival (PFS) was defined as the time between the operation date and the first progression date. Overall survival (OS) was accepted as the period between the date of operation and the date of exitus or last follow-up date for survivor patients. In addition, the follow-up period was defined between the date of diagnosis and the last control date.

Statistical analysis were performed with SPSS (Statistical Package for Social Sciences for Windows) version 21.0 and $p < 0.05$ was considered statistically significant. Univariate analysis was performed using Mann-Whitney U test for continuous variables and Kaplan –meier, log rank or Pearson's chi square test for categorical variables.

RESULTS

This study included 187 RC patients from Dışkapı Yıldırım Beyazıt Research and Training Hospital General Surgery Clinic. Thirty six point four percent of the patients were male and 63.6 % were female. The percent of patients aged 50 and under was 16.6 %, while patients aged 51 and over was 83.4 %. Median age at diagnosis was 62 years (min:26-max:88). Median Body Mass Index was 27 (min:20-max:40). Median of disease-free survival was 23 months (min:2-max:90). Median of overall survival 25 months (min:2-max:93). Thirty four of the patients (18.2 %) were operated with laparascopic surgery, and the others were operated (81.8 %) with laparotomy (Table 1). Tumor locations were in the lower rectum in 20 patients (10,7 %) and in the middle/upper rectum in 167 patients (89,3 %) (Table 1). Lymphovascular invasion was positive in 19.3 % of patients and perineural invasion rate was 19 %. Thirteen point four percent of the patients received neoadjuvant treatment. All demographic data, histopathologic features, survival and treatment characteristics of the patients are summarized in Table 1.

Table 1. Descriptive and demographic variables of the patients

	n	(%)*
Gender (n=187)		
Male	119	36.4
Female	68	63.6
Age of Diagnosis (n=187)		
Age of 50 and below	31	16.6
Age of 51 and up	156	83.4
Stage of the Tumor (n=187)		
Stage 1	31	16.6
Stage 2	62	33.2
Stage 3	71	38.0
Stage 4	23	12.3
ASA Score (n=187)		
1	25	13.4
2	76	40.6
3	86	46.0
Type of Operation-(n=187) (Laparascopy-n=34/Laparatomy-n=153)		
Age of 50 and below (Laparascopy/Laparatomy)	8/23	25.8/74.2
Age of 51 and up (Laparascopy/Laparatomy)	26/130	16.6/83.4
Location of Tumor (n=187) (Lower Rectum-n=20/Middle-Upper Rectum-n=157)		
Age of 50 and below (Lower Rectum/Midlle-Upper Rectum)	4/27	12.9/87.1
Age of 51 and up (Lower Rectum/Midlle-Upper Rectum)	16/140	10.2/89.8
Lympovascular Invasion (n=187)		
Negative	151	80.7
Positive	36	19.3
Perineural Invasion (n=187)		
Negative	150	80.2
Positive	37	19.8

Grade of the Tumor (n=187)		
Well differantiated	34	18.2
Moderately differantiated	133	71.1
Poorly differantiated	20	10.7
Histopathological Classification (n=187)		
Adenocanser	173	92.5
Musinous Adenocanser	12	6.4
Signet-Ring Cell Cancer	2	1.1
Neoadjuvant Therapy (n=187)		
Absent	162	86.6
Available	25	13.4
Reccurent Cancer (n=187)		
Absent	164	87.7
Available	23	12.3
Survival (n=186)		
Live	150	80.6
Ex	36	19.4
Body Mass Index (n=186)		
Weak	0	0
Normal	36	19.4
Overweight	108	58.1
Obese	42	22.6

* **%: Column Percentage**

Table 2. The relationship of patients age groups in terms of gender, ASA, and histopathological findings

