Clinicopathological and Survival Outcome of Young Onset Colorectal Cancer: 10 Years Retrospective Study in Upper Egypt

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Abstract:

Background: Young-onset colorectal cancers (yCRCs) have increased globally over the last several decades by 2.8%–36.5%. The publications about yCRC in developing countries in general and Egypt specifically are scarce. Moreover, there is a lack of large single-center or multicenter evaluations of yCRC in developing countries.

Patients and Methods: We evaluated the clinicopathological characteristics and survival outcomes in patients with colorectal cancer who were aged < 50 years old at South Egypt Cancer Institute from 2008 to 2017.

Results: There were 744 patients with a median age of 40 years (range: 18 – 49 years). yCRC represented 49.9% of all colorectal cancers. The commonest symptoms among the patients were bleeding (37.1%) and pain (36%) followed by obstruction (21.9%). rectal/rectosigmoid junction cancers represent 43.3% of the whole cohort. In the younger age group (18 - 29 years) we found a higher incidence of pain and obstructive manifestations, signet-ring carcinoma, lung, and peritoneal metastases in comparison with the older age group (40 - 49 years). There was a significantly higher relapse rate with a lower five- and ten-years disease free and overall survival in the lower age group.

Conclusion: There is a higher burden of yCRCs, advanced stage at presentation, and a lower survival outcome in the age group between 18 and 29 years, but the survival rates in the current study were higher compared with previous publications on yCRC worldwide. So, lowering the age for screening to be below 45 years is crucial, which is already updated. yCRC represents a nation problem necessitating further studies.

Key Words: Young-onset colorectal cancers (yCRCs); Egypt; clinicopathological characteristics; survival outcomes.

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Introduction:

Colorectal cancer (CRC) is the third most common cancer in both sexes worldwide and the second most common cause of cancer death, accounting for an estimated 1.9 million new cancer diagnoses and 935,000 deaths in 2020. In developed countries, CRC incidence rates are approximately four times higher than in developing countries [1]. In Egypt; CRC is the 7th commonest cancer, representing 3.47% of male cancers and 3% of female cancers [2].

More than 90% of cases of CRC occur in people over the age of 55, making it a disease of the elderly [3]. While the incidence and death rates of CRC have decreased in people over the age of 50, the opposite is true for people under the age of 50 [4]. Early-onset colorectal cancers (EOCRCs) or Young-onset colorectal cancers (yCRCs), which have largely been defined as adults younger than 50 years of age [5], have increased globally over the last several decades by 2.8%–36.5%; however, this does not indicate an increase in the incidence of hereditary CRCs [6,7].

The incidence of CRC is increasing among young people in the Middle East and other parts of the world [8]. In Egypt, CRC was diagnosed in 25-38% of patients aged 40 years or younger, according to national

reports [9-11] which represent a major public health issue that must be addressed. Several studies on yCRC have yielded contradictory results in terms of survival outcome when compared to survival in older people [12-14].

Aim

We performed this retrospective study at South Egypt Cancer Institute, Assiut University on CRC patients younger than 50 years to evaluate:

1- Clinicopathological characteristics of yCRC
2- Survival outcomes {disease free survival (DFS), progression free survival (PFS) and overall survival (OS) of yCRC
3- Factors of prognostic significance, updating and comparing our results with previous reports locally and internationally and providing a general national overview in Egypt on yCRC.

Patients and Methods:

Selection criteria for the study:

Our Institutional database was collected for all patients who were aged < 50 years at presentation with histologically confirmed colorectal cancers undergoing either curative or palliative multimodality management from January 1, 2008, to December 31, 2017. Patients with incomplete documents and a previous history of cancer or genetic syndromes were excluded from the study. Ethical approval was obtained from our institutional ethical committee SECI-IRB by number IORG0006563-530

Data collection and extraction:

The medical records of 744 patients who met the inclusion criteria were retrospectively reviewed to extract the study's relevant data. Data that were collected included age, gender, smoking status, family history of cancer diseases, presenting symptoms, tumor location, stage, and differentiation of the tumor, preoperative carcinoembryonic antigen (CEA), treatment adopted, treatment and survival outcome (the date of local recurrence, distant metastases, or death). Tumors were staged according to the American Joint Committee on Cancer (AJCC), TNM staging system, eighth edition.

Follow-up

Follow-up information was obtained from the patient's clinical files. The patients were followed up by regular clinical examination, colonoscopy, CT scans of the chest, CT scans or MRI scans of the pelvis and abdomen, and serum carcinoembryonic antigen (CEA) assay, every 3 months for the first two years and every 6 months thereafter. The most recent follow-up date was recorded for all patients. Recurrence at the anastomotic site, peri-anastomotic soft tissue, and regional nodes was recorded as loco-regional. Visceral and non-regional nodal recurrences were defined as distant recurrence. Overall survival (OS) was calculated from the date of diagnosis to the date of death or last follow-up; disease-free survival (DFS) was calculated from the date of diagnosis to date of relapse (locoregional or distant) or last follow-up; and progression-free survival (PFS) was calculated from the date of diagnosis to the date of disease progression or, the date of death.

Statistical analysis:

All data were collected, tabulated, and statistically analyzed using SPSS 22.0 for windows [15] and MedCalc 18 for windows [16]. Continuous Quantitative variables were expressed as the mean (+/- SD) for normally distributed data or the median (range) for abnormally distributed data, and categorical qualitative variables were expressed as absolute frequencies (number) & relative frequencies (percentage). Categorical data were compared using the Chi-square test or Fisher's exact test when appropriate. Stratification of survival was done according to prognostic factors. These time-to-event distributions were estimated using the method of Kaplan-Meier plot and compared using the two-sided exact log-rank test. Cox proportional-hazards regression analysis was used to perform univariate and multivariate models to find independent predictors for locoregional recurrence (LRR). All tests were two-sided. P-value < 0.05 was considered statistically significant.

Results:

In this study, there were 744 newly diagnosed CRC patients (387 males and 357 females) who were followed up until May 2021. The median age at presentation was 40 years (range: 18 – 49 years). The presence of comorbidities at the time of CRC diagnosis was encountered in 11.3% of the cases with hypertension being the most frequent one. Overall, 622 (83.6%) patients had an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of one at diagnosis. The commonest symptoms were bleeding (37.1%) and pain (36%) followed by obstruction (21.9%). Sixty-six percent of the patients had a left-sided primary tumor as compared with 34.0% with right-sided tumors. Colon cancer comprised 56.7% of the cases, the remaining being rectal/rectosigmoid junction cancers. For operable patients (n=622, 83.6%), the most appropriate surgical technique was selected based on the tumor location as well as the clinico-radiological status. Serum CEA levels of 577 patients were available in the clinical files and 25.3% had elevated levels at presentation. Elevated serum CA 19-9 levels were observed in 15.1% of the patients at diagnosis.

Relative frequency of young-onset CRC (yCRC)

During the period between 2008 and 2017 in South Egypt Cancer Institute, yCRC represented 44.3% to 56.9% of all CRC. The relative frequency of young-onset CRC (yCRC) among all CRC cases during the period between 2008 and 2017 was shown in Table 1.

