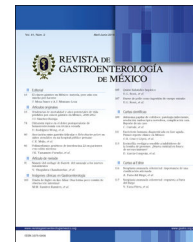




# REVISTA DE GASTROENTEROLOGÍA DE MÉXICO

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## ORIGINAL ARTICLE

# Colorectal cancer survival at an oncologic center in Colombia. A historic cohort study<sup>☆</sup>



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### KEYWORDS

Colorectal cancer;  
Clinical  
characteristics;  
Survival

### Abstract

**Introduction and aims:** In Colombia, cancer of the colon is the third most frequent cancer in relation to incidence and mortality. Five-year survival depends on stage at diagnosis, albeit that rate is not known for the country. The aim of the present study was to characterize the overall survival and disease-free survival rates in an adult population with colorectal cancer treated at an oncology center in Medellín, Colombia.

**Materials and methods:** A retrospective cohort study was conducted. The case records of patients with a histologic diagnosis of colorectal cancer, seen within the time frame of 2011 and 2015, were reviewed. The overall survival and disease-free survival curves were calculated using the Kaplan-Meier method.

**Results:** A total of 824 (54.9%) patients with cancer of the colon and 676 (45.1%) with cancer of the rectum were treated. Mean patient age was 63.3 years, female sex predominated (56.3%), and 98.1% of the tumors were adenocarcinomas. The majority of the lesions were stage III (31.9% in the colon and 35.5% in the rectum) at the time of diagnosis. Surgery was the most frequent treatment in the colon (85.2%) and radiotherapy was the most frequent in the rectum (75.4%). Overall survival at the median follow-up (27.3 months) was 66.7% for cancer of the colon and 63.9% for cancer of the rectum. Disease-free survival at the median follow-up (18.6 months in colon and 14.9 in rectum) was 72.5 and 68.9%, respectively.

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**PALABRAS CLAVE**

Cáncer colorrectal;  
Características  
clínicas;  
Supervivencia

**Conclusions:** The clinical characteristics and treatment of patients were similar to those found in other studies. Two-year survival was higher than in other Colombian reports and 5-year survival was lower than that observed in developed countries.

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### Supervivencia de cáncer colorrectal en un centro oncológico de Colombia. Estudio de cohorte histórica

#### Resumen

**Introducción y objetivos:** El cáncer de colon en Colombia es el tercero más frecuente en incidencia y mortalidad. La supervivencia a 5 años depende del estadio en el momento del diagnóstico, aunque esta no se conoce en el país. El presente estudio busca caracterizar la supervivencia global y libre de enfermedad en población adulta con cáncer colorrectal atendida en un centro oncológico de Medellín (Colombia).

**Materiales y métodos:** Estudio de cohorte retrospectivo. Se revisaron historias clínicas de pacientes atendidos entre 2011 y 2015 con diagnóstico histológico de cáncer colorrectal. Se calcularon las curvas de supervivencia global y libre de enfermedad por el método de Kaplan-Meier.

**Resultados:** Se atendieron 824 (54.9%) pacientes con cáncer de colon y 676 (45.1%) de recto. La edad media fue 63.3 años, con predominio del sexo femenino (56.3%), y un 98.1% fueron adenocarcinomas. La mayoría eran estadio III (31.9% en colon y 35.5% en recto) en el momento del diagnóstico; la cirugía fue el tratamiento más frecuente en colon (85.2%) y la radioterapia en recto (75.4%). La supervivencia global a la mediana de seguimiento (27.3 meses) para cáncer de colon fue de un 66.7% y para cáncer de recto, de un 63.9%. La supervivencia libre de enfermedad a la mediana de seguimiento (18.6 meses en colon y 14.9 en recto) fue de 72.5 y 68.9%, respectivamente.

**Conclusiones:** Las características clínicas y el tratamiento de los pacientes fueron similares a los encontrados en otros estudios. La supervivencia a 2 años fue mayor que en otros reportes colombianos y a 5 años fue menor que la observada en países desarrollados.

