ORIGINAL ARTICLE

Clinicopathological features of colorectal cancer patients under 30 years of age

Características clinicopatológicas del cáncer colorrectal en pacientes menores de 30 años

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Abstract

Background: *Colorectal cancer (CRC) is the second cause of cancer death in the world and is estimated to have been responsible for almost 935,000 deaths during 2020.* **Objective:** *Describe clinicopathological features, overall survival (OS) and progression-free survival (PFS) in CRC patients under 30 years.* **Method:** *This is a retrospective cohort study in patients under 30 years diagnosed with CRC.* **Results:** *From 2017 to 2021, 1823 patients were diagnosed with CRC, of which 54 (2.96%) were under 30 years. The OS, during 4 years, was 41.5%. The clinical stage found IV (hazard ratio [HR]: 6.212; 95% confidence interval [95%CI]: 2.504-15.414; p < 0.001), giving neoadjuvant therapy (HR: 0.705; 95%CI: 0.499-0.996; p = 0.047) and no medical history of Lynch syndrome (HR: 3.925; 95%CI: 1.355-11.364; p = 0.012) are independent predictors of mortality. The PFS, during 4 years, was 21.3%. Clinical stage IV (HR: 2.418; 95%CI: 1.000-5.850; p < 0.050), and no diagnosis of Lynch syndrome (HR: 3.800; 95%CI: 1.398-10.326; p = 0.009) are independent predictors.* **Conclusions:** *Younger patients are usually diagnosed with CRC in advanced stages. Early symptoms and evaluation, irrespective of age, are crucial.*

Keywords: *Colon cancer. Rectum cancer. Young adult. Hereditary.*

Resumen

Antecedentes: *El cáncer colorrectal (CCR) es la segunda causa de muerte por cáncer en el mundo y se estima que fue responsable de casi 935,000 muertes durante el año 2020.* **Objetivo:** *Describir las características clinicopatológicas, la supervivencia global (SG) y la supervivencia libre de progresión (SLP) en pacientes con CCR menores de 30 años.* **Método:** *Estudio de cohorte retrospectivo en pacientes con diagnóstico de CCR menores de 30 años.* **Resultados:** *Entre 2017 y 2021 se diagnosticaron 1823 pacientes con CCR, de los cuales 54 (2.96%) eran menores de 30 años. La SG a 4 años fue del 41.5%. Se encontró que la etapa clínica IV (hazard ratio [HR]: 6.212; intervalo de confianza del 95% [IC95%]: 2.504-15.414; p < 0.001), recibir tratamiento neoadyuvante (HR: 0.705; IC95%: 0.499-0.996; p = 0.047) y no tener antecedente de síndrome de Lynch (HR: 3.925; IC95%: 1.355-11.364; p = 0.012) son predictores de mortalidad independientes. La SLP a 4 años fue del 21.3%. La etapa clínica IV (HR: 2.418; IC95%: 1.000-5.850; p < 0.050) y el no contar con diagnóstico de síndrome de Lynch (HR: 3.800; IC95%: 1.398-10.326; p = 0.009) son predictores independientes.* **Conclusiones:** *Los pacientes jóvenes son diagnosticados con CCR en etapas avanzadas. Los síntomas iniciales, junto con la evaluación, independientemente de la edad, son cruciales.*

Palabras clave: *Cáncer de colon. Cáncer de recto. Adultos jóvenes. Hereditario.*

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Introduction

Colorectal cancer (CRC) is the second leading cause of cancer death worldwide, estimated to be responsible for nearly 935,000 deaths in 2020. It is the third most frequent neoplasm in men and the second in women[1]. In Mexico, CRC ranks fourth in incidence, accounting for 7.6% (14,901 people) and 6245 deaths in 2020, placing it second in mortality[2].

The incidence and mortality of CRC have dropped from 1975 to 2006; however, this trend is mainly influenced by older age groups[3]. Between 2009 and 2013, the incidence of CRC decreased by 4.6% per year in people aged 65 and older, likely due to a combination of screening tests, changes in the distribution of risk factors (less smoking, more aspirin use), and treatment improvements. However, epidemiological studies show an alarming increase in incidence among people younger than 50 years, at a rate of 1.6% per year[4]. Similarly, CRC mortality rates for adults younger than 50 increased by approximately 1% per year from 2005 through 2014, while they dropped by 1% to 3% per year for older patients. For individuals aged 20 to 34 years, compared to 2010, the incidence is forecasted to increase by 90% and up to 124% by 2030[3,5]. Other studies report that for patients younger than 50 years, the incidence is projected to increase from 11% in 2010 up to 22% in 2030[6]. The specific cause of the increase in cases among young patients remains unknown. It is believed to be closely related to lifestyle changes over the past 45 years (sedentary behavior, diet, substance abuse, etc.) and an increase in the prevalence of chronic non-communicable diseases and hereditary origins[1,7].