Clinical parameters

The mean age of the studied patients was 38.5 years. Four hundred and twelve patients (55.4%) had an age between 40 and 49 years. Male represented 52% of patients. Most of the patients didn't have comorbidities and the most frequent comorbidity was hypertension (5%). Most of the patients (83.6%) had ECOG performance status 1. The most common presentation was bleeding (37.1%) followed by pain (36%) and obstruction (21.9%). The most frequent site of the tumor was the rectum (39.8%) followed by the right colon (32.8%). Four hundred and ninety-one patients (66%) had left-sided colon cancer. The most common type of operation was lower anterior resection (34%) followed by right hemicolectomy (25.1%). One hundred and eighty-eight patients (25.3%) had elevated serum CEA. One hundred and twelve patients (15.1%) had elevated serum CA19-9. The most common sites of metastases were the liver (9.9%) followed by peritoneum (6.9%) and the lung (2.6%) Bone metastasis was detected in 0.9% of patients. Detailed clinical parameters and staging among the studied young-onset CRC patients were shown in Table 2.

Pathological parameters

A review of pathologic reports revealed that the majority of patients had pathological T3 (44.1%) tumors and in 439 patients (59.0%) there was clinical lymph node involvement, 60 (8.1%) with LVI, 11 (1.5) with PNI. The most common histologic subtype was adenocarcinoma (79.2%). Moderately differentiated tumors were detected in 66.4% of the cases, whereas 21.2% of the cases had poorly differentiated tumors. One hundred and thirty-six (18.3%) cases presented with metastasis, and of those, nine cases were in the liver. Detailed pathological parameters and staging among the studied young-onset CRC patients were shown in Table 3.

Treatment in patients with yCRCs:

Patients with stage II or III rectal cancer were treated with neoadjuvant chemoradiation (CRT) with concomitant capecitabine or 5FU. Patients were scheduled for curative surgery 6-8 weeks after completion of CRT [17]. A total of 622 (83.6%) patients underwent curative surgical resection. Patients with high-risk stage II and III disease received 6 months of oxaliplatin-based therapy with either modified FOLFOX6 or CAPEOX. Chemotherapy regimens included, CapeOX: oxaliplatin 130 mg/m2 on day 1, capecitabine 1000 mg/m2 twice daily days 1-14 every 3 weeks; mFOLF¬OX6: Oxaliplatin 85 mg/m2 IV, day 1, leucovorin 400 mg/m2 IV day 1, 5-FU 400 mg/m2 IV bolus on day 1, then 1200 mg/m2/day ×2 days (total 2400 mg/m2 over 46-48 hours) continuous infusion to be repeated every two weeks or Capecitabine: 1000-1250 mg/m2 PO twice daily days 1-14 every 3 weeks. A total of 136 (18.3%) were metastatic at presentation and 133 patients (17.9%) were treated with combination chemotherapy (oxaliplatin and/or irinotecan with a fluoropyrimidine). In addition, 20 (2.7%) patients with metastatic disease underwent palliative colostomy. Management of the studied young-onset CRC patients was shown in table 4.

Treatment Outcome

The median follow-up duration was 5 years (range from 4 months to 120 months). Actuarial local recurrence, distant metastasis, and relapse rates were 11%, 20.9%, and 29.3%, respectively, among 608 patients presented with stage I to stage III disease. The actuarial progression rate was 80.1% among 136 patients who presented with stage IV disease. Three-year progression-free survival was 8.8%. The actuarial mortality rate in the whole study cohort was 20.6%. Ten-year DFS and OS were 66.3% and 69.4%, respectively. The outcome among the studied young-onset CRC patients was shown in Figure 1.

Relationship between age group and clinicopathological parameters

In the age group between 18 and 29 years old, we found higher incidence of female predominance (p-value=0.006), pain and obstructive manifestations (p-value<0.001), mucinous and signet ring carcinoma (p-value<0.001), positive surgical margins (p-value=0.033), advanced TNM staging (stage III/IV) (p-value<0.001), lung metastases (p-value=0.049), and peritoneal metastases (p-value<0.001) in comparison with the age group between 40 and 49 years old. On the opposite side, patients in the age group 40 to 49 years old have significant hypertensive and diabetic patients (p-value<0.001), bleeding and bowel habits changes (p-value<0.001), poorly differentiated (p-value<0.001), LVI (p-value<0.001), and raising CEA and CA19.9 (p-value<0.001) in comparison with the age group between 18and 29 years old. Detailed relationships between age group and clinicopathological parameters were shown in Table 5, 6.

Relationship between age group and outcome

There was significantly higher actuarial local recurrence (LR) in the age group 18 and 29 years in comparison with the age group between 40 and 49 years (21.3% vs. 5.6%, p-value<0.001). Moreover, higher incidence of distant metastases (DM) (32% vs. 17.1%, p-value=0.010) in comparison with the age group 40 and 49 years old. Five and ten years DFS (72.8 % and 72.2% vs. 50.0 % and 50.5 %, p-value<0.001) and OS (76.2 % and 72.3% vs. 62.2% and 33.5%, p-value<0.001) were significantly higher in age group between 40 and 49 in comparison with age group 18 and 29 years, respectively. There was a higher rate of progression in metastatic setting in the age group between 40 and 49 when compared with those between 18 and 29 years (95.9% vs. 45.2%, p-value<0.001). Relationship between age group and the outcome was shown in Table 7.

Relationship between type of disease at presentation and clinicopathological parameters

There was higher incidence of metastatic patients in the age group between 40 and 49 years in relation to those with 18 and 29 years (53.7% vs. 22.8%, p-

value<0.001). Female gender (69.9% vs. 30.1%, p-value<0.001), Left colon cancer (50.7% vs. 49.3%, p-value<0.001), grade III (33.1% vs. 1.5% for grade I, p-value<0.001), T3/T4 (6.6% and 5.1% vs. 0% and 0.7% for T1/T2, respectively, p-value<0.001), and N2 (6.6% vs. 0% for N1, p-value<0.001) were common in metastatic disease. Detailed relationship between type of disease at presentation and clinicopathological parameters were shown in Table 8, 9.

Relationship between type of disease at presentation and outcome

Five and ten years OS was significantly lower in metastatic patients in comparison with non-metastatic patients (42.8% and 0% vs. 84.3% and 79.3%, respectively, p-value<0.001, respectively). Relationship between type of disease at presentation and the outcome was shown in Table 10.

Predictors of survival in Univariate and Multivariate Analyses

Overall survival

Both the histopathological grade and type of operation (P< 0.001) stood as the most powerful predictors of the OS in the multivariable analysis, followed in significance by AJCC (American Joint Committee on Cancer) staging group and comorbidities (P= 0.004); while other statistically significant prognostic factors in the univariate analysis as the age, surgical margins lost their significance in the multivariate model. Predictors of OS in the univariable and multivariable analysis were described in Table 11.

Disease free survival

The stage (P< 0.001) was found as the most powerful predictors of the DFS in the multivariable analysis followed in significance by age group (P= 0.001), histopathological grade (P= 0.010), and comorbidities (P= 0.046). Predictors of DFS in the univariable and multivariable analysis were described in Table 12.

Discussion:

In our current study during the period between 2008 and 2017, yCRCs represented 2.9% and 49.9% of all diagnosed cancers and colorectal carcinoma patients, respectively. So, there is a dramatic increase in the incidence of yCRC as compared with previous reports in Egypt with 25-39.8% of yCRC diagnosed in patients younger than 50 years old [9,10, 18-22]. Moreover, this incidence rate is higher also than previously recorded in other Middle East countries [23-27], Europe [28- 30], and the United States [31-33].

The maximum annual increase in the relative frequency of colon cancers overall diagnoses colorectal carcinoma patients in the current study was 11.1 percent which is markedly higher than that reported by Murphy et al, 2020 concluding that there was a 2.2% annual increase in the incidence rate of CRC for patients under 50 years old during the period between 2012 and 2016 [34]. This increase may be attributed to the westernization of lifestyle with a diet rich in processed meat, increasing prevalence of smoking, and obesity which all are known risk factors for CRC [35-38].

