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ORIGINAL ARTICLE

Clinical profile of early- and late-onset colorectal cancer patients in a referral medical center in Medellín, Colombia: A comparative analysis

Perfil clínico de pacientes con cáncer colorrectal de aparición temprana y tardía en un centro médico de referencia en Medellín, Colombia: Un análisis comparativo

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Abstract

Introduction. Incidence of early-onset colorectal cancer (EOCRC), defined as colorectal cancer (CRC) in individuals aged < 50 years, is rising worldwide. Despite the increasing international scientific production on EOCRC, research is limited in Colombia. The objective of this study was to characterize the clinical features of adults with EOCRC and late-onset CRC (LOCRC, CRC in individuals aged ≥ 50 years).

Methods. An observational, retrospective, cross-sectional study was conducted with CRC patients ≥ 18 years old at one medical center in Medellín, Colombia. Clinical and pathological data were retrieved from the Institutional Cancer Registry. Two analysis groups were established: EOCRC and LOCRC. The Chi-Square test was applied to compare the variables of interest between both groups.

Results. The sample included 1,202 patients, 53.5% were female (N=643) and the median age was 65 years (interquartile range: 55-73). EOCRC represented 15.9% (N=192). LOCRC tended to have more history of cardiometabolic diseases and smoking (p<0.001) than EOCRC. CRC family history was proportionally more frequent in EOCRC (7.3% vs 3.8%; p=0.028) than in LOCRC. Right-sided tumors were more common in LOCRC (30.4% vs 21.9%; p=0.041) and left-sided tumors in EOCRC (30.7% vs 23.2%; p=0.041). Only one patient had inflammatory bowel disease history.

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Conclusion. EOCRC is clinically distinct from LOCRC regarding pathological and toxicological history as well as tumor location. Our findings provide valuable insights for enhancing clinical decision-making, particularly in relation to age at onset in Colombian CRC patients.

Keywords: colorectal neoplasms; age of onset; epidemiology; observational study; colorectal surgery; Colombia.

Resumen

Introducción. La incidencia de cáncer colorrectal (CCR) de aparición temprana (CCR-ATem), definido como CCR en individuos menores de 50 años, está aumentando en todo el mundo. A pesar del incremento en la producción científica internacional sobre CCR-ATem, la investigación es limitada en Colombia. El objetivo de este estudio fue caracterizar clínicamente los adultos con CCR-ATem y CCR de aparición tardía (CCR-ATar, CCR en individuos ≥ 50 años).

Métodos. Estudio observacional, retrospectivo, transversal, en el que se incluyeron los pacientes adultos con CCR atendidos en un centro médico de Medellín, Colombia. Los datos se obtuvieron del Registro Institucional de Cáncer. Se establecieron dos grupos de análisis: CCR-ATem y CCR-ATar. Se aplicó la prueba de Chi cuadrado para comparar las variables de interés entre ambos grupos.

Resultados. La muestra incluyó 1.202 pacientes, 53,5 % fueron mujeres (N=643), y la mediana de edad fue de 65 años (rango intercuartil: 55-73). CCR-ATem representó el 15,9 % (N=192). CCR-ATar tuvo más casos de enfermedades cardiometabólicas y tabaquismo (p<0,001). El antecedente familiar de CCR fue proporcionalmente más frecuente en CCR-ATem (7,3 % vs. 3,8 %; p=0,028). Los tumores del colon derecho fueron más frecuentes en CCR-ATar (30,4 % vs. 21,9 %; p=0,041) y los del colon izquierdo en CCR-ATem (30,7 % vs. 23,2 %; p=0,041). Solo un paciente tuvo antecedente de enfermedad inflamatoria intestinal.

Conclusión. CCR-ATem es clínicamente distinto de CCR-ATar con respecto a antecedentes patológicos y toxicológicos, y localización tumoral. Nuestros hallazgos proporcionan información útil para mejorar la toma de decisiones clínicas, particularmente en relación con la edad de inicio en pacientes colombianos con CCR.

Palabras clave: neoplasias colorrectales; edad de inicio; epidemiología; estudio observacional; cirugía colorrectal; Colombia.

Introduction

Colorectal cancer (CRC) is one of the most common and deadly cancers globally [1]. By 2019, the incidence of CRC exceeded 2.17 million cases, with associated deaths nearly doubling from around 500,000 to 1.09 million over the past three decades [2]. Data from the Global Burden of Disease 2019 revealed a significant increase in new cases of CRC from 1990 to 2019, particularly in regions with low to middle sociodemographic indices such as South Asia, sub-Saharan Africa, and Latin America [2]. In the latter, for instance, CRC incidence age-standardized rates saw a noteworthy 145.8% rise during this period [2]. Projections indicate a concerning threefold increment in CRC incidence by 2040 worldwide [3].