Diagnosing CRC in people younger than 30 is challenging because most young adults do not have obvious risk factors (such as family history) and are categorized as average risk according to current CRC screening and management algorithms. Age and family history of cancer remain the cornerstone of CRC risk stratification algorithms. However, only a minority of early-onset CRC patients report having a first-degree relative with CRC, and even fewer have a predisposing condition (such as inflammatory bowel disease)[8-10]. The failure to consider the possibility of CRC by both patients and doctors contributes to delays in diagnosis in younger adults, even in the presence of warning symptoms (such as hematochezia or iron deficiency anemia), resulting in a substantial proportion of young patients having metastatic disease at diagnosis.

Hereditary syndromes play an important role in the development of CRC in young patients[11]; 20% have a family history of CRC, and up to 33% of cases in those younger than 35-40 years are related to hereditary syndromes, such as Lynch syndrome (hereditary CRC)[6]. This syndrome is caused by mutations in DNA mismatch repair genes (MLH1, MSH2, MSH6, and PMS2) and accounts for 1% to 2% of all CRC cases[12].

The objective of this study is to describe the clinicopathological characteristics, overall survival (OS), and progression-free survival (PFS) in patients younger than 30 years diagnosed with CRC.

Method

Data source

Data source was the physical and electronic health records of the National Cancer Institute, which provide demographic data (age at diagnosis, sex, tumor location, TNM staging according to the American Joint Committee on Cancer (AJCC) 8th edition, histological type, tumor grade, and number of lymph nodes evaluated), as well as dates of diagnosis, recurrence, and last consultation. We obtained permission to access the research data files with reference number 2022/106. The study did not involve interaction with human subjects nor the use of personally identifiable information, did not require informed consent, and was approved by the research committee of the National Cancer Institute.

Patient selection

We included patients with CRC who were younger than 30 years at the time of diagnosis, from January 2017 through December 2021. Patients older than 30 at diagnosis, those with TNM in situ, and those with incomplete information were excluded (Fig. 1).

Data analysis

Data analysis was conducted on patients younger than 30 years at the time of diagnosis. Clinicopathological characteristics, genetic disorders (microsatellite instability), type of treatment (resective surgery, palliative surgery, neoadjuvant, adjuvant, and palliative), and survival were