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## Introduction and aims

Colorectal cancer holds third place in incidence and prevalence worldwide, at 9.7 and 10.9%, respectively, following breast cancer and lung cancer.<sup>1,2</sup> The yearly prevalence of colon cancer in Colombia also makes it the third most frequent cancer in the country, behind prostate cancer and breast cancer. It accounts for 8.3% of all malignant neoplasias and its mortality rate places it in fourth place.<sup>2</sup>

Death from colorectal cancer has decreased over time, most likely due to changes in risk factors, such as diet, the introduction of screening programs, and the availability of better treatments in developed countries.<sup>3</sup> Colorectal cancer prognosis is known to essentially depend on pathologic stage at the time of presentation. According to large cohorts, such as the SEER register (the United States), 5-year survival ranges from 74% for stage I disease to 5.7% in stage IV.<sup>4</sup>

In Colombia, Montenegro et al. reported that in colorectal cancer patients from the cities of Medellín and Nieva<sup>5</sup>

that are under 40 years of age, the greatest frequency was found in those between 28 and 30 years old, with lesions mainly in the rectum. The most frequent symptoms were abdominal pain, rectal bleeding, and weight loss. In 2008, Barrero et al. described rectal cancer as the most frequent type in the city of Ibagué.<sup>6</sup> In 2012, the authors of a study conducted in Bucaramanga<sup>7</sup> found that the disease was more frequent in women (61%), abdominal pain (86%) and constipation (50%) were the most prevalent symptoms, and they identified the consumption of red meat (61%), low ingestion of vegetables (36%), and the presence of relatives with colorectal cancer (22%) as important background histories. In Cali,<sup>8</sup> more women (58%) and individuals with a body mass index under 25 kg/m<sup>2</sup> (61%) were found to be affected, and the main location of the cancer was in the right colon (34%). The principal symptoms were abdominal pain (24%) and intestinal bleeding (13.4%). Lastly, in the Colombian study with the largest number of patients,<sup>9</sup> a greater number of women were found to be affected (53%), with a mean age of 57.4 years. The most frequent risk factors were obesity (33%), alcohol consumption (50%), and smoking (48%).

The cancer was located in the rectum in the majority of the cases (42%) and was in advanced stages (40%).

Apart from the abovementioned studies on the clinical and pathologic characteristics of patients with colorectal cancer, there is no information in Colombia on survival rates or its associated factors. Therefore, the aim of the present study was to describe, in addition to the demographic and clinical characteristics and risk factors, the overall survival (OS) and disease-free survival (DFS) in patients with colorectal cancer treated at the *Instituto de Cancerología (IDC) Las Américas*, in Medellín, Colombia, within the time frame of 2011 and 2015.

## Materials and methods

A historic cohort study was conducted on patients above 18 years of age, diagnosed with colorectal cancer and treated at the *IDC* within the time frame of 2011-2015. The researchers collected the data from the clinical histories of the patients and the institutional register of patients with colorectal cancer.

The sociodemographic variables collected were age at diagnosis, sex, type of social security coverage, place of residency, and socioeconomic level. The clinical variables were a family history of cancer (first-degree relatives: parents, brothers and sisters, and children; other-degree relatives: grandparents, grandchildren, aunts and uncles, nieces and nephews), a personal history of inflammatory bowel disease, diabetes, smoking, alcoholism, previous abdominal radiation, androgen deprivation therapy, acromegalia, and cholecystectomy, and a family history of syndromes associated with colorectal cancer, symptoms at the time of disease presentation (rectal bleeding, anemia, asthenia, changes in bowel habit, abdominal pain, weight loss, rectal tenesmus, and others), and disease stage at the time of initial medical attention at the *IDC*. In addition, the results of the diagnostic studies of colonoscopy, biopsy, and carcinoembryonic antigen were recorded, as well as the treatment received (curative surgery, neoadjuvant and/or adjuvant chemotherapy, adjuvant radiotherapy, palliative care). The World Health Organization classification was used to determine nutritional status according to the body mass index.

