

# Clinicopathological Comparison of Colorectal Cancer in Young and Old Patients

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## Abstract

**Background & Objectives:** Colorectal cancer is the commonest malignancy in the gastrointestinal tract third and the second leading cause of cancer death worldwide. The advanced stages and poor tumor grade of colorectal cancer are likely to be found in younger patients than in older one. The aim of our study was to study the various demographic features that are known to influence developing colorectal cancer and to compare clinicopathological features of colorectal cancer between young and old patients.

**Methods:** This is a retrospective study, conducted over the period from 2015- 2020, where we reviewed medical files, histopathological reports and radiological findings of 200 newly diagnosed colorectal cancer cases that were admitted to Rizgari Hospital/ Clinical Oncology Department, Erbil, Kurdistan of Iraq. The patients aged below 40 years were classified as the “young group”, and those aged 60 years and more were classified as the “old group”. The clinicopathological features in both groups had been compared.

**Results:** The young group and old group consisted of (60) 30% and (140) 70% of patients, respectively. The young group showed a higher percentage of positive family history of cancer in comparison to the old one, and BMI also was statistically significant. Regarding the histopathological grading and pathological staging: grade -II was the most common, (82%) in both groups, and stage III &IV were significantly higher in the young group (83.3%) in comparison to the old group (74.3%).

**Conclusion:** Younger patients had advanced stage and poor tumor grade compared to the old patients.

**Key words:** Clinicopathological ,Colorectal cancer, Young patients.

## Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer in both men and women and it is the commonest malignancy in the gastrointestinal system and the second leading cause of cancer death worldwide.<sup>1-2</sup> Annually, around one million cases over the world are diagnosed as CRC, of which half of them die within 5 years.<sup>3</sup> Colorectal cancer accounts for 9.4% of cancer cases in males and 10.1% in females worldwide however, is not universally common in the world<sup>4</sup>.The definition of what age would be considered young for a patient developing CRC is controversial. Most of studies

defined “young” as those patients under 40 years of age.<sup>5</sup>Generally, CRC is a cancer of the middle aged and older people, and most of them are diagnosed after the age of 55 years, while 2-10% of all CRC cases noted in young patients.<sup>6-7</sup>Some studies have reported that CRC were more aggressive in young patients, and presented with a higher stage, and to have worse histopathological report and radiological findings. On the other hand, CRC detected early in young patients with early pathological tumors, revealed a better survival rate over 5 years.<sup>7</sup>The incidence of CRC is linked to many risk

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factors. Of which age and hereditary factors that human cannot control them. Furthermore, a large number of life style and environmental risk factors that might have an important role in initiation of CRC.<sup>4-8</sup> Hereditary conditions are resulting in nearly 5 to 10% of CRC cases.<sup>9</sup> To decrease the CRC associated morbidity and mortality, there are factors that could affect them such as: healthy diet and weight, daily physical activity and screening strategy programs together with early management and proper intervention treatment.<sup>4</sup> Reviews have reported that emergence of CRC in young age patient groups required workup of presenting bowel symptoms. For that reason, it is

### Materials and methods

From 2015-2020, where we reviewed the medical files, histopathological reports and radiological findings of 200 newly diagnosed CRC cases that were admitted to Rizgari Hospital/ Clinical Oncology Department, Erbil, Kurdistan of Iraq. The study, is approved by the Scientific Research and Ethical Committees of the Kurdistan Board of Medical Specialties. All patients with colorectal cancer (proved by histopathological examination) that had attended the Oncological Department of Rizgary Teaching Hospital/ Erbil and their age <40 years and  $\geq 60$  years with complete records of medical files, and with histopathology report and radiological findings to report the tumor stage and grade are included to this study. Patients aged < 40 years were classified as the "young group" (Group Y, n = 60), and the patients aged  $\geq 60$  years were classified as the "old group" (Group O, n = 140). We excluded in this study patients with previous history of cancer or their medical files and documents are incomplete. During the research period, 245 patients' files matched the age criterion, of which, 200 patients were chosen to this research, while 40 patients have been excluded because their files records are incomplete

important for CRC in young patient and put strong strategies for the diagnosis and early management of the cancer. Patients neglect these early symptoms such as persistent abdominal cramps, changing in bowel habits, weakness, fatigue and unexplained weight loss or much common, the doctors insufficiently investigate them.<sup>10-11</sup> The aim of our study was to study the various demographic features that are known to influence the development of CRC as family history of cancer, BMI, smoking, drinking, blood group, Rhesus group, residency, marital status, and to compare clinicopathological features of CRC between young and old patients.