The median age of the study cohort was 40 years (18–49) and the Majority of the patients belonged to the age group of 40–49 years (n = 412; 55.5%). These results are in agreement with some previous studies [20-21, 23, 39-42] and also contradictory with others that show most patients aged between 30 and 39 years [10, 43-47].

Similar to the majority of the studies, the most common presenting symptom is bleeding per rectum followed by abdominal pain [10, 24,27,42,43,45,47]. The rectum was the commonly affected site followed by the right colon which was consistent with various studies [7, 10, 24, 32, 41-43, 46].

The patients in the current study presented with more advanced stage (III and IV), higher pathological grading, and signet ring adenocarcinoma reflecting the aggressive nature of yCRC. These results are in good agreement with other studies showing the same bad characteristics [45-46, 48-49]. The combined stage III and IV in the current study represented 75% which was higher than previous studies in Egypt [9, 20, 22, 32] and globally [26, 42, 50, 51].Similarly, signet ring adenocarcinoma was found in 8.6% of patients which was higher than that by Khougali et al, who was found that the rate of signet ring adenocarcinoma in Sudan was 4.9% [23], also rate of signet ring adenocarcinoma in our study was higher than in other studies [10, 39], but lower rate than a study done by Motepalli et al, who found that the rate of signet ring carcinoma was 35.2% [52].

The most common sites of metastases at presentation were the liver (9.9%) followed by peritoneal metastasis (6.9%). These results were similar to a study done by Haleshappa et al, who reported that the most common sites of metastases at presentation were liver (46.9%) followed by metastases in the peritoneum (34.3%) [43].

In the current study, the actuarial local recurrence rate was 11%, the actuarial distant metastasis rate was 20.9%, and the actuarial relapse rate was 29.3%. The mean DFS was 89.76 months and the 3-year, 5-year, and 10 years DFS rates were 75.3%, 67.6%, and 66.3% respectively. Moreover, the mean OS was 97.8 months and 3-year, 5-year, and 10 years OS rate was 84%, 77.4%, and 69.4% respectively.

As regards the survival rates, we reported the higher DFS and OS in comparison with other studies in the Middle East [24-26, 53, 54], European Union [41], USA [32, 33], and East Asian countries [55]. Improvement in survival may be explained by overall good performance status, fewer comorbidities, and tolerability of combination chemotherapy. Moreover, the 5- years DFS and OS were statistically significant in the age group from 40-49 years old in comparison with the age group 18-29 years old which have worse prognostic clinicopathological features, this is in agreement with other studies showing the survival advantage in the same age group between 40-49 years old [39, 41].

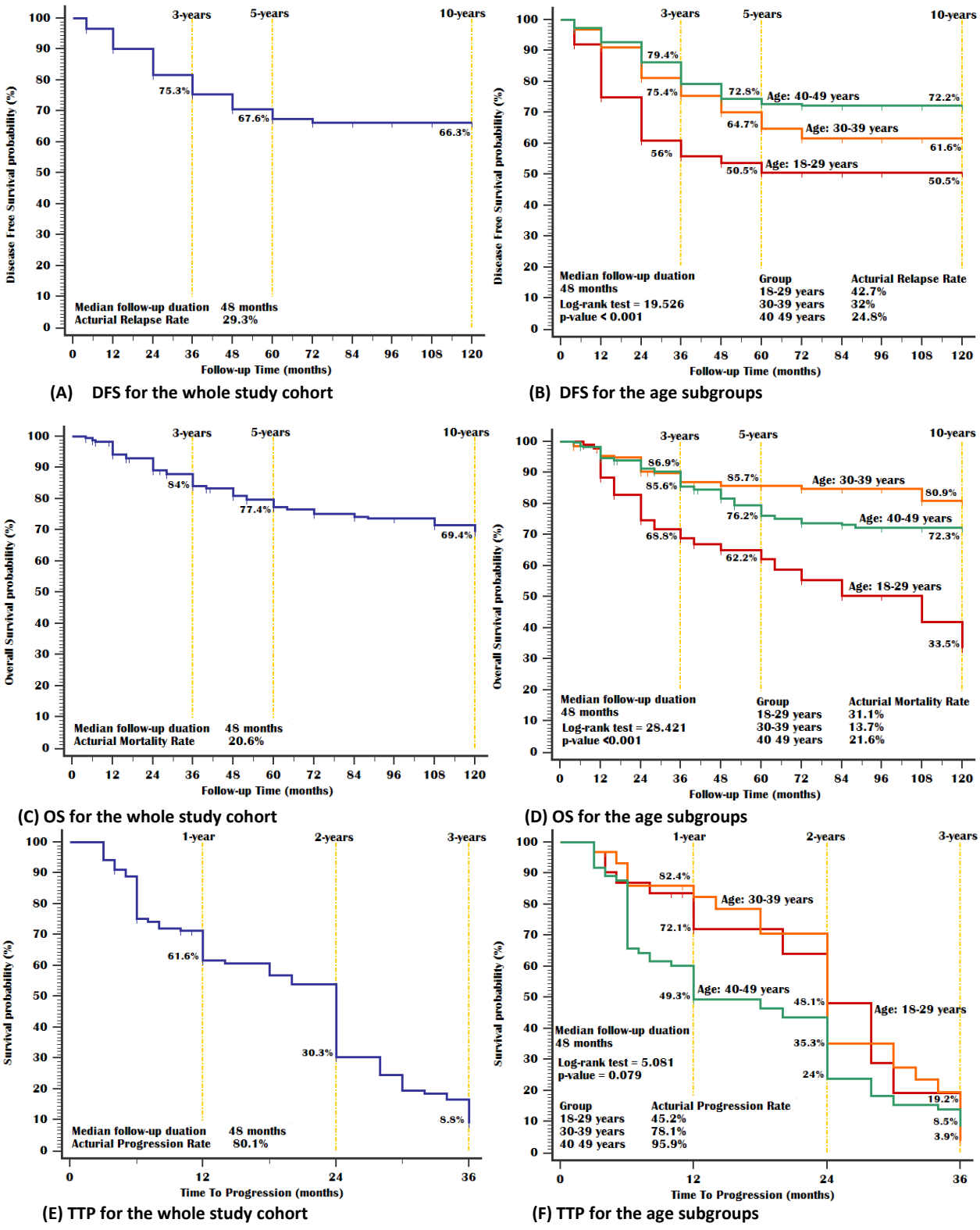

Figure (1): Kaplan Meier Plot showing treatment outcomes.

(A) DFS for the whole study cohort (B) DFS for the age subgroups
(C) OS for the whole study cohort (D) OS for the age subgroups
(E) TTP for the whole study cohort (F) TTP for the age subgroups

Table 1: Relative frequency of young onset CRC (yCRC) in South Egypt Cancer Institute (SECI) during the period between 2008 and 2017.

	Both sex		Male		Female	
Year	**yCRC/All cancer**	**yCRC/CRC**	**yCRC/All cancer**	**yCRC/CRC**	**yCRC/All cancer**	**yCRC/CRC**
2008	2.8%	55.6%	3.6%	60.4%	2.0%	48.6%
2009	2.8%	49.5%	3.9%	57.1%	1.5%	36.6%
2010	2.6%	47.2%	2.5%	48.1%	2.7%	46.4%
2011	3.1%	50.0%	2.7%	47.5%	3.4%	51.9%
2012	2.5%	47.5%	3.1%	46.3%	2.1%	49.1%
2013	2.2%	45.8%	3.3%	52.3%	1.2%	35.7%
2014	2.8%	56.9%	3.7%	56.5%	2.2%	57.4%
2015	3.7%	52.5%	4.9%	56.8%	2.8%	48.1%
2016	2.8%	44.3%	4.0%	52.3%	1.9%	35.4%
2017	3.3%	51.3%	3.6%	51.5%	3.1%	51.0%
Total	2.9%	49.9%	3.5%	52.9%	2.3%	46.6%

Table (2): Clinical parameters among the studied young-onset CRC patients (N=744).