The chemotherapy received depended on cancer type and stage. Cases of stages IIb and III colon cancer were treated with the Mayo and FOLFOX-4 adjuvant regimens with no radiotherapy and cases of stage IV disease were treated with regimens according to the criterion of the cancer clinic, following the guidelines of the National Comprehensive Cancer Network. They varied depending on the ECOG, if the patient had received adjuvant treatment or not, and KRAS/NRAS status: FOLFOX-6, FOLFIRI, bevacizumab was added in first-line and second-line treatment for metastatic disease, cetuximab was added in patients that did not have the KRAS/NRAS mutations, and on occasion, when 5-FU was not commercially available, it was substituted with capecitabine.

On the other hand, the chemotherapy regimens for non-metastatic cancer of the rectum depended on whether or not the surgery was performed at the *IDC*. If carried out there, preoperative pelvic magnetic resonance imaging was ordered, and if there was regional lymph node

or mesorectal lymph node involvement, primary radiotherapy/chemotherapy was employed (5 weeks of radiotherapy, with bolus 5-FU and leucovorin during the first and fifth weeks); if surgery was not performed at the *IDC*, the regimen was the same as that given to patients with stage IIB or stage III cancer of the colon.

Clinical staging was carried out through colonoscopy and complete contrast-enhanced chest and abdominal tomography and the postoperative pathology report. The medical records of patients that began treatment at the *IDC* or elsewhere were included, and thus not all of the cases had the clinical and pathologic stage data. When available in the case record, the pathologic stage was used, and when not, the clinical stage was used. The American Joint Committee on Cancer staging system was employed.

OS was defined as the time from diagnosis to death by any cause, and DFS was defined as the time from the end of treatment to the appearance of signs and/or symptoms of the disease. The date of death was obtained from the hospital medical records, the database of the National Civil Status Register, or the FOSYGA. November 30, 2016, was chosen as the closing date for the collection of data on OS and DFS. The patients whose vital status could not be established through the abovementioned sources were given the date of their final contact with the *IDC*.

The results were analyzed using the STATA 12 program. The data from the qualitative nominal variables were described through absolute and relative frequencies and the quantitative variables were expressed through the descriptive statistics of central tendency and dispersion (mean and standard deviation [SD]) or of position (median and interquartile range [IQR]), according to the symmetry of the variable. Survival was calculated using the Kaplan-Meier method.

The study was approved by the Independent Ethics Committee of the *IDC Las Américas*, which meets the Good Clinical Practice guidelines in all its activities.

## Results

Within the study time frame, 1,549 clinical histories of patients with colorectal cancer were found, 49 of which were not included due to insufficient information (33), no pathology study (8), patient was under 18 years of age (4), and unknown primary cancer (4). Of the 1,500 patients included in the study, 824 (54.9%) had colon cancer and 676 (45.1%) had rectal cancer.

The mean age of the patients with colon cancer was 63.4 years (SD 13.8), and there was a predominance of women (56.3%). The mean age of the patients with rectal cancer was 62.6 years (DE 14.1) and there was also a predominance of women (47.5%). The most frequent personal histories were smoking and diabetes mellitus (27.8 and 15.6%, respectively). At the time of diagnosis, the majority of the patients, 642 (42.8%), had normal nutritional status (Table 1).