	Age of Diagnosis				
	≤50		>50		p
	n	(%)*	n	(%)*	
Gender (n=187)					
Female	15	22.1	53	77.9	0.187[1]
Male	16	13.4	103	86.6	
$\chi 2$ =1.740					
Lymphovascular Invasion (n=187)					
Absent	25	16.6	126	83.4	1[1]
Present	6	16.7	30	83.3	
$\chi 2$ =0.000					
Perineural Invasion (n=187)					
Absent	26	17.3	124	82.7	0.754[1]
Present	5	13.5	32	86.5	
$\chi 2$ =0.098					
Neoadjuvant Therapy (n=187)					
Absent	22	13.6	140	86.4	0.754[1]
Present	9	36.0	16	64.0	
$\chi 2$ =0.098					
Reccurent Disease (n=187)					
Absent	26	15.9	138	84.1	0.681[1]
Present	5	21.7	18	78.3	
$\chi 2$ =0.169					

ASA Score (n=187)					
1	14	56.0	11	44.0	**<0.001[2]**
2	15	19.7	61	80.3	
3	2	2.3	84	97.7	
χ2 =41.274					
Grade of tumor (n=187)					
Well-differantiated	3	8.8	31	91.2	**0.008[2]**
Moderate differantiated	20	15.0	113	85.0	
Poor differantiated	8	40.0	12	60.0	
χ2=9.640					
Histology of tumor (n=187)					
Adenocancer	27	15.6	146	84.4	
Musinous Adenocancer	4	33.3	8	66.7	
Signet-cell Cancer	0	0	2	100	
Stage (n=187)					
Stage 1	6	19.4	25	80.6	0.941[2]
Stage 2	10	16.1	52	83.9	
Stage 3	12	16.9	59	83.1	
Stage 4	3	13.0	20	87.0	
χ2=0.395					

*: Column Percentage, [1]Yates Corrected Chi Square Test, [2]Pearson Chi Square Test

ASA score and Grade of Tumor variables between two groups were statistically significant (p: <0.001, and p: 0.008, respectively) (Table 2). The relationship of patients age groups in terms of gender, ASA, and histopathological findings is summarized in Table 2.

Disease-free survival was found to be 29 (3-75) months in patients ≤ 50 years and 22.5 (2-90) months in patients 50 > years. Overall survival was found to be 33 (6-25) months in patients ≤ 50 years and 24 (2-93) months in patients 50 > years (Table 3). Lack of perineural invasion significantly affected disease-free survival and overall survival (p <0.035-p <0.001) (Table 4).

Table 3. Relations Between Groups of Patients with Survival

	Groups	Median (Month)	Z	p
Disease Free Survival	≤50	29 (3-75)	-0.291	0.771
	>50	22.5 (2-90)		
Overall Survival	≤50	30 (6-75)	-0.967	0.334
	>50	24 (2-93)		

Table 4. Analysis of Survival

		Median (Month)	95 % Confidence Interval	Log Rank	p
Disease Free Survival					
Age	≤50	62.2	52.0-72.4	0.542	0.462
	>50	77.2	70.7-83.6		
Perineural Invasion	Absent	77.6	72.7-84.6	**4.453**	**0.035**
	Present	44.4	36.9-52.0		
Overall Survival					
Age	≤50	68.2	59.0-77.4	1.804	0.179
	>50	63.4	55.4-71.4		
Perineural Invasion	Absent	67.4	60.0-87.9	**15.766**	**<0.001**
	Present	53	37.5-53.2		

Kaplan –meier, log rank test was used

DISCUSSION

The incidence of RC is relatively rare among young patients. RC is one of the common cancers in those aged 55 to 65 years (6). However, increased incidence of RC in young-onset has been shown in several current academic studies. (6-8). No agreement has been reached regarding the cut-off age for the diagnosis of RC in young-onset patients. But most of the studies have corroborated the cut-off age as 50 (9). We defined age 50 years and under as young, because this is the age when initial screening is recommended for average risk individuals.