Clinical parameters	All studied patients (N=744)	
	No.	%
Age (years)		
Mean±SD	38.56 ±7.81	
Median (Range)	40 (18 – 49)	
18-29 years	106	14.2%
30-39 years	226	30.4%
40-49 years	412	55.4%
Sex		
Male	387	52%
Female	357	48%
Comorbidity		
Absent	660	88.7%
HTN	37	5%
DM	33	4.4%
Cardiac	2	0.3%
Hepatic	1	0.1%
HTN & DM	11	1.5%
ECOG PS		
ECOG 1	622	83.6%
ECOG 2	119	16%
ECOG 3	3	0.4%
Presentation		
Obstruction	163	21.9%
Perforation	3	0.4%
Pain	268	36%
Bleeding	276	37.1%
Change in bowel habit	34	4.6%
Site of tumor		
Right colon	224	32.8%
Transverse colon	9	1.2%
Left colon	111	14.9%
Sigmoid colon	58	7.8%
Rectosigmoid	26	3.5%
Rectum	296	39.8%

Clinical parameters	All studied patients (N=744)	
	No.	%
Sidedness		
Right colon cancer	253	34%
Left colon cancer	491	66%
Type of operation		
No surgery	102	13.7%
Rt hemicolectomy	187	25.1%
Trans. hemicolectomy	4	0.5%
Lt hemicolectomy	89	12%
Sigmoidectomy	27	3.6%
LAR	253	34%
APR	48	6.5%
Total/Subtotal colectomy	14	1.9%
Colostomy	20	2.7%
CEA		
Normal	389	52.3%
Raised	188	25.3%
Missed	167	22.4%
CA19-9		
Normal	427	57.4%
Raised	112	15.1%
Missed	205	27.6%
Site of metastases		
Absent	608	81.7%
Liver	61	8.2%
Lung	13	1.7%
Peritoneal	44	5.9%
Bone	3	0.4%
Liver + Lung	4	0.5%
Liver + Peritoneal	7	0.9%
Liver + Bone	2	0.3%
Lung + Bone	2	0.3%

Categorical variables were expressed as number (percentage); Continuous variables were expressed as mean ± SD & median (range).

Table (3): Pathological parameters among the studied young-onset CRC patients (N=744).

Clinicopathological parameters	All studied patients (N=744)		Clinicopathological parameters	All studied patients (N=744)	
	No.	%		No.	%
Histopathology			T		
Conventional adenocarcinoma	589	79.2%	T1	25	3.4%
Mucinous adenocarcinoma	91	12.2%	T2	121	16.3%
Signet ring carcinoma	64	8.6%	T3	328	44.1%
			T4	151	20.3%
			Not applicable	119	16%
Grade			N		
Grade I	92	12.4%	N0	186	25%
Grade II	494	66.4%	N1	275	37%
Grade III	158	21.2%	N2	164	22%
			Not applicable	119	16%
Surgical margins			M		
Negative	621	83.5%	M0	608	81.7%
Positive	4	0.5%	M1	136	18.3%
Not applicable	119	16%			
LVI			AJCC stage group		
Absent	403	54.2%	Stage I	39	5.2%
Present	60	8.1%	Stage II	147	19.8%
Missed	162	21.8%	Stage III	422	56.7%
Not applicable	119	16%	Stage IV	136	18.3%
PNI					
Absent	453	60.9%			
Present	11	1.5%			
Missed	161	21.6%			
Not applicable	119	16%			

Categorical variables were expressed as number (percentage).

Table (4): Management of the studied young-onset CRC patients (N=744).

Management	All studied patients (N=744)		Age group					
			18-29 years (N=106)		30-39 years (N=225)		40-49 years (N=412)	
	No.	%	No.	%	No.	%	No.	%
Chemotherapy								
No	82	11%	6	5.7%	27	11.9%	49	11.9%
Neoadjuvant/Adjuvant	529	71.1%	69	65.1%	167	73.9%	293	71.1%
Palliative	133	17.9%	31	29.2%	32	14.2%	70	17%
Type of chemotherapy								
No	82	11%	6	5.7%	27	11.9%	49	11.9%
XELOX	37	5%	6	5.7%	8	3.5%	23	5.6%
FOLFOX	484	65.1%	76	71.7%	137	60.6%	271	65.8%
FOLFIRI	10	1.3%	1	0.9%	1	0.4%	8	1.9%
Xeloda	18	2.4%	1	0.9%	3	1.3%	14	3.4%
5FU/Leucovorin	113	15.2%	16	15.1%	50	22.1%	47	11.4%

Categorical variables were expressed as number (percentage); a: Chi-square test; p-value < 0.05 is significant.

Table (5): Relationship between age group and clinical parameters.

Clinical parameters	All studied patients (N=744)		Age group						p-value[a]
			18-29 years (N=106)		30-39 years (N=225)		40-49 years (N=412)		
	No.	%	No.	%	No.	%	No.	%	
Sex									
Male	387	52%	43	40.6%	110	48.7%	234	56.8%	0.006
Female	357	48%	63	59.4%	116	51.3%	178	43.2%	
Comorbidity									
Absent	660	88.7%	99	93.4%	222	98.2%	339	82.3%	<0.001
HTN	37	5%	1	0.9%	2	0.9%	34	8.3%	
DM	33	4.4%	4	3.8%	1	0.4%	28	6.8%	
Cardiac	2	0.3%	1	0.9%	0	0%	1	0.2%	
Hepatic	1	0.1%	0	0%	0	0%	1	0.2%	
HTN & DM	11	1.5%	1	0.9%	1	0.4%	9	2.2%	
ECOG PS									
ECOG 1	622	83.6%	91	85.8%	197	87.2%	334	81.1%	0.196
ECOG 2	119	16%	15	14.2%	29	12.8%	75	18.2%	
ECOG 3	3	0.4%	0	0%	0	0%	3	0.7%	
Presentation									
Obstruction	163	21.9%	29	27.4%	33	14.6%	101	24.5%	<0.001
Perforation	3	0.4%	1	0.9%	1	0.4%	1	0.2%	
Pain	268	36%	48	45.3%	96	42.5%	124	30.1%	
Bleeding	276	37.1%	28	26.4%	91	40.3%	157	38.1%	
Change in bowel habit	34	4.6%	0	0%	5	2.2%	29	7%	
Site of tumor									
Right colon	224	32.8%	26	24.5%	74	32.7%	144	35%	0.224
Transverse colon	9	1.2%	4	3.8%	3	1.3%	2	0.5%	
Left colon	111	14.9%	16	15.1%	36	15.9%	59	14.3%	
Sigmoid colon	58	7.8%	8	7.5%	14	6.2%	36	8.7%	
Rectosigmoid	26	3.5%	4	3.8%	8	3.5%	14	3.4%	
Rectum	296	39.8%	48	45.3%	91	40.3%	157	38.1%	
Sidedness									
Right colon cancer	253	34%	30	28.3%	77	34.1%	146	35.4%	0.384
Left colon cancer	491	66%	76	71.7%	149	65.9%	266	64.6%	
Type of operation									
No surgery	102	13.7%	20	18.9%	28	12.4%	54	13.1%	<0.001
Rt hemicolectomy	187	25.1%	13	12.3%	55	24.3%	119	28.9%	
Trans. hemicolectomy	4	0.5%	3	2.8%	1	0.4%	0	0%	
Lt hemicolectomy	89	12%	9	8.5%	29	12.8%	51	12.4%	
Sigmoidectomy	27	3.6%	6	5.7%	10	4.4%	11	2.7%	
LAR	253	34%	25	23.6%	86	38.1%	142	34.5%	
APR	48	6.5%	15	14.2%	8	3.5%	25	6.1%	
Total/Subtotal colectomy	14	1.9%	7	6.6%	4	1.8%	3	0.7%	
Colostomy	20	2.7%	8	7.5%	5	2.2%	7	1.7%	

Table (6): Relationship between age group and pathological parameters.