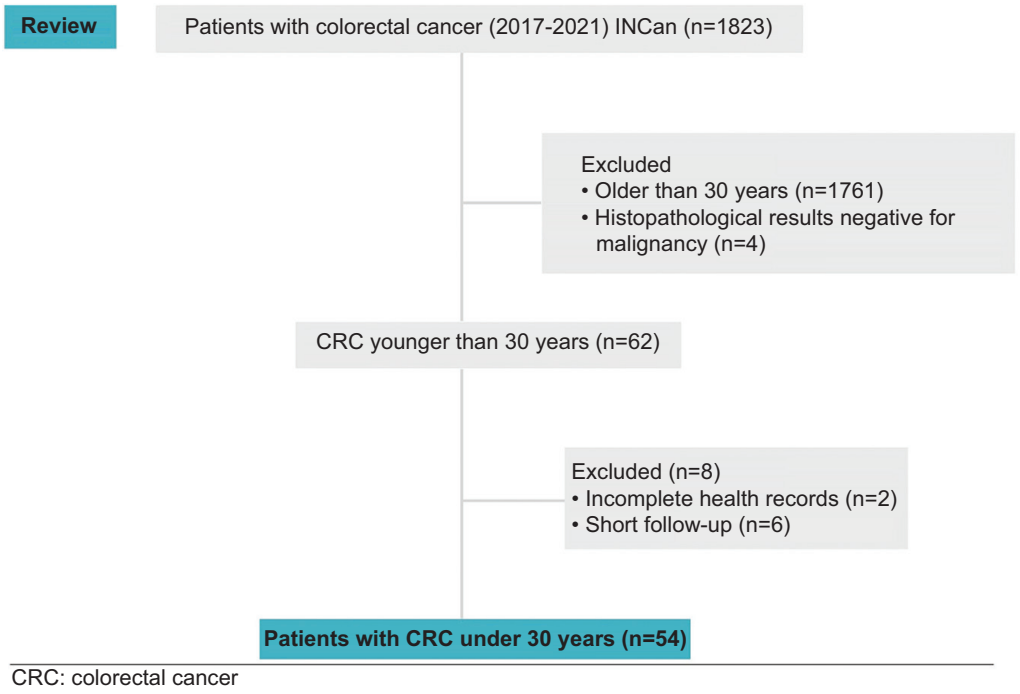

Figure 1. *STROBE diagram.*

evaluated. Anatomical location analysis included the right colon (cecum, ascending colon, hepatic flexure, and transverse colon), the left colon (splenic flexure, descending colon, and sigmoid colon), and the rectum (rectosigmoid junction and rectum). Staging was performed according to the criteria described in the 8th edition of the AJCC classification. Histological type was categorized into 3 classes: adenocarcinoma, mucinous adenocarcinoma, and signet ring cell adenocarcinoma. Tumor grade was categorized as well differentiated (G1), moderately differentiated (G2), and poorly differentiated (G3). Of note that patients with Lynch syndrome were diagnosed using the following guidelines: 1) clinical criteria, 2) molecular techniques for detecting microsatellite instability and immunohistochemistry, and 3) a combination of both. Deaths attributed to CRC were treated as events, overall survival (OS) was calculated from the date of diagnosis to the date of death or end of follow-up (cut-off date: December 2021), and progression-free survival (PFS) was calculated from the start date of treatment to the date of progression or end of follow-up (cut-off date: December 2021).

Statistical analysis

Continuous data were expressed as medians and standard deviations. Categorical data were compared using the chi-square test or Fisher's exact test. Survival curves were generated using Kaplan-Meier estimates, and differences between the curves were analyzed using the log-rank test. Cox univariate and multivariate regression models were developed to analyze the influence of each characteristic on survival. Data were summarized as hazard ratios (HR) and their 95% confidence intervals (CI95%). A p-value $\leq$ 0.05 was considered statistically significant. Data were analyzed using SPSS software version 26 (SPSS, IBM, Inc., Chicago, IL, United tates).

Results

From January 2017 through December 2021, a total of 1823 patients were diagnosed with CRC, 54 of whom (2.96%) were younger than 30 years (Fig. 1). Table 1 describes the general characteristics. The mean age at diagnosis was 24.7 years (range, 17-30). Notably, a low percentage of the population was overweight (12; 22.2%) or obese (4; 7.40%). A total of 27.80% of the patients had a family history of CRC. The most common initial symptoms were abdominal pain (38; 70.3%), weight loss (38; 70.3%), and hematochezia (32; 59.26%). The most frequent location of the primary tumor was the rectum (25; 46.3%). Simple adenocarcinoma was the most frequent histological subtype (37; 68.5%); however, signet ring cell

adenocarcinoma accounted for 25.9% (14), and the most common histological grade was poorly differentiated (31; 57.4%). Non-metastatic stages (I-III) predominated over metastatic stage (IV), with 34 (62.4%) and 20 (37%) patients, respectively. Lynch syndrome was diagnosed in 15 (27.8%) patients, with MLH1 being the most affected mismatch repair gene (7; 46.7%). Resective surgery prevailed over other initial treatments (30; 63.3%). The most widely implemented systemic treatment was neoadjuvant therapy (25; 68%).

Overall survival

The 4-year OS rate was 35.6% (Fig. 2). Using a stepwise logistic regression model, it was found that stage IV at diagnosis (HR, 6.212; 95%CI, 2.504-15.414; p < 0.001), having received neoadjuvant therapy (HR, 0.705; 95%CI, 0.499-0.996; p = 0.047), and not having been diagnosed with Lynch syndrome (HR, 3.925; 95%CI, 1.355-11.364; p = 0.012) are independent mortality predictors (Table 2).

Progression-free survival

The 4-year PFS rate was 21.3% (Fig. 2). Multivariate analysis found that stage IV at diagnosis (HR, 2.418; 95%CI, 1.000-5.850; p < 0.050) and not having been diagnosed with Lynch syndrome (HR, 3.800; 95%CI, 1.398-10.326; p = 0.009) are independent predictors of disease progression (Table 3).

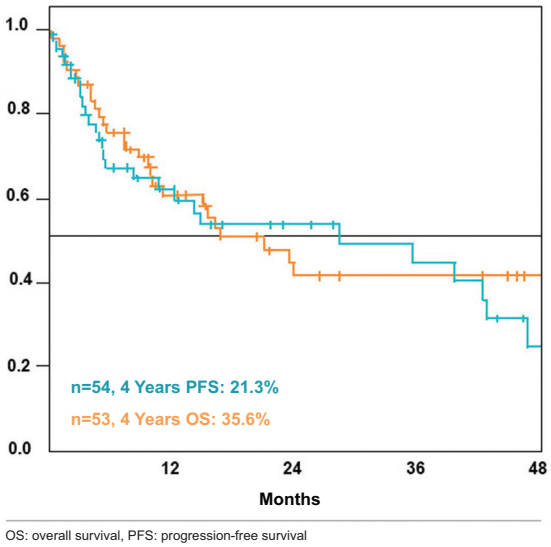

Figure 2. *Overall and disease-free survival.*

Discussion

Currently, an unequivocal definition of early-onset CRC in young adults is needed, as there is no clear consensus in the literature or guidelines. Therefore, direct comparisons among available studies are not possible due to differing age cutoffs (ranging from 30 to 50 years). However, this study is based on the Adolescent and Young Adult (AYA) guideline, which includes CRC patients diagnosed between the ages of 15 and 29 years[13].