The increase in RC in young patients have yet unknown reasons. Most of the cases are sporadic rather than hereditary, though hereditary factors were accused to be the essential reason for RC in young patients (10). Many social and behavioral risk factors, such as smoking, alcohol, red diet intake, and obesity have been showed to be related with the RC in young patients (11,12). However, these factors in question could not totally explain the increase of RC in young individuals because they are not routinely screened for RC, and this leads them at an increased risk of being diagnosed only once RC becomes symptomatic. In our study, 90.32 % of the patients fewer than 50 years of age were determined histopathologically as moderate or poor grade at the initial diagnosis, and this value was a statistically significant finding. Other studies in literature have generally been reported as advanced stage in parallel with our study (13,14). In our study, 80.65 % of patients fewer than 50 years of age were reported as stage 2, 3, 4 and this was the most important statistically significant data. Almost 25 % of patients fewer than 50 years of age are poorly differentiated while the other group is around 7 percent. As stated in the literature, unfortunately, the tumor aggressiveness of patients under the age of 50 is more than the other group and is more advanced at the time of diagnosis. In a current study, Tawadros et al investigated 6775 CRC patients, and a greater proportion of younger patients (88%) had advanced disease compared to older patients (15). In another study which was conducted with 3318 CRC patients from Australia also reported that a greater proportion of patients < 40 (80.4%) presented with metastatic disease compared to patients aged older patients (64.4%) (16).

The reasons of seeing RC at a young age with more severe symptoms have been tryied to explain with various hypotheses in the literature. Advanced stage at diagnosis does not seem to be explained simply by longer time to diagnosis suggests that biologic factors may be important determinants of stage at diagnosis (17). Although there is no proof about the symptom severity at presentation, it is possible that more severe symptoms in patients with advanced disease could have led to more detailed evaluation. It has been suggested that malignancies in young adults display a distinct biology (18). Outcomes are affected by underlying biology and genetics (19-22). In addition, several studies showed that there is higher incidence of genetic CRC syndromes and family history in younger patients (13).

In current study, disease-free survival, and overall survival between young and the elderly population were not statistically significant, though majority of the young patients were represented with advanced disease. In the current study, although there is no difference in terms of overall survival and disease-free survival in terms of age variable, the results in question is found against young-onset. A study conducted with SEER database has shown no statistically significant difference in overall and disease-free survival at 5 years between a cohort of young and elderly patients (23). On the contrary some studies have reported poor prognosis of the favor on young patients (24). Despite the poor prognostic factors in the young group, the survival of the patients with specific to Lynch syndrome is better than their counterparts (25). In the current study, when both overall survival and disease-free survival are examined in detail with prognostic factors, the perineural invasion is suggested as a crucial prognostic factor and all patients with perineural invasion have statistically lower survival. In other recent studies, the most important prognostic factors affecting survival were advanced disease, and adverse histological subtypes (mucinous, and signet ring cell adenocarcinoma) (26).

On the other hand, the main issue seems that how it affects the cost effectiveness and efficacy when bringing down the 50 years criteria for endoscopic screening tests, especially in patients without a family history once the literature analyzed. Increased incidence of RC in young patients, and often diagnosed at high-grades in this group, makes this type of screening favorable to bring down the age criteria. On the contrary, the high cost of screening endoscopic programs and the fact that RC is still less common in this age group compared to the age group over 50 makes it difficult to bring down the age criteria. Considering all these factors, single sigmoidoscopy can be applied to the 40-year and under as a screening test. In a recent multicenter randomized study, a single screening rectosigmoidoscopy reduced CRC incidence by 33 % and mortality 43 % (27).

Our study has some limitations. Our data does not include TNM stage or presence of a residual tumor following surgery with curative intent (the R classification for mesorectal dissection). These are the most crucial prognostic factors in RC (28). Another issue isthe lack of genetic testing for HNPCC or any other genetic disorders predisposing the RC. Eventually the current study is a retrospective study, so prospective studies with more sample size are needed for whether changing the screening age is cost effective or efficacious.

CONCLUSION

RC in young-onset is related with poor prognostic factors such as aggressive histological features, high grade and stage tumors. Above all, because there are no screening tests used widely for especially without history young population, a younger patient tends to frequently present with RC at a higher stage than their older followers. So that, clinicians should pay more attention and interest to

the symptoms and sings of the bowel in younger patients and should not hesitate to perform screening tests such as blood test, or especially rectosigmoidoscopy, etc to be initiate early diagnosis and further treatment.

Competing interests: The authors declare that they have no competing interest.

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