Pathological parameters	All studied patients (N=744)		Age group						p-value[a]
			18-29 years (N=106)		30-39 years (N=225)		40-49 years (N=412)		
	No.	%	No.	%	No.	%	No.	%	
Histopathology									
Conventional	589	79.2%	57	53.8%	181	80.1%	351	85.2%	<0.001
Mucinous	91	12.2%	32	30.2%	23	10.2%	36	8.7%	
Signet ring	64	8.6%	17	16%	22	9.7%	25	6.1%	
Grade									
Grade I	92	12.4%	18	17%	30	13.3%	44	10.7%	<0.001
Grade II	494	66.4%	78	73.6%	128	56.6%	288	69.9%	
Grade III	158	21.2%	10	9.4%	68	30.1%	80	19.4%	
Surgical margins									
Negative	621	83.5%	77	72.6%	193	85.4%	351	85.2%	0.033
Positive	4	0.5%	1	0.9%	1	0.4%	2	0.5%	
Not applicable	119	16%	28	26.4%	32	14.2%	59	14.3%	
LVI									
Absent	403	54.2%	42	39.6%	133	58.8%	228	55.3%	<0.001
Present	60	8.1%	2	1.9%	15	6.6%	43	10.4%	
Missed	162	21.8%	34	32.1%	46	20.4%	82	19.9%	
Not applicable	119	16%	28	26.4%	32	14.2%	59	14.3%	
PNI									
Absent	453	60.9%	43	40.6%	146	64.6%	264	64.1%	0.001
Present	11	1.5%	1	0.9%	4	1.8%	6	1.5%	
Missed	161	21.6%	34	32.1%	44	19.5%	83	20.1%	
Not applicable	119	16%	28	26.4%	32	14.2%	59	14.3%	
T									
T1	25	3.4%	2	1.9%	13	5.8%	10	2.4%	0.001
T2	121	16.3%	13	12.3%	26	11.5%	82	19.9%	
T3	328	44.1%	38	35.8%	113	50%	117	43%	
T4	151	20.3%	25	23.6%	42	18.6%	84	20.4%	
Not applicable	119	16%	28	26.4%	32	14.2%	59	14.3%	
N									
N0	186	25%	9	8.5%	78	34.5%	99	24%	<0.001
N1	275	37%	34	32.1%	84	37.2%	157	38.1%	
N2	164	22%	35	33%	32	14.2%	97	23.5%	
Not applicable	119	16%	28	26.4%	32	14.2%	59	14.3%	
M									
M0	608	81.7%	75	70.8%	194	85.8%	339	82.3%	0.004
M1	136	18.3%	31	29.2%	32	14.2%	73	17.7%	
AJCC stage group									
Stage I	39	5.2%	1	0.9%	16	7.1%	22	5.3%	<0.001
Stage II	147	19.8%	8	7.5%	62	27.4%	77	18.7%	
Stage III	422	56.7%	66	62.3%	116	51.3%	240	58.3%	
Stage IV	136	18.3%	31	29.2%	32	14.2%	73	17.7%	
Site of metastases									
Absent	608	81.7%	75	70.8%	194	85.8%	339	82.3%	<0.001
Liver	61	8.2%	4	3.8%	19	8.4%	38	9.2%	
Lung	13	1.7%	3	2.8%	1	0.4%	9	2.2%	
Peritoneal	44	5.9%	23	21.7%	6	2.7%	15	3.6%	
Bone	3	0.4%	0	0%	3	1.3%	0	0%	
Liver + Lung	4	0.5%	0	0%	0	0%	4	1%	
Liver + Peritoneal	7	0.9%	1	0.9%	1	0.4%	5	1.2%	
Liver + Bone	2	0.3%	0	0%	2	0.9%	0	0%	
Lung + Bone	2	0.3%	0	0%	0	0%	2	0.5%	
CEA									
Normal	389	52.3%	48	45.3%	126	55.8%	215	52.2%	<0.001
Raised	188	25.3%	17	16%	47	20.8%	124	30.1%	
Missed	167	22.4%	41	38.7%	53	23.5%	73	17.7%	
CA19-9									
Normal	427	57.4%	40	37.7%	142	62.8%	245	59.5%	<0.001
Raised	112	15.1%	11	10.4%	27	11.9%	74	18%	
Missed	205	27.6%	55	51.9%	57	25.2%	93	22.6%	

Categorical variables were expressed as number (percentage); a: Chi-square test; p-value < 0.05 is significant.

Table (7): Relationship between age group and outcome.

Outcome	All studied patients		Age group						p-value
			18-29 years		30-39 years		40-49 years		
	No.	%	No.	%	No.	%	No.	%	
LR	(N=608)		(N=75)		(N=194)		(N=339)		
Absent	541	89%	59	78.7%	162	83.5%	320	94.4%	<0.001[a]
Present	67	11%	16	21.3%	32	16.5%	19	5.6%	
DM									
Absent	481	79.1%	51	68%	149	76.8%	281	82.9%	0.010[a]
Present	127	20.9%	24	32%	45	23.2%	58	17.1%	
Relapse									
Absent	430	70.7%	43	57.3%	132	68%	225	75.2%	0.005[a]
Present	178	29.3%	32	42.7%	62	32%	84	24.8%	
Disease Free Survival									
Mean DFS (months)	89.76months		71.15months		87.26months		95.12months		<0.001[b]
(95%CI)	(86.06-93.46)		(58.68-83.62)		(80.65-93.86)		(90.53-99.72)		
3-years DFS	75.3%		56%		75.4%		79.4%		
5-years DFS	67.6%		50.5%		64.7%		72.8%		
10-years DFS	66.3%		50.5%		61.6%		72.2%		
Progression	(N=136)		(N=31)		(N=32)		(N=73)		
Absent	27	19.9%	17	54.8%	7	21.9%	3	4.1%	<0.001[a]
Present	109	80.1%	14	45.2%	25	78.1%	70	95.9%	
Time To Progression									
Median TTP (months)	24months		24months		24months		12months		0.079[b]
(95%CI)	(22.06-25.93)		(18.37-29.62)		(20.86-27.13)		(5.08-18.91)		
1-year PFS	61.6%		72.1%		82.4%		49.3%		
2-years PFS	30.3%		48.1%		35.3%		24%		
3-years PFS	8.8%		19.2%		3.9%		8.5%		
Mortality	(N=744)		(N=106)		(N=226)		(N=412)		
Absent	591	79.4%	73	68.9%	195	86.3%	323	78.4%	0.001[a]
Present	153	20.6%	33	31.1%	31	13.7%	89	21.6%	
Overall Survival									
Mean OS (months)	97.88months		77.67months		105.28months		97.88months		<0.001[b]
(95%CI)	(94.78-100.97)		(66.31-89.04)		(100.50-110.07)		(93.87-101.90)		
3-years OS	84%		68.8%		86.9%		85.6%		
5-years OS	77.4%		62.2%		85.7%		76.2%		
10-years OS	69.4%		33.5%		80.9%		72.3%		

Categorical variables were expressed as number (percentage); a: Chi-square test; b: Log-rank test; p-value < 0.05

Table (8): Relationship between type of disease at presentation and clinical parameters.