Early-onset CRC predominantly affects racial and ethnic minorities vs non-Hispanic whites. Although 10% to 12% of all patients diagnosed with CRC are younger than 50 years, the proportion nearly doubles among non-Hispanic blacks (16%) vs non-Hispanic whites (9%)[14]. Early-onset CRC incidence rates have consistently been higher among blacks, though the gap with whites has recently narrowed[9]. Incidence rates have also rapidly increased among young Hispanics[15,16].

According to CRC records from the SEER (Surveillance, Epidemiology, and End Results) database of the National Cancer Institute, the incidence of this neoplasm in individuals younger than 35 years is 2.2%[17]. Özaydın et al.[18], in their study on CRC in individuals younger than 30, found an incidence of 3.59%. In our study, it was 2.96% (54/1823), with a slight male predominance (51.85% vs. 49.15%), but no statistically significant difference. These percentages show that the rate has increased in this population; according to data from the GLOBOCAN (2020) database of the Global Cancer Observatory, a significant increase in new cases in this population group has been documented in recent years[19].

The role of body mass index (BMI) in the OS of CRC patients is still unclear. Birmingham et al.[20] published on the possible negative effect of leptin on tumor progression and metastasis by stimulating vascular endothelial growth factor. On the other hand, studies by Ogino et al.[21] assert that a high BMI may positively influence survival, as it was reported higher in obese CRC patients with p27 gene alterations or increased STMN1 gene expression. García-Oria et al.[22] state in their study that BMI is not a prognostic factor for long-term survival in CRC patients. In our study, we observed that only a small percentage of individuals had a BMI categorized as overweight or obese. However, it should be considered that the weight used for

Table 1. Clinical characteristics of patients with colorectal cancer

Characteristic	n	%
Age, years	24.7 (17-30)	
Sex		
Male	28	51.85
Female	26	48.15
BMI		
Underweight	10	18.50
Normal	28	51.90
Overweight	12	22.20
Obesity	4	7.40
Family history of CRC		
Yes	16	29.60
No	38	70.37
Clinical presentation		
Abdominal pain	38	70.37
Weight loss	38	70.37
Hematochezia	32	59.26
Constipation	15	27.78
Fecaluria	1	1.85
Primary tumor location		
Right colon	13	24.07
Left colon	13	24.07
Rectum	25	46.30
Synchronous	3	5.56
Histological type		
Adenocarcinoma	37	68.50
Signet ring cell adenocarcinoma	14	25.90
Mucinous adenocarcinoma	3	5.60
Histological grade		
G1: Well-differentiated adenocarcinoma	4	7.41
G2: Moderately differentiated adenocarcinoma	19	35.19
G3: Poorly differentiated adenocarcinoma	31	57.41
TNM staging		
Stage 1	4	7.40
Stage 2	17	31.50
Stage 3	13	24.10
Stage 4	20	37.00
Lynch syndrome		
Yes	15	27.80
No	39	72.20
Type of MSI in patients with Lynch syndrome		
MLH1	7	12.96
MSH2	3	5.55
Combination of MSI*	5	9.25
None	39	72.2
Type of surgery		
Resective surgery	30	63.3
Palliative surgery	16	18.8
No surgery	8	37.5
Systemic treatment		
Adjuvant	16	25
Neoadjuvant	25	76
Palliative	13	15.4

CRC: colorectal cancer; BMI: body mass index; MSI: microsatellite instability.
*Including MLH1, MSH2, MSH6, and PMS2.

this study was the weight at diagnosis, after initial symptoms, and one of the most common symptoms prior to diagnosis is weight loss (a little more than 70% of the studied population had this symptom).

CRC in young patients tends to occur more frequently in the distal sigmoid or rectum[23,24]. According to our study, the location was similar in the right (24.07%) and left (24.07%) colon, and the most frequent was in the rectum (46.30%). In contrast, in patients older than 50, proximal colon cancer is more common[25].