The most frequent symptoms in the patients with colon cancer were lower gastrointestinal bleeding (212; 25.7%), abdominal pain (382; 46.4%), and changes in bowel habit (121; 14.7%). In the patients with rectal cancer, they were lower gastrointestinal bleeding (475; 70.3%), abdominal

**Table 1** Sociodemographic and medical background characteristics of the patients.

Characteristics	Colon 824 (54.9) n (%)	Rectum 676 (45.1) n (%)	Total 1,500 n (%)
<i>Mean age in years (SD)</i>	63.4 (13.8)	62.6 (14.1)	63.3 (13.9)
<b>Sex</b>			
Female	464 (56.3)	321 (47.5)	785 (52.3)
Male	360 (43.7)	355 (52.5)	715 (47.7)
<b>Social security regimen</b>			
Contributory	709 (86)	554 (82)	1,263 (84.2)
Subsidized	115 (14)	122 (18.1)	237 (16)
<b>City of residency</b>			
Medellín	454 (55.1)	321 (47.5)	775 (51.7)
Metropolitan area of Medellín	216 (26.2)	174 (25.7)	390 (26)
The rest of Antioquia	134 (16.3)	165 (24.4)	299 (10)
The rest of the country	20 (2.4)	16 (2.4)	36 (2.4)
<b>Smoking</b>	243 (29.5)	174 (25.7)	417 (27.8)
<b>Diabetes mellitus</b>	142 (17.2)	92 (13.6)	234 (15.6)
<b>Alcohol consumption</b>	68 (8.3)	61 (9)	129 (8.6)
<b>Cholecystectomy</b>	64 (7.8)	43 (6.4)	107 (7.1)
<b>Abdominal radiation for other neoplasias</b>	5 (0.6)	6 (0.9)	11 (0.7)
<b>History of adenomatous polyp</b>	8 (1)	5 (0.7)	13 (0.9)
<b>Personal history of cancer</b>	41 (5)	39 (5.8)	80 (5.3)
Genital tract	17 (41.6)	14 (35.9)	31 (38.8)
Skin	10 (24.4)	7 (17.9)	17 (21.2)
Gastrointestinal tract	3 (7.3)	5 (12.8)	8 (10)
Breast	3 (7.3)	5 (12.8)	8 (10)
Thyroid	3 (7.3)	3 (7.7)	6 (7.5)
Urinary tract	3 (7.3)	2 (5.1)	5 (6.2)
Others (brain, blood, lung)	2 (4.8)	3 (7.8)	5 (6.2)
<b>Family history of colorectal cancer</b>	78 (9.4)	63 (9.3)	141 (9.4)
First-degree relatives	59 (75.6)	43 (68.3)	102 (72.3)
Other-degree relatives	19 (24.4)	20 (31.7)	39 (27.7)
<b>Nutritional status (IMC)</b>			
Malnutrition	58 (7)	46 (6.8)	104 (6.9)
Normal	366 (44.4)	276 (40.8)	642 (42.8)
Overweight	237 (28.8)	150 (22.2)	387 (25.8)
Obese	71 (8.6)	59 (8.7)	130 (8.7)
No information	92 (11.2)	145 (21.5)	237 (15.8)

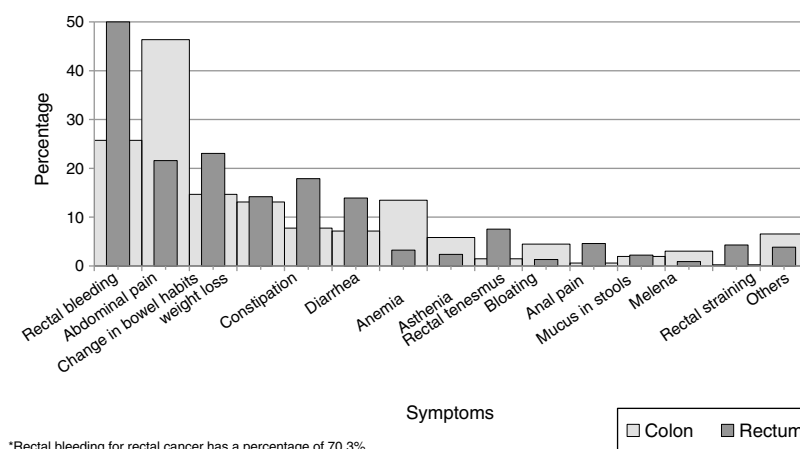
BMI: body mass index; SD: standard deviation.

pain (146; 21.6%), and changes in bowel habit (156; 23.1%). Additional symptoms of weight loss, asthenia, rectal tenesmus, and anorexia, among others, were identified (fig. 1). Only 12 (0.8%) patients, 7 (0.8%) with colon cancer and 5 (0.7%) with rectal cancer, had no symptoms at diagnosis.