or their contact number is incorrect. Patient's age between 40-59 years, previous history of cancer and patients with incomplete documents are excluded from the study. For all patients, vital parameters including weight, height, the body mass index (BMI) were calculated on the basis of routine procedure of weight in kilograms divided by height in meters squared and a BMI of <18.5 is underweight, 25–29.9 is overweight, BMI of >30 is obese, while, BMI of 18.5–24.9 is considered as normal<sup>12</sup>. A level of serum Carcinoembryonic Antigen (CEA) equal to 5 ng/ml or more than that was recorded as abnormal. We staged the tumors according to the American Joint Committee on Cancer (AJCC), TNM staging system, eighth edition<sup>13</sup>. We have performed the statistical analyses using SPSS version 24.0. The categorical demographic variables and the descriptive measures were presented as percentages and frequencies while the continuous variables have been reported as the mean  $\pm$  SD and range. The percent of categorical variables had been compared between both groups by using the Pearson's Chi-square test and Fisher's exact test if it was appropriate. Relations between grades,

stages and histopathology were determined by using the chi-square test. All tests are

two sided. A p-value is considered statistically significant when it is ( $\leq 0.05$ ).

### Results

In this study, there were 200 newly diagnosed 96 (48%) females and 104 (52%) males through the period, from January 2015 to January 2020. At diagnosis, the mean age of the patients was  $58.39 \pm 17.2$  years with a range of 16–86 years. For the young group the mean age was  $33.67 \pm 5.26$  years and a range of 16–39 years while in the old group the mean age was  $68.99 \pm 5.61$  years ranged from 64–86 years. sixty (30%) patients aged < 40 years from total numbers of the CRC patients that were included in the research

(the young group Y) and the remaining 140 (70%) patients were  $\geq 60$  years (the old group O) including 28 males (46.7%) and 76 (54.35%), respectively, with no statistically significant difference in gender between the above two groups ( $p = 0.323$ ). Young CRC patients group showed a higher percentage of positive family history of cancer in comparison to the old CRC patients' group, ( $p < 0.001$ ). Also, BMI, was statistically significant ( $p = 0.006$ ).

**Table (1):** Patients demographical features based on patients' age group.

Variable	Category	Total (n = 200 (100%))	Young group (n = 60(30%))	Old group (n=140(70%))	p value
Gender					0.323
	Male	104 (52%)	28 (46.7%)	76 (54.3%)	
	Female	96 (48%)	32 (53.3%)	64 (45.7%)	
Family history of cancer					<0.001
	Positive	52 (26%)	32 (53.3%)	20 (14.3%)	
	Negative	148 (74%)	28 (46.7%)	120 (85.7%)	
Blood group					0.210
	A	66 (33%)	16 (26.7%)	50 (35.7%)	
	B	42 (21%)	10 (%)	32 (22.9%)	
	AB	18 (9%)	8 (%)	10 (7.1%)	
	O	74 (37%)	26 (%)	48 (34.3 %)	
Rh					0.781
	positive	184 (92%)	56 (93.3%)	128 (91.4%)	
	negative	16 (8%)	4 (6.7%)	12 (8.6%)	
Residency					0.746
	Rural	70 (35%)	22 (36.7%)	48 (34.3%)	
	Urban	130 (65%)	38 (63.3%)	92 (65.7%)	
Education					<0.001

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	Educated	78 (39%)	38 (63.3%)	40 (28.6%)	
	Non-educated	122 (61%)	22 (36.7%)	100 (71.4%)	
Marital status					<0.001
	Married	174 (87%)	36 (60%)	138 (98.6%)	
	Single	26 (13%)	24 (40%)	2 (1.4%)	
Smoking					0.805
	Yes	96 (48%)	28 (46.7%)	68 (48.6%)	
	No	104 (52%)	32 (53.3%)	72 (51.4%)	
Alcohol					0.304
	Yes	20 (10%)	4 (6.7%)	16 (11.4%)	
	No	180 (90%)	56 (93.3)	124 (88.6%)	
BMI					0.006
	≤ 25	100 (50%)	24 (40%)	76 (54.3%)	
	26-30	50 (25%)	12 (20%)	38 (27.1%)	
	>30	50 (25%)	24 (40%)	26 (18.6%)	