At the time of diagnosis, most patients in our study were in stage IV (37%). In the study by Fu et al.[26], the age group of young patients had a higher percentage in clinical stages III and IV vs the group older than 35, in whom stages I and II predominated. Their survival analysis in clinical stages I-III was similar for both age groups, while in stage IV, being younger than 35 a poor prognosis factor. Similarly, a study of 32 patients younger than 30 with CRC showed a higher percentage in advanced clinical stages III (46.8%) and IV (31.2%)[18].

Regarding histological type, simple adenocarcinoma was present in most individuals (68.5%), followed by adenocarcinoma with a signet ring cell pattern (25.90%). The predominant histological grade in our study was G3 (poorly differentiated), at 57.41%. In the study by You et al.[27], the mucinous and signet ring cell pattern (12.6% vs 10.8%), as well as poorly or undifferentiated (20.4% vs 18%), were the most common findings and were also independent predictors. In a comparison between age groups 20-40 years and 60-80 years, O'Connell et al.[28,29] evidenced that tumors in younger populations often exhibit a mucinous and signet ring cell pattern, with low differentiation (27.3% vs 17.2%) vs an older group.

In the absence of distinctive biological characteristics, current treatment guidelines do not distinguish early-onset CRC from the disease in older adults. Surgical resection should meet the appropriate standards for the corresponding tumor site. Care should be taken to avoid overtreatment in these patients, despite the lower risk of morbidity and the years of life gained. In our sample, curative intent surgery was predominant, with 30 cases (63.3%), followed by palliative surgery with 16 cases (18.8%), and no surgical intervention in 8 cases (37.5%). These rates are similar to one of the largest studies of young adults with metastatic CRC, with more than 6700 patients, which reported surgical treatment outcomes, showing that 2653 (39.5%) underwent primary tumor resection only, 1547 (23.1%) underwent primary tumor resection plus

Table 2. Analysis of factors associated with overall survival in patients

Factor	Total (events)	Univariate analysis (48 months)	Multivariate analysis (48 months)
	n (%)	% (95%CI) p	HR (95%CI) p
Overall	54 (12)	67.4 (49.8-85.0)	
Sex		0.276	
Female	26 (11)	53.60 (31.45-75.69)	
Male	28 (18)	33.6 (14.39-52.8)	
BMI		0.112	
≤ 18.5	10 (8)	15.0 (11.65-41.65)	
> 18.5	44 (21)	47.5 (30.84-64.16)	
Family history of CRC		0.227	
Yes	16 (6)	50.10 (19.13-81.06)	
No	38 (23)	37.7 (20.64-54.65)	
Tumor location		0.53	
Right colon	13 (5)	39.60 (1.57-77.62)	
Left colon	13 (9)	33.70 (5.47-61.92)	
Rectum	25 (14)	42.5 (21.33-63.66)	
Synchronous	3 (1)	66.7 (13.38-120)	
Pathological stage		< 0.001	6.212 (2.504-15.414)
≤ III	33 (10)	69.10 (50.28-87.91)	< 0.001
IV	21 (19)	5.10 (4.7-14.9)	
Histological type		0.002	1.153 (0.651-2.042)
Adenocarcinoma	37 (19)	47.00 (29.16-64.83)	0.626
Signet ring cell adenocarcinoma	14 (10)	0 (0.0-0.0)	
Mucinous adenocarcinoma	3 (0)	0 (0.0-0.0)	
Tumor differentiation		0.268	
Poor-moderate	23 (12)	50.8 (29.82-71.77)	
Well	31 (17)	29.8 (8.24-51.36)	
Type of surgery		0.003	0.875 (0.500-1.529)
No surgery	8 (5)	25.00 (13.80-63.80)	0.638
Curative	30 (11)	62.20 (43.18-81)	
Palliative	16 (13)	15.50 (3.90-34.9)	
Systemic treatment		< 0.001	0.705 (0.499-0.996)
Adjuvant	16 (12)	22.50 (0.94-44.06)	0.047
Neoadjuvant	25 (6)	77.80 (75.72-79.87)	
Palliative	13 (11)	0 (0.0-0.0)	
Lynch syndrome		0.007	3.925 (1.355-11.364)
No	39 (25)	29.0 (12.53-45.46)	0.012
Yes	15 (4)	73.5 (47.04-99.96)	

CRC: colorectal cancer; HR: hazard ratio; 95%CI: 95% confidence interval; BMI: body mass index.