Population-based reports in Colombia support these findings, indicating an increase in both CRC incidence and mortality rates. Between 2015 and 2022, CRC diagnoses went from 1.967 to 3.910, representing a 98.7% increase. Furthermore, CRC-related deaths also increased from 1.436 to 3.036 cases during the same period [4,5]. According to the Cali Cancer Registry, Colombia, the CRC age-standardized incidence rates (100,000 persons/year) changed from 7.3 and 7.0 between 1962-1966 to 15.8 and 14.1 between 2003-2007 among men and women, respectively [6]. Similar patterns are evident in studies based on cancer registries from other Colombian cities [7-9].

This scenario mirrors an epidemiological trend observed across numerous countries con-

cerning age-related CRC burden. Over the last decades, there has been a documented increment in cases of early-onset colorectal cancer (EOCRC), defined as CRC in individuals aged < 50 years, without a clear underlying cause [10,11]. Currently, EOCRC accounts for approximately 10% of all CRC cases [11]. The annual incidence of EOCRC has increased by 36.5% worldwide [12] and by 1-4% in high-income countries [13]. Moreover, CRC has become the 2nd and 4th most common cancer in men and women < 50 years of age, respectively. It is estimated that, by the year 2030, the incidence of colon cancer will rise by 90%, and for rectal cancer is expected to be 124.2% among individuals aged 20 to 34 years [14].

Consequently, there is a growing international research field aimed at elucidating this phenomenon. However, in Colombia the number of studies focused on CRC, let alone EOCRC, remains limited. Local evidence directly addressing CRC in younger adults is scarce. To date, two published studies [15,16] have explored EOCRC in Colombian patients, and none has conducted a comparative analysis with late-onset CRC (LOCRC, CRC in individuals aged 50 years or older). Both studies sought to characterize the clinical features of young adults in three regions of Colombia. They found that tumors in EOCRC were mainly in the descending colon and rectum. The primary clinical signs and symptoms were weight loss, changes in bowel habits, and abdominal pain; and the diagnosis tended to be more frequently established in advanced stages.

Due to the limited local evidence, alongside the increasing incidence of EOCRC globally, further research is needed. Thus, we aimed to characterize the clinical features of EOCRC and LOCRC patients at one referral medical center in Medellín, Colombia.

Methods

An observational, retrospective, cross-sectional study was conducted at one cancer care-focused referral medical center in Medellín, Colombia. CRC diagnosis was established according to the 10th edition of the International Classification of Diseases [17]. This study followed the recommendations of the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) initiative [18].

The sample consisted of adults ≥ 18 years old diagnosed with CRC treated between January 1st, 2018 and December 31st, 2022. Patients with metastasis to the colon and/or rectum from another primary tumor, recurrent CRC, and a history of a non-colorectal malignant tumor were excluded.

Data were retrieved from the Institutional Cancer Registry. Included characteristics were demographics (i.e., age at the time of diagnosis, sex), pathological history, toxicological history, CRC family history, time between the onset of clinical signs and/or symptoms and diagnosis (in months), clinical signs and/or symptoms at onset, tumor location, histological subtype, tumor grading, TNM staging according to the 7th edition of the American Joint Committee on Cancer [19], and metastases location.

Bias was reduced through review, adjustment and cleaning of the database provided by the medical center. All inconsistent data were discussed by the authors and, when possible, the respective electronic medical records were reviewed to clarify the information.

Two analysis groups were established: EOCRC (adults diagnosed at < 50 years of age) and LOCRC (adults diagnosed at ≥ 50 years of age). All available items of each variable were considered. Mean and standard deviation or median and interquartile range (IQR) were calculated for continuous variables according to data distribution, and frequencies and percentages for categorical variables. The Chi-square test was performed to compare the variables of interest between both groups. Missing data were not included in the statistical analyses. All patient's characteristics were analyzed according to age at the time of diagnosis. All analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 25.0.0.0 (IBM). *P*-values < 0.05 were considered statistically significant.