In contract, no statistically significant difference was reported between the two groups in relevance to site of the tumor, diagnostic radiology, pre-operative serum CEA, colonoscopy, surgery and treatment Table(2). Tumors were found in the segments as following: 74 (37%) in the left

side of colon 38(19%) in the right side of colon, and 88 (44%) were in the rectum. Adjuvant chemotherapy was the choice of treatment in (73.3%) of young CRC patients and (87.5%) of old CRC patients with no statistically significant difference between the two groups. Table(2).

**Table (2):** Patients clinical features based on patients' age group.

Variable	Category	Total (n = 200 (100%))	Young group (n =60(30%))	Old group (n=140(70%))	p value
Site					0.178
	right	38 (19%)	8 (13.3%)	30 (21.4%)	
	left	74 (37%)	20 (33.3%)	54 (38.6%)	
	rectum	88 (44%)	32 (53.3%)	56 (40%)	
Diagnostic Radiology					0.526
	CT	164 (82%)	48 (80%)	116 (82.9%)	
	MRI	2 (1%)	0 (0%)	2 (1.4%)	
	PET	2 (1%)	0 (0%)	2 (1.4%)	
	ALL	32 (16%)	12 (20%)	20 (14.3%)	
CEA					0.120

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	<5	110 (55%)	28 (46.7%)	82 (58.6%)	
	>5	90 (45%)	32 (53.3%)	58 (41.4%)	
Performance status					0.032
	0	158 (79%)	54 (90%)	104 (74.3%)	
	1	28 (14%)	4 (6.7%)	24 (17.1%)	
	2	8 (4%)	0 (0%)	8 (5.7%)	
	3	6 (3%)	2 (3.3%)	4(2.9%)	
Colonoscopy					0.999
	Yes	198 (99%)	60 (100%)	138 (98.6%)	
	No	2 (1%)	0 (0%)	2 (1.4%)	
Surgery					0.746
	Yes	130 (65%)	40 (66.7%)	90 (64.3%)	
	No	70 (35%)	20 (33.3%)	50 (35.7%)	
Treatment					0.365
	Adjuvant Chemotherapy	154 (77%)	44 (73.3%)	110 (78.5%)	
	Concurrent Chemoradiation	24 (12%)	10 (16.7%)	14 (10%)	
	BST	4 (2%)	0 (0%)	4 (2.9%)	
	Observation	18 (9%)	6 (10%)	12 8.6%)	

The most common histopathological type in both groups was adenocarcinoma (93.3%) in young group and (92.9%) in old group with no statistically significant difference. Grade -II was the most common histopathological grade in both groups (82%), followed by grade III (14%), grade I (4%), in young group grade II (70%), grade III (26.7%) and grade I (3.3%) while in old group grade II (87.1%), grade III (8.6%) and grade I (4.3%) with statistically significant

difference between them ( $p < 0.003$ ). According to the pathological stage: stage III & IV was common in both groups (67%), stage III & IV was higher in the young group (83.3%) than in old group (74.3%) with statistically significant difference between them ( $p < 0.001$ ). Lymphovascular invasion and Perineural invasion were significantly different between the two groups ( $p = 0.031$ ), and (0.005), respectively. Table(3).