metastasectomy, 231 (3.4%) received metastasectomy without primary tumor resection, and 2277 patients (32.9%) had no surgery. Their results showed significant differences in OS: the median for patients who underwent primary tumor resection was 29 months vs13 months for those who did not[30]. Akinkuotu et al.[31] grouped individuals into ≤ 25 years and > 25 years and found that the first group had higher rates of total colectomy (8.9% vs 2.7%) and total proctocolectomy (5.0% vs 0.5%), higher rates of contiguous organ resection (12.9% vs 8.0%), external beam radiation treatment (3.9% vs. 1.9%), and chemotherapy treatment (76.6% vs 40.1%). Younger patients had significantly lower 30- and 90-day mortality (0.6% vs 4.2% and 2.1% vs 7.6%) vs those older than 25 years. Although colectomy was associated with a lower risk of death, contiguous organ resection associated with colectomy was linked to a higher risk of death[31]. Despite these results for sporadic early-onset CRC patients, extended

Table 3. Analysis of factors associated with progression-free survival in patients

Factor	Total (events)	Univariate analysis (48 months)	Multivariate analysis (48 months)	p-value
		% (95%CI) p	HR (95CI)	p
Overall	50 (12)	67.4% (49.7-85.0)		
Sex		0.065		
Female	26 (10)	30.50% (25.54-35.45)		
Male	28 (17)	14.7% (3.72-25.67)		
BMI		0.028	0.384 (0.138-1.069)	0.067
≤ 18.5	10 (8)	0.0% (0.0-0.0)		
> 18.5	44 (19)	26.6% (5.04-48.16)		
Family history of CRC		0.367		
Yes	16 (7)	38.70% (7.92-69.47)		
No	38 (20)	11.10% (7.52-29.62)		
Tumor location		0.885		
Right colon	13 (5)	31.30% (14.56-77.16)		
Left colon	13 (7)	30.80% (1.14-62.74)		
Rectum	25 (14)	14.30% (8.82-37.42)		
Synchronous	3 (1)	0.0% (0.0-0.0)		
Pathological stage		0.005	2.418 (1.000-5.850)	0.050
≤ III	33 (16)	27.10% (4.75-49.44)		
IV	21 (11)	24.00% (0.67-47.32)		
Histological type		0.185		
Adenocarcinoma	37 (21)	22.10% (3.48-40.72)		
Signet ring cell adenocarcinoma	14 (6)	0.0% (0.0-0.0)		
Mucinous adenocarcinoma	3 (0)	0.0% (0.0-0.0)		
Tumor differentiation		0.832		
Poor-moderate	23 (14)	12.60% (8.37-33.57)		
Well	31 (13)	32.20% (6.91-57.48)		
Type of surgery		0.068		
No surgery	8 (2)	0.0% (0.0-0.0)		
Curative	30 (13)	32.40% (6.72-58.07)		
Palliative	16 (12)	15.80% (4.19-35.79)		
Type of systemic treatment		0.005	0.899 (0.557-1.450)	0.662
Adjuvant	16 (7)	29.60% (1.76-60.96)		
Neoadjuvant	25 (10)	28.60% (2.14-55.06)		
Palliative	13 (10)	15.80% (4.46-38.26)		
Lynch Syndrome		0.005	3.800 (1.398-10.326)	0.009
Yes	15 (5)	17.70% (1.9-37.3)		
No	39 (22)	49.50% (16.18-82.82)		

CRC: colorectal cancer; HR: hazard ratio; 95%CI: 95% confidence interval; BMI: body mass index,

resections, such as total colectomy or proctocolectomy, have not shown any advantage in disease-free survival or OS[5].

Our results regarding systemic treatment indicate that neoadjuvant therapy was the most implemented, followed by adjuvant therapy and palliative treatment, with a statistically significant difference. In the study by Arhin et al.[30], 5552 (82.8%) patients received systemic chemotherapy and 1156 (17.2%) received radiotherapy, and they found that receiving chemotherapy and radiotherapy was significantly associated with better survival (HR, 0.65 and 0.88, respectively). However, in the study by Kneuertz et al.[32], it was found that the use of more aggressive systemic therapy did not lead to significant gains in survival. Over-treatment with multiple doses of chemotherapy, due to the maximum tolerated dose that can be administered, limits or perhaps eliminates any chemotherapy options at the time of relapse[31]. It is more likely that AYA patients in low-risk stage I or II will receive unindicated adjuvant

regimens, highlighting the risk of over-treatment faced by this population. Given the higher proportion of advanced-stage disease in early-onset CRC, along with the trend of over-treatment, multidisciplinary coordination of care is necessary to define individualized and appropriate treatment plans[5].