Clinical parameters	All studied patients (N=744)		Type of disease				p-value[a]
			Non-Metastatic disease (N=608)		Metastatic disease (N=136)		
	No.	%	No.	%	No.	%	
Age group							
18-29 years	106	14.2%	75	12.3%	31	22.8%	0.004
30-39 years	226	30.4%	194	31.9%	32	23.5%	
40-49 years	412	55.4%	339	55.8%	73	53.7%	
Sex							
Male	387	52%	346	56.9%	41	30.1%	<0.001
Female	357	48%	262	43.1%	95	69.9%	
Comorbidity							
Absent	660	88.7%	548	90.1%	112	82.4%	0.002
HTN	37	5%	30	4.9%	7	5.1%	
DM	33	4.4%	24	3.9%	9	6.6%	
Cardiac	2	0.3%	1	0.2%	1	0.7%	
Hepatic	1	0.1%	1	0.2%	0	0%	
HTN & DM	11	1.5%	4	0.7%	7	5.1%	
ECOG PS							
ECOG 1	622	83.6%	581	95.6%	41	30.1%	<0.001
ECOG 2	119	16%	27	4.4%	92	67.6%	
ECOG 3	3	0.4%	0	0%	3	2.2%	
Presentation							
Obstruction	163	21.9%	127	20.9%	36	26.5%	0.001
Perforation	3	0.4%	2	0.3%	1	0.7%	
Pain	268	36%	205	33.7%	63	46.3%	
Bleeding	276	37.1%	248	40.8%	28	20.6%	
Change in bowel habit	34	4.6%	26	4.3%	8	5.9%	
Site of tumor							
Right colon	224	32.8%	181	29.8%	63	46.3%	0.001
Transverse colon	9	1.2%	5	0.8%	4	2.9%	
Left colon	111	14.9%	91	15%	20	14.7%	
Sigmoid colon	58	7.8%	52	8.6%	6	4.4%	
Rectosigmoid	26	3.5%	22	3.6%	4	2.9%	
Rectum	296	39.8%	257	42.3%	39	28.7%	
Sidedness							
Right colon cancer	253	34%	186	30.6%	67	49.3%	<0.001
Left colon cancer	491	66%	422	69.4%	69	50.7%	

Categorical variables were expressed as number (percentage); a: Chi-square test; p-value < 0.05 is significant.

Table (9): Relationship between type of disease at presentation and pathological parameters

Pathological parameters	All studied patients (N=744)		Type of disease				p-value[a]
			Non-Metastatic disease (N=608)		Metastatic disease (N=136)		
	No.	%	No.	%	No.	%	
Type of operation							
No surgery	102	13.7%	3	0.5%	99	72.8%	<0.001
Rt hemicolectomy	187	25.1%	176	28.9%	11	8.1%	
Trans. hemicolectomy	4	0.5%	4	0.7%	0	0%	
Lt hemicolectomy	89	12%	85	14%	4	2.9%	
Sigmoidectomy	27	3.6%	27	4.4%	0	0%	
LAR	253	34%	252	41.4%	1	0.7%	
APR	48	6.5%	47	7.7%	1	0.7%	
Total/Subtotal colectomy	14	1.9%	14	2.3%	0	0%	
Colostomy	20	2.7%	0	0%	20	14.7%	
Histopathology							
Conventional	589	79.2%	488	80.3%	101	74.3%	0.290
Mucinous	91	12.2%	71	11.7%	20	14.7%	
Signet ring	64	8.6%	49	8.1%	15	11%	
Grade							
Grade I	92	12.4%	90	14.8%	2	1.5%	<0.001
Grade II	494	66.4%	405	66.6%	89	65.4%	
Grade III	158	21.2%	113	18.6%	45	33.1%	
Surgical margins							
Negative	621	83.5%	604	99.3%	17	12.5%	<0.001
Positive	4	0.5%	4	0.7%	0	0%	
Not applicable	119	16%	0	0%	119	87.5%	
LVI							
Absent	403	54.2%	394	64.8%	9	6.6%	<0.001
Present	60	8.1%	60	9.9%	0	0%	
Missed	162	21.8%	154	25.3%	8	5.9%	
Not applicable	119	16%	0	0%	119	87.5%	
PNI							
Absent	453	60.9%	444	73%	9	6.6%	<0.001
Present	11	1.5%	11	1.8%	0	0%	
Missed	161	21.6%	153	25.2%	8	5.9%	
Not applicable	119	16%	0	0%	119	87.5%	
T							
T1	25	3.4%	25	4.1%	0	0%	<0.001
T2	121	16.3%	120	19.7%	1	0.7%	
T3	328	44.1%	319	52.5%	9	6.6%	
T4	151	20.3%	144	23.7%	7	5.1%	
Not applicable	119	16%	0	0%	119	87.5%	
N							
N0	186	25%	186	30.6%	0	0%	<0.001
N1	275	37%	267	43.9%	8	5.9%	
N2	164	22%	155	25.5%	9	6.6%	
Not applicable	119	16%	0	0%	119	87.5%	
CEA							
Normal	389	52.3%	357	58.7%	32	23.5%	<0.001
Raised	188	25.3%	116	19.1%	72	52.9%	
Missed	167	22.4%	135	22.2%	32	23.5%	
CA19-9							
Normal	427	57.4%	395	65%	32	23.5%	<0.001
Raised	112	15.1%	47	7.7%	65	47.8%	
Missed	205	27.6%	166	27.3%	39	28.7%	

Categorical variables were expressed as number (percentage); a: Chi-square test; p-value < 0.05 is significant.

Table (10): Relationship between type of disease at presentation and outcome.

Outcome	All studied patients (N=744)		Type of disease				p-value
			Non-Metastatic disease (N=608)		Metastatic disease (N=136)		
	No.	%	No.	%	No.	%	
Mortality							
Absent	591	79.4%	519	85.4%	72	52.9%	<0.001a
Present	153	20.6%	89	14.6%	64	47.1%	
Overall Survival							
Mean OS (months)	97.88months		104.47months		64.81months		<0.001b
(95%CI)	(94.78-100.97)		(101.53-107.42)		(55.65-73.97)		
3-years OS	84%		89.9%		55.6%		
5-years OS	77.4%		84.3%		42.8%		
10-years OS	69.4%		79.3%		0%		

Categorical variables were expressed as number (percentage); a: Chi-square test; b: Log-rank test; p-value < 0.05 is significant

Table (11): Cox regression analysis for predictors for Overall Survival (OS).