The result of carcinoembryonic antigen testing was positive in the medical records of 139 of 275 (50.5%) of the patients with colon cancer and 122 of 219 (55.7%) of those with rectal cancer. The majority of the patients had stage III disease at diagnosis (33.5%), whereas only 1.1% had *in situ* tumors. A total of 98.1% of the patients had adenocarcinomas (Table 2), with the predominant location in the rectum (676; 45.1%), followed by the ascending colon

(344; 22.9%), whereas the lowest frequencies were in the descending colon (372; 24.8%) and the transverse colon (64; 4.3%). Tumor location could not be established in 44 (2.9%) patients.

Of the patients with colon cancer, 702 (85.2%) underwent surgery, as did 355 (52.5%) of the patients with rectal cancer. Forty-six (5.6%) of the patients with colon cancer and 47 (6.9%) with rectal cancer received no treatment, either because they died before surgery could be performed, they refused to undergo surgery, or they were lost to follow-up. Of the patients that did not have metastasis at diagnosis, 117 (14.2%) with colon cancer and 112 (16.6%) with rectal cancer presented with metastasis within the study period (Table 2).



**Figure 1** Symptoms by cancer type. A patient can have presented with more than one symptom. Other symptoms: lumbar pain, flatulence, food intolerance, stoppage of bowel movements, sensation of an anal mass, sensation of an abdominal mass, syncope, emesis, anorexia.

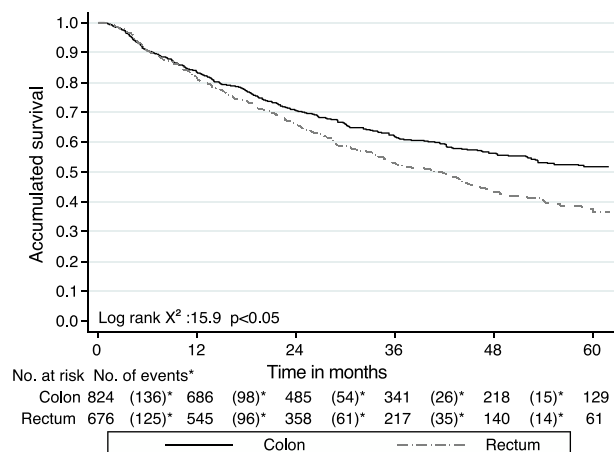
By November 2016, 679 (45.3%) of the 1,500 study patients had died: 339 (41.1%) from colon cancer and 340 (50.3%) from rectal cancer. The vital status of 12 (0.8%) patients could not be established. The median follow-up for the patient total was 27.3 months (IQR: 14.7-46.6), 29.1 months (IQR: 15.1-50.6) for the patients with colon cancer, and 25.4 months (IQR: 13.9-43.6) for those with rectal cancer. At the median follow-up for patients with colon cancer, OS was 66.7% (95% CI: 63.2-69.9) and 63.9% (95% CI: 59.9-67.5) for those with rectal cancer.

The two-year OS from diagnosis for both types of cancer was 68.4% (95% CI: 65.9-70.7) and 5-year OS was 45.5% (95% CI: 42.3-48.6). The 2-year OS for patients with colon cancer was 70.5% (95% CI: 66.6-73) and the 5-year OS was 51.7% (95% CI: 47.4-55.7), whereas the 2-year OS for patients with rectal cancer was 65.7% (95% CI: 61.9-69.3) and the 5-year OS was 37.5% (95% CI: 32.7-42.3). The Kaplan-Meier curves demonstrated a better OS for colon cancer ( $p < 0.05$ ) (fig. 2). Figure 3 shows the OS by stages in colon cancer and rectal cancer.