Hereditary syndromes play a very important role in the development of CRC; they cause 1% up to 3% of all CRC cases[33]. In young patients, it is estimated that 20% have a family history of CRC and up to 34.2% of cases in those younger than 35 years are related to hereditary syndromes, such as Lynch syndrome[12]. In our study, 27.8% of the population was diagnosed with Lynch syndrome, which is similar to the findings made by Schofield et al.:[12] a total of 1434 tumors in patients younger than 60 years, 33 of whom (2.30%) were younger than 30 years, 9 (27.3%) with microsatellite instability, and 24 (72.7%) without instability[12]. The most widely affected mismatch repair gene was MLH1 (n = 9, 60.3% of all Lynch syndrome cases). In the study by Durhuus et al.[6], in their group younger than 40 years, the most widely affected mismatch repair gene was MSH2 (39.4%), followed by MLH1 (33%). Additionally, 36.2% were diagnosed in clinical stages III and IV, with a 5-year OS rate of 55%, and in clinical stages I and II, a 5-year OS rate of 97%. Similar results regarding OS in early stages were obtained by Domínguez et al.[34], who reported that tumors related to Lynch syndrome in clinical stages I, II, and III have a 10-year survival of over 82%. Our results, when categorizing clinical stages into 2 groups in patients with Lynch syndrome, considering clinical stage IV and clinical stages I-III, show 1 (6.7%) and 14 (93.3%) cases, respectively, indicating a clear predominance of early stages that positively influence the OS of patients in this group. All patients with Lynch syndrome had resective surgery as their initial treatment with adjuvant therapy. It is obvious that this group benefited from early-stage diagnosis and initial resective surgery treatment.

The descriptive nature, small sample size, and having been conducted in a single center are all limitations of our study; however, it is the first national study addressing this topic.

Conclusions

As far as we know, this is the largest series to date examining the clinical and histological characteristics of people diagnosed with CRC up to 30 years of age in Mexico.

CRC in young patients is a public health problem as they have pathological characteristics leading to late diagnosis (advanced clinical stages) and worse prognosis. Alarm symptoms, along with evaluation regardless of age, family history, and genetic syndromes, are crucial.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

References

1. Sawicki T, Ruszkowska M, Danielewicz A, Niedźwiedzka E, Arłukowicz T, Przybyłowicz KE. A review of colorectal cancer in terms of epidemiology, risk factors, development, symptoms and diagnosis. Cancers (Basel). 2021;13:2025.
2. International Agency for Research on Cancer. Mexico Source: Globocan 2020. (Consultado el 18-08-2022.) Disponible en: https://gco.iarc.fr/today/data/factsheets/populations/484-mexico-fact-sheets.pdf/
3. Edwards BK, Ward E, Kohler BA, Eheman C, Zauber AG, Anderson RN, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. Disponible en: http://cisnet.cancer.gov/projections
4. SEER*Stat Databases: November 2015 Submission. 2015. (Consultado el 18-08-2022.) Disponible en: https://seer.cancer.gov/data-software/documentation/seerstat/nov2015/
5. You YN, Lee LD, Deschner BW, Shibata D. Colorectal cancer in the adolescent and young adult population. JCO Oncol Pract. 2020;16:19-27.
6. Durhuus JA, Therkildsen C, Kallemose T, Nilbert M. Colorectal cancer in adolescents and young adults with Lynch syndrome: a Danish register-based study. BMJ Open. 2021;11:53538.