Results

Over the 5-year period, 1,202 patients were diagnosed with CRC. Among these, 53.5% (N=643) were women, and 15.9% (N=192) belonged to the EOCRC group. The median age of all patients was 65 years (IQR: 55-73), with EOCRC patients having a median age of 42 years (IQR: 36.25-46.75) and LOCRC patients of 68 years (IQR: 60-75). A detailed presentation of the clinical features, stratified by age, is provided in table 1.

The LOCRC group exhibited a higher prevalence of cardiometabolic diseases (i.e., arterial hypertension, diabetes mellitus, and dyslipidemia) and smoking history compared to the EOCRC group (all p<0.001). Conversely, the EOCRC group displayed a higher proportion of CRC family history in first- or second-degree relatives (7.3% vs 3.8%; p=0.028) compared to the LOCRC group.

Statistically significant differences were found regarding tumor location. Tumors in the right colon were more common in individuals with LOCRC (30.4% vs 21.9%; p=0.041), and those in the left colon predominated in the EOCRC group (30.7% vs 23.2%; p=0.041). No significant differences were identified on TNM stage (p=0.965), histological subtype (p=0.886), and tumor grading (p=0.124).

Time between the onset of clinical signs and/or symptoms and diagnosis did not differ between EOCRC and LOCRC, with a median of 5 (IQR: 2.0-8.5) and 4 (IQR: 1.0-8.0) months, respectively. Moreover, inflammatory bowel disease (IBD) history represented only 0.1% of the total sample. One patient with ulcerative colitis was identified within the LOCRC group.

Discussion

Given the limited research on CRC in younger populations in Colombia, we aimed to characterize a representative sample of CRC patients in Medellín by analyzing the clinical differences between EOCRC and LOCRC. Our findings revealed distinct profiles. LOCRC patients exhibited a higher prevalence of cardiometabolic diseases and smoking history. EOCRC individuals showed a significant prevalence of CRC family history over LOCRC. Disparities in tumor locations were also evident, with right colon tumors being more prevalent in LOCRC and left colon tumors in EOCRC.

As individuals age, they are often exposed for longer periods to external risk factors associated with cardiometabolic diseases, particularly in Western-influenced cultures [20]. Unhealthy habits such as low physical activity and heavy alcohol intake are commonly associated with a heightened incidence of those conditions [20]. In our study, we observed a significantly higher prevalence of arterial hypertension, diabetes mellitus, and dyslipidemia among adults with LOCRC compared to those with EOCRC. These disparities are often overlooked in many studies, likely because such non-communicable chronic diseases are prevalent among the elderly population, whether they have CRC or not [21]. Moreover, it is important to highlight that the incidence of cardiovascular diseases is on the rise among young individuals, especially in high-income countries [22]. This is attributed to the adoption of westernized lifestyles and their associated risk factors, including obesity and high consumption of sugary beverages [22,23]. Consequently, age may no longer be a relevant clinical aspect to consider when establishing CRC risk in the future [14,24].

EOCRC is often linked to a familial background, either through known hereditary syndrome or family history [25]. Our findings revealed that CRC family history was proportionally more common in EOCRC patients compared to LOCRC patients. These findings are supported by observational studies from Colombia and Chile, which reported similar proportions (17.4 vs 10.2% and 9.72 vs 6.7%, respectively) [26,27]. Furthermore, within the EOCRC group of our study, a significant majority (92.7%) of cases were sporadic. Evidence suggests that 70-85% of all EOCRC patients are average-risk individuals, meaning that around three out of four EOCRC cases have no family history or known genetic predisposition [22]. Considering this fact, coupled with the recent rise in EOCRC incidence, surveillance in symptomatic cases becomes pivotal. Early detection through these measures could significantly enhance prognosis in young individuals [28,29].

Table 1. Characteristics of adults with early- and late-onset colorectal cancer in Medellín, Colombia.