The median follow-up for DFS was 18.6 months (IQR: 9.5-35.9) in the patients with colon cancer and 14.9 months (IQR: 7.8-28.6) in the patients with rectal cancer. DFS for colon cancer was 72.5% (95% CI: 68.5-76.1), whereas it was 68.9% (95% CI: 64.5-73) for rectal cancer (fig. 4).

Upon differentiating stage and type of cancer, patients with colon cancer had a DFS of 87.4% (95% CI: 77-93.3), 77.4% (95% CI: 70.7-82.7), and 68% (95% CI: 61.6-73.7) for stages I, II, and III, respectively, whereas for patients with rectal cancer it was 75.3% (95% CI: 62.2-84.3), 69.2% (95% CI: 59.7-76.9), and 70.3% (95% CI: 63.4-76.1) (fig. 5).

Upon classifying the 1,500 patients with colorectal cancer according to location in the right colon (from the ascending colon to the splenic flexure) and the left colon (from the splenic flexure to the rectum), the 2-year OS was better for the right colon (72.3%; 95% CI: 67.9-76.8) than for the left (67.5%; 95% CI: 64.5-70.3). Results were similar for 5-year OS, which was 54.3% (95% CI: 48.9-60.4) for the right colon and 42.5% (95% CI: 38.7-46.4) for the left. The behavior in relation to DFS was also similar: for the right colon, 2-year DFS was 61.3% (IC 95% CI: 55.6-66.5) and 5-year DFS



**Figure 2** Overall survival by cancer type.

was 41.9% (95% CI: 34.6-49.2), whereas for the left colon, 2-year DFS was 50.1% (95% CI: 46.5-53.6) and 5-year DFS was 26.9% (95% CI: 22.4-31.7). Figures 6 and 7 show the OS and DFS in relation to disease laterality and according to disease stage.

## Discussion and conclusions

The incidence of colorectal cancer has been on the rise in Colombia for several years,<sup>10-12</sup> and the same is projected for gastric cancer by the year 2045.<sup>13</sup> Likewise, even though death by colorectal cancer has decreased in developed countries, it has increased in countries with a lack of resources, such as Colombia.<sup>14-17</sup> That increase is most likely due to greater exposure to the risk factors attributable to urban growth in many of those countries, to later detection resulting from the poor availability of screening and prevention programs, and to a lower level of access to adequate treatment. Thus, it is important to have information on the clinical characteristics, diagnosis, and management of patients in our environment, as well as their outcomes in terms of survival.

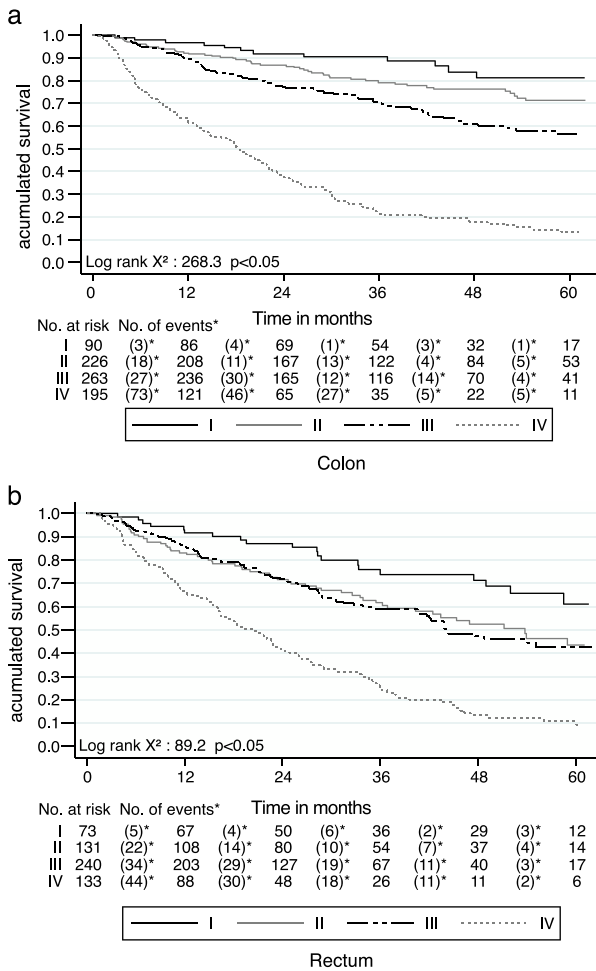
**Table 2** Histopathologic, laboratory, clinical and treatment characteristics.