7. Colorectal Cancer Facts & Figures 2020-2022. Colorectal cancer screening test use* (%), adults 50 years and older by state, 2018. Disponible en: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/colorectal-cancer-facts-and-figures/colorectal-cancer-facts-and-figures-2020-2022.pdf
8. Chang DT, Pai RK, Rybicki LA, Dimaio MA, Limaye M, Jayachandran P, et al. Clinicopathologic and molecular features of sporadic early-onset colorectal adenocarcinoma: an adenocarcinoma with frequent signet ring cell differentiation, rectal and sigmoid involvement, and adverse morphologic features. Modern Pathology. 2012;25:1128-39.
9. Murphy CC, Wallace K, Sandler RS, Baron JA. Racial disparities in incidence of young-onset colorectal cancer and patient survival. Gastroenterology. 2019;156:958-65.
10. Stoffel EM, Koeppe E, Everett J, Ulintz P, Kiel M, Osborne J, et al. Germline genetic features of young individuals with colorectal cancer. Gastroenterology. 2018;154:897-905.e1.
11. Balaguer F. Genética del cáncer colorrectal. Gastroenterol Hepatol. 2013;36(Suppl 2):73-9.
12. Schofield L, Watson N, Grieu F, Li WQ, Zeps N, Harvey J, et al. Population-based detection of Lynch syndrome in young colorectal cancer patients using microsatellite instability as the initial test. Int J Cancer. 2009;124:1097-102.
13. Bleyer A. Adolescent and Young Adult (AYA) Oncology: The First A. Pediatr Hematol Oncol. 2007;24:325-36.
14. Murphy CC, Sanoff HK, Stitzenberg KB, Baron JA, Lund JL, Sandler RS. Patterns of sociodemographic and clinicopathologic characteristics of stages II and III colorectal cancer patients by age: examining potential mechanisms of young-onset disease. J Cancer Epidemiol. 2017;2017:1-10.
15. García S, Pruitt SL, Singal AG, Murphy CC. Colorectal cancer incidence among Hispanics and non-Hispanic Whites in the United States. Cancer Causes Control. 2018;29:1039-46.
16. Wang DY, Thrift AP, Zarrin-Khameh N, Wichmann A, Armstrong GN, Thompson PA, et al. Rising incidence of colorectal cancer among young Hispanics in Texas. J Clin Gastroenterol. 2017;51:34-42.
17. Colorectal cancer — Cancer Stat Facts. (Consultado el 18-08-2022.) Disponible en: https://seer.cancer.gov/statfacts/html/colorect.html
18. Özaydın Ş, Ataş E, Tanrıseven M, Kaplan MA, Hartendorp P, Ünlü A, et al. Colorectal cancer in patients aged ≤ 30 years: 17 years of experience. Erciyes Med J. 2019;41:62-70.
19. Cancer over time. Global Cancer Observatory. (Consultado el 18-08-2022.) Disponible en: https://gco.iarc.fr
20. Birmingham JM, Busik JV, Hansen-Smith FM, Fenton JI. Novel mechanism for obesity-induced colon cancer progression. Carcinogenesis. 2009;30:690-7.
21. Ogino S, Shima K, Nosho K, Irahara N, Baba Y, Wolpin BM, et al. A cohort study of p27 localization in colon cancer, body mass index and patient survival. Cancer Epidemiol Biomarkers Prev. 2009;18:1849.
22. García-Oria MJ, Armengol Carrasco M, Caballero Millán A, Ching C, Codina Cazador A. ¿Es el índice de masa corporal un factor pronóstico de supervivencia en el cáncer de colon? Análisis multivariable. Cir Esp. 2022;89:152-8.
23. Abdelsattar ZM, Wong SL, Regenbogen SE, Jomaa DM, Hardiman KM, Hendren S. Colorectal cancer outcomes and treatment patterns in patients too young for average-risk screening. Cancer. 2016;122:929-34.
24. Teng A, Lee DY, Cai J, Patel SS, Bilchik AJ, Goldfarb MR. Patterns and outcomes of colorectal cancer in adolescents and young adults. J Surg Res. 2016;205:19-27.
25. Zahir Ahmed S, Cirocchi N, Saxton E, Brown MK. Incidence of age migration of colorectal cancer in younger population: retrospective single centred-population based cohort study. Ann Med Surg (Lond). 2021; 74:103214.
26. Fu J, Yang J, Tan Y, Jiang M, Wen F, Huang Y, et al. Young patients (≤ 35 years old) with colorectal cancer have worse outcomes due to more advanced disease. Medicine. 2014;93:e135.
27. You YN, Xing Y, Feig BW, Chang GJ, Cormier JN. Young-onset colorectal cancer: is it time to pay attention? Arch Intern Med. 2012;172:287-9.
28. O'Connell JB, Maggard MA, Livingston EH, Yo CK. Colorectal cancer in the young. Am J Surg. 2004;187:343-8.
29. O'Connell JB, Maggard MA, Liu JH, Etzioni DA, Livingston EH, Ko CY. Do young colon cancer patients have worse outcomes? World J Surg. 2004;28:558-62.
30. Arhin ND, Shen C, Bailey CE, Matsuoka LK, Hawkins AT, Holowatyj AN, et al. Surgical resection and survival outcomes in metastatic young adult colorectal cancer patients. Cancer Med. 2021;10:4269-81.
31. Akinkuotu AC, Maduekwe UN, Hayes-Jordan A. Surgical outcomes and survival rates of colon cancer in children and young adults. Am J Surg. 2021;221:718-24.
32. Kneuertz PJ, Maithel SK, Staley CA, Kooby DA. Chemotherapy-associated liver injury: impact on surgical management of colorectal cancer liver metastases. Ann Surg Oncol. 2011;18(1):181-190.
33. Castro-Mujica MC, Barletta-Carrillo C. Síndrome de Lynch: aspectos genéticos, clínicos y diagnósticos. Rev Gastroenterol Peru. 2018;38:265-79.
34. Domínguez-Valentín M, Seppälä TT, Sampson JR, Macrae F, Winship I, Evans DG, et al. Survival by colon cancer stage and screening interval in Lynch syndrome: a prospective Lynch syndrome database report. Hered Cancer Clin Pract. 2019;17:28.