Characteristic	EOCRC n=192 15.9%	LOCRC n=1,010 84.1%	Total n=1,202 100%	P-value
Age, median (IQR)	42 (36.25-46.75)	68 (60-75)	65 (55-73)	—
Sex, n (%)				
Female	104 (54.2)	539 (53.4)	643 (53.5)	0.839
Male	88 (45.8)	471 (46.6)	559 (46.5)	
Pathological history, n (%)				
Arterial hypertension	17 (8.9)	395 (39.1)	412 (34.3)	<0.001
Diabetes mellitus (type I or II)	7 (3.6)	161 (15.9)	168 (14.0)	<0.001
Dyslipidemia[1]	4 (2.1)	119 (11.8)	123 (10.2)	<0.001
Ulcerative colitis	0 (0.0)	1 (0.1)	1 (0.1)	—
Crohn's disease	0 (0.0)	0 (0.0)	0 (0.0)	—
Colorectal polyps	15 (7.8)	61 (6.0)	76 (6.3)	0.355
Diverticular disease[2]	0 (0.0)	5 (0.5)	5 (0.4)	—
Toxicological history, n (%)				
Smoking	32 (16.7)	289 (28.6)	321 (26.7)	<0.001
Alcohol consumption	19 (9.9)	126 (12.5)	145 (12.1)	0.314
CRC family history[3], n (%)	14 (7.3)	38 (3.8)	52 (4.3)	0.028
Clinical signs and/or symptoms, n (%)				
Lower gastrointestinal tract bleeding	83 (54.2)	380 (49.7)	463 (50.4)	0.301
Abdominal pain	69 (45.1)	281 (36.7)	350 (38.1)	0.052
Weight loss	29 (19.0)	139 (18.2)	168 (18.3)	0.819
Bowel habits changes	47 (30.7)	280 (36.6)	327 (35.6)	0.165
Bowel obstruction	21 (13.7)	72 (9.4)	93 (10.1)	0.106
Anorectal pain[4]	11 (7.2)	42 (5.5)	53 (5.8)	0.411
Time to diagnosis in months[5], median (IQR)	5 (2.0-8.5)	4 (1.0-8.0)	4 (1.0-8.0)	—
Tumor location, n (%)				
Right colon[6]	42 (21.9)	307 (30.4)	349 (29.0)	0.041
Left colon[7]	59 (30.7)	234 (23.2)	293 (24.4)	
Rectum	91 (47.4)	467 (46.2)	558 (46.4)	
Not specified	0 (0.0)	2 (0.2)	2 (0.2)	
Histological subtype, n (%)				
Adenocarcinoma, NOS	186 (96.9)	971 (96.1)	1157 (96.3)	0.886
Neuroendocrine carcinoma	2 (1.0)	13 (1.3)	15 (1.2)	
Other histological subtypes[8]	4 (2.1)	26 (2.6)	30 (2.5)	
Tumor grading, n (%)				
Well differentiated	73 (47.7)	493 (56.6)	566 (55.3)	0.124
Moderately differentiated	69 (45.1)	328 (37.7)	397 (38.8)	
Poorly differentiated	11 (7.2)	50 (5.7)	61 (6.0)	
Stage, n (%)				
0	3 (2.3)	21 (3.1)	24 (3.0)	0.965
I	16 (12.0)	73 (10.8)	89 (11.0)	
II	34 (25.6)	163 (24.1)	197 (24.4)	
III	42 (31.6)	219 (32.4)	261 (32.3)	
IV	38 (28.6)	200 (29.6)	238 (29.4)	
Metastasis location, n (%)				
Liver	15 (55.6)	108 (61.4)	123 (60.6)	0.565
Lungs	8 (29.6)	49 (27.8)	57 (28.1)	0.847
Peritoneum	5 (18.5)	24 (13.6)	29 (14.3)	0.500
Tumor size and extend, n (%)				
T0	1 (0.8)	7 (1.0)	8 (1.0)	0.953
T1	29 (22.3)	153 (22.9)	182 (22.8)	
T2	19 (14.6)	80 (12.0)	99 (12.4)	
T3	57 (43.8)	289 (43.3)	346 (43.4)	
T4	21 (16.2)	118 (17.7)	139 (17.4)	
T in situ	3 (2.3)	21 (3.1)	24 (3.0)	
Regional lymph nodes involvement, n (%)				
N0	57 (43.8)	279 (41.8)	336 (42.1)	0.463
N1	50 (38.5)	292 (43.7)	342 (42.9)	
N2	23 (17.7)	97 (14.5)	120 (15.0)	
Metastasis, n (%)				
M0	95 (71.4)	476 (70.4)	571 (70.6)	0.814
M1	38 (28.6)	200 (29.6)	238 (29.4)	

EOCRC: early-onset colorectal cancer; LOCRC: late-onset colorectal cancer; CRC, colorectal cancer: NOS, not otherwise specified.

[1]Includes hypercholesterolemia and hypertriglyceridemia; [2]Diverticulosis or diverticulitis; [3]First- or second-degree relatives; [4]Includes rectal tenesmus, rectal straining, sensation of mass in the rectum, anal burning sensation, and dyschezia; [5]Time between onset of clinical signs and/or symptoms and diagnosis; [6]Cecum, ascending colon, hepatic flexure, and transverse colon; [7]Splenic flexure, descending colon, sigmoid colon and rectosigmoid junction; [8]Mucinous adenocarcinoma, signet ring cell carcinoma, squamous cell carcinoma, sarcoma, lymphoma, and undifferentiated carcinoma.