Characteristics	Colon 824 n (%)	Rectum 676 n (%)	Total 1,500 n (%)
<i>Histologic type</i>			
Adenocarcinoma	805 (97.7)	666 (98.5)	1,471 (98.1)
Others <sup>a</sup>	19 (2.3)	10 (1.5)	29 (1.9)
<i>Histologic grade</i>			
Well-differentiated	417 (50.6)	322 (47.6)	739 (49.2)
Moderately differentiated	221 (26.8)	223 (32.9)	444 (29.6)
Poorly differentiated	58 (7)	26 (3.8)	84 (5.6)
Undifferentiated	6 (0.7)	5 (0.7)	11 (0.7)
No information	122 (14.8)	100 (14.8)	222 (14.8)
<i>Stage</i>			
<i>In situ</i>	6 (0.7)	10 (1.5)	16 (1.1)
I	90 (10.9)	73 (10.8)	163 (10.9)
II	226 (27.4)	130 (19.2)	356 (23.7)
III	263 (31.9)	240 (35.5)	503 (33.5)
IV	198 (24)	134 (19.8)	332 (22.1)
No information	41 (4.9)	89 (13.2)	130 (8.7)
<i>Treatment</i>			
Surgery	702 (85.2)	355 (52.5)	1,057 (70.5)
Radiotherapy	55 (6.7)	510 (75.4)	565 (37.7)
Neoadjuvant chemotherapy	N/A	370 (54.7)	370 (24.7)
Adjuvant chemotherapy	315 (38.2)	122 (18.1)	437 (29.1)
Pain and palliative care	263 (31.9)	231 (34.2)	494 (32.9)
Palliative chemotherapy	167 (20.3)	120 (17.8)	287 (19.1)
No treatment	46 (5.6)	47 (6.9)	93 (6.2)
<i>Metastasis by stage</i>			
<i>In situ</i>	117 (14.2)	112 (16.6)	229 (15.3)
I	1 (0.9)	1 (0.9)	2 (0.9)
II	7 (5.9)	13 (11.6)	20 (8.7)
III	29 (24.8)	24 (21.4)	53 (23.1)
IV	77 (65.8)	56 (50)	133 (58.1)
No information	3 (2.6)	18 (16.1)	21 (9.2)
<i>Metastasis extension</i>			
Local	4 (3.4)	4 (3.6)	8 (3.5)
Regional	9 (7.7)	18 (16.1)	27 (11.8)
Distant	104 (88.9)	90 (80.3)	194 (84.7)
<i>Metastasis site<sup>b</sup></i>			
Liver	62 (52.9)	47 (41.9)	109 (47.6)
Lung	42 (35.9)	35 (31.2)	77 (33.6)
Peritoneum	30 (25.6)	12 (10.7)	42 (18.3)
Bone	15 (12.8)	20 (17.8)	35 (15.3)
Lymph nodes	22 (18.8)	11 (9.8)	33 (14.4)
Others <sup>c</sup>	32 (27.3)	53 (47.3)	85 (37.1)
<i>Second primary site<sup>b</sup></i>			
Gastrointestinal tract	40 (4.9)	33 (4.9)	73 (4.9)
Genital tract	16 (40)	12 (36.4)	28 (38.4)
Urinary tract	7 (17.5)	8 (24.2)	15 (20.5)
Others <sup>c</sup>	7 (17.5)	5 (15.2)	12 (16.4)
Others <sup>c</sup>	12 (30)	9 (27.3)	21 (28.8)