	Univariate model		Multivariate model	
Variables	HR (95%CI)	p-value	HR (95%CI)	p-value
Age group		<0.001		0.089
18-29 years	2.220 (1.485 – 3.319)	<0.001	2.588 (1.031 – 6.492)	0.043
30-39 years	0.645 (0.429 – 0.971)	0.036	1.659 (0.784 – 3.512)	0.186
40-49 years	Reference		Reference	
Sex				
Male	Reference		Reference	
Female	1.325 (0.965 – 1.821)	0.082	0.954 (0.514 – 1.770)	0.881
Family history				
Negative				
Positive	59.776 (7.772 – 459.733)	<0.001		
Comorbidities		<0.001		0.004
Absent	Reference		Reference	
HTN	1.403 (0.736 – 2.673)	0.304	5.130 (0.878 – 29.964)	0.069
DM	1.583 (0.831 – 3.017)	0.163	0.530 (0.145 – 1.936)	0.337
Cardiac	6.067 (0.841 – 43.755)	0.074	14.976 (1.022 – 219.347)	0.048
Hepatic	8.958 (1.244 – 64.489)	0.029	32.423 (2.767 – 379.887)	0.006
HTN & DM	4.621 (2.345 – 9.108)	<0.001	1.060 (0.164 – 6.858)	0.951
ECOG Performance status		<0.001		
ECOG 1	Reference		Reference	
ECOG 2	3.357 (2.397 – 4.703)	<0.001	0.330 (0.026 – 4.111)	0.389
ECOG 3	9.329 (2.953 – 29.477)	<0.001		
Presentation		0.050		0.779
Obstruction	0.586 (0.299 – 1.149)		0.660 (0.193 – 2.262)	0.509
Perforation	0.000 (0.000 –)			
Pain	0.443 (0.231 – 0.849)		0.718 (0.264 – 1.952)	0.516
Bleeding	0.398 (0.207 – 0.766)		Reference	
Change in bowel habits	Reference			
Site of Tumour		0.070		0.323
Right colon	1.194 (0.822 – 1.735)	0.352	1.106 (0.000 –)	0.998
Transverse colon	3.488 (1.498 – 8.122)	0.004	242.093 (0.000 –)	0.906
Left colon	1.184 (0.727 – 1.929)	0.498	57.631 (0.000 –)	0.930
Sigmoid colon	0.793 (0.391 – 1.606)	0.519	0.028 (0.000 –)	0.476
Rectosigmoid	1.554 (0.621 – 3.888)	0.346	17.221 (1.145 – 258.997)	0.040
Rectum	Reference		Reference	
Sidedness				
Right Colon Cancer	1.233 (0.893 – 1.703)	0.203		
Left Colon Cancer	Reference			
Type of operation		<0.001		<0.001
No surgery	Reference			
Right hemicolectomy	0.313 (0.201 – 0.487)	<0.001	Reference	
Transverse hemicolectomy	0.308 (0.042 – 2.248)	0.246	0.000 (0.000 –)	0.622
Left hemicolectomy	0.277 (0.151 – 0.505)	<0.001	0.027 (0.000 –)	0.815
Sigmoidectomy	0.378 (0.161 – 0.889)	0.026	37.111 (0.000 –)	0.941
LAR	0.102 (0.058 – 0.182)	<0.001	0.090 (0.000 –)	0.961
APR	0.912 (0.532 – 1.563)	0.737	3.669 (0.000 –)	0.979
Total/Subtotal colectomy	0.447 (0.139 – 1.441)	0.178	0.006 (0.000 –)	0.740
Colostomy	2.685 (1.464 – 4.924)	0.001		
Histopathology		0.019		0.663
Conventional Adenocarcinoma	Reference		Reference	
Mucinous Adenocarcinoma	1.741 (1.144 – 2.648)	0.010	1.485 (0.601 – 3.669)	0.391
Signet ring Carcinoma	0.778 (0.408 – 1.484)	0.446	1.273 (0.331 – 4.896)	0.725

HR: Hazard Ratios; 95%CI: 95%confidence interval; p-value<0.05 is significant; Significant is bold.

Table (11): Contd.

	Univariate model		Multivariate model	
Variables	HR (95%CI)	p-value	HR (95%CI)	p-value
Grade		**0.001**		**<0.001**
Grade I	Reference		Reference	
Grade II	0.459 (0.307 – 0.686)	<0.001	0.099 (0.039 – 0.247)	<0.001
Grade III	0.673 (0.423 – 1.072)	0.096	0.259 (0.085 – 0.785)	0.017
Surgical margins		**<0.001**		
Negative	Reference		Reference	
Positive	2.200 (0.306 – 15.840)	0.434	35.072 (0.000 –)	0.944
Not applicable	4.796 (3.447 – 6.672)	<0.001		
LVI		**<0.001**		0.400
Absent	Reference		Reference	
Present	0.988 (0.471 – 2.073)	0.974	0.517 (0.189 – 1.419)	0.200
Missed	2.074 (1.336 – 3.220)	0.001	1.827 (0.235 – 14.220)	0.565
Not applicable	5.749 (3.969 – 8.327)	<0.001		
PNI		**<0.001**		0.789
Absent	Reference		Reference	
Present	1.718 (0.420 – 7.023)	0.452	0.677 (0.081 – 5.637)	0.718
Missed	2.019 (1.306 – 3.123)	0.002	0.569 (0.089 – 3.642)	0.551
Not applicable	5.751 (4.013 – 8.243)	<0.001		
Size (cm)	1.031 (0.939 – 1.132)	0.525	1.097 (0.934 – 1.288)	0.262
No. of Dissected LN	0.951 (0.907 – 0.997)	0.039	1.000 (0.954 – 1.048)	0.996
T		**<0.001**		
T1	Reference			
T2	1.006 (0.000 –)	1.000		
T3	4060.073 (0.000 –)	0.804		
T4	12826.859 (0.000 –)	0.777		
Not applicable	23057.932 (0.000 –)	0.764		
N		**<0.001**		
N0	Reference			
N1	2.678 (0.747 – 9.599)	0.130		
N2	43.626 (13.762 – 138.299)	<0.001		
Not applicable	52.244 (16.338 – 167.054)	<0.001		
M		**<0.001**		
M0	Reference			
M1	4.924 (3.558 – 6.814)	<0.001		
AJCC stage group		**<0.001**		**0.004**
Stage I	Reference		Reference	
Stage II	1594.887 (0.000 –)	0.856	1.823 (0.000 –)	0.892
Stage III	17664.842 (0.000 –)	0.810	17.098 (0.003 –)	0.524
Stage IV	59968.074 (0.000 –)	0.787		
Chemotherapy		**<0.001**		0.868
No	Reference		Reference	
Neoadjuvant/Adjuvant	5.175 (1.637 – 16.357)	0.005	5.542 (0.010 –)	0.595
Palliative	21.240 (6.651 – 67.826)	<0.001	0.915 (0.000 –)	0.994
Type of Chemotherapy		**0.001**		0.193
No	Reference		Reference	
XELOX	9.263 (2.454 – 34.971)	0.001	1.382 (0.227 – 8.429)	0.726
FOLFOX	7.326 (2.325 – 23.081)	0.001	2.473 (1.019 – 6.001)	0.045
FOLFIRI	31.103 (6.947 – 139.245)	<0.001		
Xeloda	8.754 (2.091 – 36.651)	0.003	2.922 (0.596 – 14.336)	0.186
5FU/Leucovorin	6.258 (1.889 – 20.731)	0.003		

HR: Hazard Ratios; 95%CI: 95%confidence interval; p-value<0.05 is significant; Significant is bold.

Table (12): Cox regression analysis for predictors for Disease Free Survival (DFS).