While CRC is often treated as a single clinical entity, evidence indicates notable differences between colon and rectal cancer [30,31]. In our study, patients in the LOCRC group showed a higher tendency to develop tumors in the right colon, while left colon tumors were more prevalent in the EOCRC group. After analyzing a cohort of 1,877 stage IV CRC patients, Willauer et al. [32] reported similar results. Left-sided tumors were more frequent in younger adults (51.5% vs 42.1%) and right-sided tumors in older adults (35.9% vs 24.9%). In parallel, Bohorquez et al. [26] characterized the clinical manifestations of 1,525 Colombian CRC patients. In one of their sub-analyses comparing the sample by age, EOCRC presented predominantly in the rectum (48.9% vs 40.1%), while LOCRC occurred more often in the right colon (29.8% vs 21.1%). Notably, no significant age-based differences in left-sided tumor location were found.

Accordingly, tumor location becomes an important factor implied in key CRC oncological outcomes [33]. However, when it comes to survival-related outcomes, the evidence is inconsistent. Some observational studies suggest a more favorable prognosis for tumors in the distal colon (including rectum) compared to the proximal colon, while others report the opposite, regardless of age at diagnosis [24,34]. Notably, research examining the relationship between tumor location and age is limited. While some studies have focused on survival differences between EOCRC and LOCRC, which appear to be more favorable for younger patients, little consideration has been given to its link to tumor location, underscoring the need for further investigation [35].

An important point of interest is the unusual low frequency of IBD found in our study sample. Only one patient in the LOCRC group had a history of ulcerative colitis. This contrasts with multiple research reviews, given the well-established association between IBD and CRC development [21,22,25,36]. A plausible explanation for this discrepancy lies in the rigorous clinical surveillance that individuals with IBD often undergo because of the recognized risk for CRC in this population [36]. The monitoring of IBD patients enables the early detection of premalignant lesions, easing prompt interventions by clinicians and, ultimately, improving overall prognosis [10].

This study has multiple limitations. First, its retrospective design and data source introduce a potential bias as data accuracy could not be assessed in many cases. Second, data for many variables were unavailable and could not be used in the statistical analyses. And third, this was a single-center study, which could represent a selection bias. However, the authors would like to highlight the strengths of this study. This is one of the few studies conducted in Colombia that characterizes and analyzes a relatively large sample of EOCRC compared to LOCRC. Our study contributes to the global scientific knowledge framework on CRC by exploring it in individuals under the age of 50 in a South American region. Moreover, conducting studies focused on the age of onset of CRC is decisive for enhancing our understanding of CRC patients' profile within our local context. Such studies can offer significant insights that could improve clinical decision-making processes by clinicians and shape the design of future research approaches in the region.

Conclusion

Patients with EOCRC are clinically distinct from those with LOCRC. Younger individuals display a higher prevalence of CRC family history and a tendency to develop left-sided tumors. Conversely, LOCRC cases are characterized by a higher frequency of cardiometabolic diseases, smoking history, and right colon tumors. Our study contributes to the limited scientific production on EOCRC in Colombia and provides compelling insights for enhancing clinical decision-making, particularly in relation to age at onset in CRC patients.

Compliance with ethical standards

Informed consent: This research followed the standards outlined in the Helsinki Declaration of 1975, as modified in 2013 in its 7th revision. Additionally, in alignment with Resolution 8430 of 1993 of Colombia and considering that patient's identification was not documented and no

interventions or deliberate modifications to the biological, physiological, psychological, or social variables of the individuals were carried out; the risk of this study was classified as less than minimal. Furthermore, in compliance with Resolution 1409 of 2022 of Colombia and Law 1581 of 2012 of Colombia, informed consent was not required. The study received approval from the Committee of Ethics in Clinical Research of the medical center (Acta Nº. 209).

Conflicts of Interest: The authors report no conflict of interest.

Artificial Intelligence: The authors declare the use of OpenAI ChatGPT to improve text writing and coherence in some parts of the manuscript.

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Authors' contributions

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- Data acquisition: Yeimys Eliana Pérez-García, Álvaro Esteban Ruiz-Grajales.
- Data analysis and interpretation of data: Álvaro Esteban Ruiz-Grajales, Esteban Castrillón-Martínez.
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