**Table (3):** Pathological characteristics of the CRC patients.

Variable	Category	Total (n = 200 (100%))	Young group (n =60(30%))	Old group (n=140(70%))	p value
Histopathological type					0.999

	Adenocarcinoma	186 (93%)	56 (93.3%)	130 (92.9%)	
	others	14 (7%)	4 (6.7%)	10 (7.1%)	
Grade					0.003
	I	8 (4%)	2 (3.3%)	6 (4.3%)	
	II	164 (82%)	42 (70%)	122 (87.1%)	
	III	28 (14%)	16 (26.7%)	12 (8.6%)	
Stage					<0.001
	I	18 (9%)	6 (10%)	12 (8.6%)	
	II	28 (14%)	4 (6.7%)	24 (17.1%)	
	III	78 (39%)	36 (60%)	42 (30%)	
	IV	76 (38%)	14 (23.3%)	62 (44.3%)	
Lymphovascular invasion					0.031
	Yes	30 (15%)	14 (23.3%)	16 (11.4%)	
	No	170 (85%)	46 (76.7%)	124 (88.6%)	
Perineural invasion					0.005
	Yes	42 (21%)	20 (33.3%)	22 (15.7%)	
	No	158 (79%)	40 (66.7%)	118 (84.3%)	

## Discussion

There is no agreement on the exact meaning of the word (young) in CRC patients. In few reviews, they considered patients who were under 50 years as young patients,<sup>14-16</sup> while other authors considered young patients till the age of 30 years.<sup>17</sup> However, most of studies agreed on the age 40 years or below as the young CRC patients, as has been used in current research.<sup>18-21</sup> The relative incidence of CRC in the < 40 years age group varies by country. Numerous Asian and African countries have significantly higher proportional figures. In the present study, 30% of cases were < 40yrs of age in agreement with studies.<sup>22-26</sup> This suggests a possible hidden familial risk for colon cancer and identifies the need for a mass screening programs for CRC. In contrast, previous studies revealed that CRC is more common in the patients < 40 years age group, and it is only in 7% of patients

< 40 years.<sup>18-19</sup> Iriniz et al reported a prevalence of 17.5% in the cases aged < 40 years.<sup>27</sup> In 2009, Charua published a research that contained patient data from the previous 20 years and observed a CRC prevalence of 6.4% in the patients aged < 40 years.<sup>28</sup> There was no significant difference among CRC patients < 40 years and  $\geq$  60 years according to the gender. In this research, 52% of the total patients and 46.7% of the patients were < 40 years old and 54.3% of the patients  $\geq$  60 years old were males. This agrees with some previous studies,<sup>29</sup> unlike others where, the proportion of females exceeded that of males.<sup>8</sup> The tumor stage and grade are important negative factors which influence the survival of the cases. Stage I disease in patients had a better prognosis compared to patients with stage IV disease. In addition, decreased survival was related to a high-grade tumor (grade I). The

proportion of patients with stage IV disease was higher among young patients. The young group patients had more aggressive tumor type and higher advanced stages of the disease particularly stage IV<sup>30-31</sup>. In this study, the most common histopathological type was adenocarcinoma (93%) with no significant difference between young and old groups ( $p=0.999$ ), and we reported a significant difference in the stage of CRC between the old group and young group patients ( $p<0.001$ ). A poor grade (grade III) was more in the young group (26.7%) compared to old group (8.6%) and ( $p=0.003$ ) which was also observed in previous researches.<sup>31-32</sup> Delayed diagnosis

### Conclusion

Younger age (< 40 years) is an important risk factor leading to a higher aggressive tumor type or more advanced stage. Additionally, the younger patients had a poor prognosis compared to the older patients. Screening and other strategies

### Recommendation

Further researches are needed to better understand the characteristics of the disease in CRC patients below 40 years, especially, the factors that may be led to differences in clinicopathological features

### Conflicts of interest

There were no conflicts of interest.

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in the young group patients may be the cause of the higher stages of CRC, but the old group patients visit hospitals for different reasons which might make early diagnosis in the Iraqi people. In addition, in other countries among older patients, the increase of the probability of diagnosis at lower stages due to programs for CRC screening.<sup>31-33</sup> In this study, 44% of tumors were found in the rectum (53.3% in young group, 40% in old group) and 37% of the tumors were located in left site colon (33.3% in young group, 38.6% in old group) ( $p=0.178$ ). Many studies found more than 33% of tumors are in the sigmoid colon and the rectum<sup>28-29</sup>.

what other strategies (either shortly explain or remove) of early detection for young age people may be lead to early detection of the tumor and improve the survival of young patients.

between young and old groups. The results of these researches will help modify strategies of the treatment and, finally, the CRC patient's outcomes.

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