	Univariate model		Multivariate model	
Variables	HR (95%CI)	p-value	HR (95%CI)	p-value
Age group		**<0.001**		**0.001**
18-29 years	2.375 (1.578 – 3.574)	<0.001	1.960 (1.080 – 3.556)	0.027
30-39 years	1.360 (0.979 – 1.888)	0.066	2.136 (1.420 – 3.214)	<0.001
40-49 years	Reference		Reference	
Sex				
Male	Reference			
Female	1.279 (0.953 – 1.716)	0.101		
Comorbidities		**0.038**		**0.046**
Absent	Reference		Reference	
HTN	0.615 (0.272 – 1.389)	0.242	0.434 (0.155 – 1.213)	0.112
DM	0.390 (0.124 – 1.220)	0.106	0.140 (0.019 – 1.018)	0.052
Cardiac	9.631 (1.333 – 69.558)	0.025	7.160 (0.865 – 59.301)	0.068
Hepatic	4.960 (0.692 – 35.555)	0.111	3.636 (0.347 – 38.124)	0.282
HTN & DM	0.718 (0.100 – 5.126)	0.741	0.635 (0.073 – 5.496)	0.680
ECOG Performance status				
ECOG 1	Reference			
ECOG 2	0.960 (0.451 – 2.045)	0.916		
Presentation		0.268		
Obstruction	0.772 (0.361 – 1.651)	0.505		
Perforation	0.000 (0.000 –)	0.950		
Pain	0.545 (0.258 – 1.152)	0.112		
Bleeding	0.771 (0.372 – 1.595)	0.483		
Change in bowel habits	Reference			
Site of Tumour		0.232		
Right colon	1.027 (0.734 -1.436)	0.879		
Transverse colon	1.216 (0.299 – 4.946)	0.785		
Left colon	0.936 (0.601 – 1.457)	0.769		
Sigmoid colon	0.344 (0.150 – 0.789)	0.012		
Rectosigmoid	1.004 (0.407 – 2.479)	0.993		
Rectum	Reference			
Sidedness				
Right Colon Cancer	1.149 (0.844 – 1.564)	0.376		
Left Colon Cancer	Reference			
Type of operation		0.157		
No surgery	Reference			
Right hemicolectomy	1.255.230 (0.000 –)	0.821		
Transverse hemicolectomy	793.551 (0.000 –)	0.832		
Left hemicolectomy	1124.04 (0.000 –)	0.824		
Sigmoidectomy	760.988 (0.000 –)	0.833		
LAR	1004.397 (0.000 –)	0.826		
APR	2169.575 (0.000 –)	0.807		
Total/Subtotal colectomy	1048.416 (0.000 –)	0.825		
Histopathology		**0.012**		**0.010**
Conventional Adenocarcinoma	Reference		Reference	
Mucinous Adenocarcinoma	0.960 (0.602 – 1.529)	0.863	1.029 (0.539 – 1.964)	0.931
Signet ring Carcinoma	0.177 (0.056 – 0.554)	0.003	0.105 (0.025 – 0.450)	0.002
Grade		0.086		
Grade I	Reference			
Grade II	0.973 (0.626 – 1.513)	0.903		
Grade III	1.436 (0.873 – 2.362)	0.154		

HR: Hazard Ratios; 95%CI: 95%confidence interval; p-value<0.05 is significant; Significant is bold.

Table (12): Contd.

	Univariate model		Multivariate model	
Variables	HR (95%CI)	p-value	HR (95%CI)	p-value
Surgical margins				
Negative	Reference			
Positive	2.500 (0.620 – 10.079)	0.198		
LVI		**<0.001**		0.145
Absent	Reference		Reference	
Present	3.030 (2.072 – 4.429)	<0.001	1.597 (0.994 – 2.566)	0.053
Missed	2.100 (1.484 – 2.971)	<0.001	1.937 (0.261 – 14.388)	0.518
PNI		**<0.001**		0.456
Absent	Reference		Reference	
Present	3.438 (1.602 – 7.81)	0.002	1.595 (0.635 – 4.001)	0.320
Missed	1.744 (1.253 – 2.427)	0.001	0.640 (0.083 – 4.958)	0.669
Size (cm)	1.087 (1.019 – 1.160)	**0.012**	1.016 (0.935 – 1.104)	0.707
No. of Dissected LN	1.023 (0.998 – 1.049)	0.078		
T		**<0.001**		
T1	Reference			
T2	2356.921 (0.000 –)	0.835		
T3	10617.366 (0.000 –)	0.803		
T4	26051.747 (0.000 –)	0.785		
N		**<0.001**		
N0	Reference			
N1	10.684 (4.660 – 24.495)	<0.001		
N2	26.505 (11.594 – 60.596)	<0.001		
AJCC stage group		**<0.001**		**<0.001**
Stage I	Reference		Reference	
Stage II	1.406 (0.164 – 12.034)	0.756	134.664 (0.000 –)	0.933
Stage III	20.542 (2.876 – 146.725)	0.003	4497.806 (0.000 –)	0.885
Chemotherapy				
No	Reference		Reference	
Neoadjuvant/Adjuvant	31.045 (4.349 – 221.634)	**0.001**	1346.773 (0.000 –)	0.876
Type of Chemotherapy		**<0.001**		0.053
No	Reference		Reference	
XELOX	48.831 (6.345 – 375.822)	<0.001	1.849 (0.806 – 4.244)	0.147
FOLFOX	35.261 (4.932 – 252.098)	<0.001	0.774 (0.448 – 1.335)	0.357
Xeloda	20.750 (2.319 – 185.655)	0.007	1.476 (0.376 – 5.798)	0.577
5FU/Leucovorin	16.354 (2.200 – 121.585)	0.006		

HR: Hazard Ratios; 95%CI: 95%confidence interval; p-value<0.05 is significant; Significant is bold.

As expected the 5 years OS was significantly higher in non-metastatic than in the metastatic patients at presentation (mean OS: 104.4 versus 64.8 months respectively, 5-year OS: 84.3% versus 42.8% respectively), but this 5 years OS in the metastatic setting is higher than in other previously reported studies [26, 43, 53] which may be partly by the younger age of large percentage of metastatic patients (46.3% < 40 years) who have good general conditions and can tolerate extensive surgery for tumor resection and intensive chemotherapy. Consistent with other studies, the cancer stage was the most powerful factor affecting survival in multivariate analysis [24, 25, 53, 56].

To the best of our knowledge, this study is one of the largest single cancer institutional studies in developing countries focusing on clinicopathological and demographic data of yCRC and comparing it among different age groups, but the current study has some limitations, including an element of referral bias because our cancer center is a tertiary center, the retrospective nature of the study, and the lack of molecular and genetic characteristics.

Conclusions:

There is a higher burden of yCRC , advanced stage at presentation with a high incidence of bad prognostic factors, lower survival outcomes in the age group between 18 and 29 (in comparison with age group 40 and 49 years) but the survival rates in the current study was higher compared with previous publications on yCRC worldwide. So, lowering the age for screening to be below 45 years is crucial, which is already updated. This represents a nation problem necessitating further studies. Further large prospective studies with a long time of follow-up are needed to reach a conclusive decision about long-term outcomes in yCRC patients.

List of Abbreviations:

yCRCs: Young-onset colorectal cancers; AJCC: American Joint Committee on Cancer; CEA: carcinoembryonic antigen; DFS: Disease-free survival; OS: Overall survival; PFS: Progression-free survival; LRR: locoregional recurrence; ECOG: Eastern Cooperative Oncology Group; PS:Performance status; CRT: chemoradiation; LVI: Lymphovascular invasion.

Competing Interests

The authors declare that they have no conflict of interests.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Ahmed Mubarak Hefni, Mohammed Bayomy, Alia Mohammed Attia and Salah Mabrouk Khallaf. The first draft of the manuscript was written by Ahmed Mubarak Hefni and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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