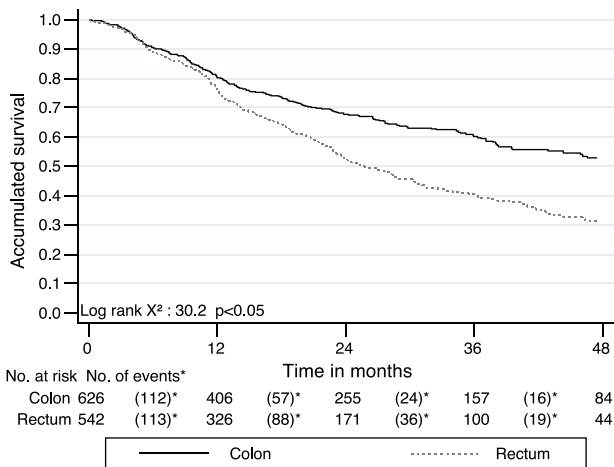
<sup>a</sup> Squamous cell carcinoma, melanoma, sarcoma, neuroendocrine cancer, PEComa.

<sup>b</sup> A person could have had more than one metastasis site and more than one second primary site.

<sup>c</sup> Reproductive system, central nervous system, soft tissues, pleura, bladder, kidney, pancreas, abdominal wall, mediastinum, skin, amygdala, small bowel.

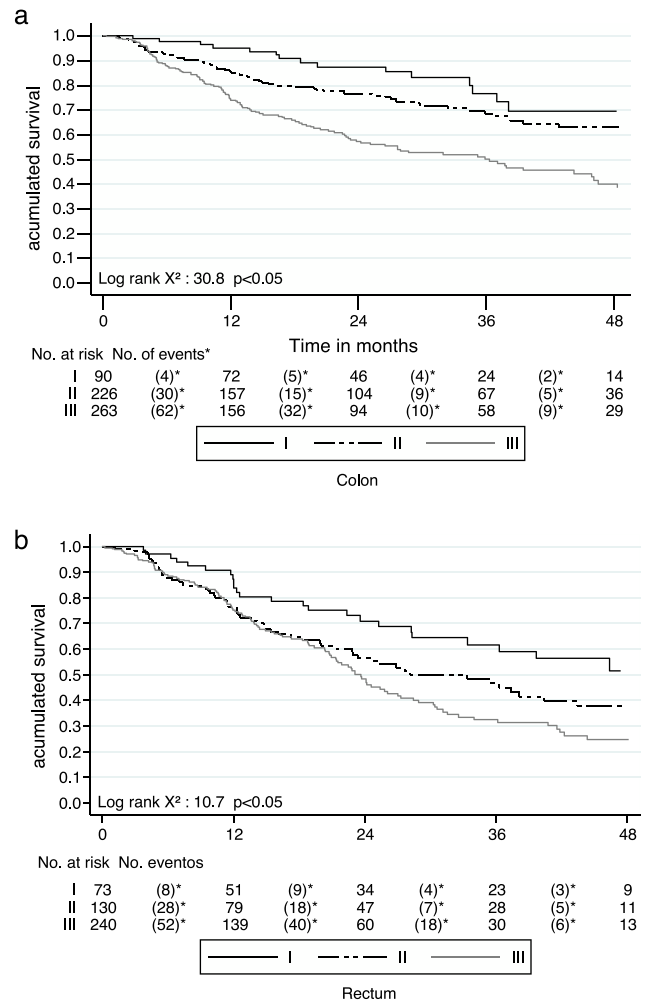


**Figure 3** Overall survival by stage in colon cancer (a) and rectal cancer (b).



**Figure 4** Disease-free survival by cancer type.

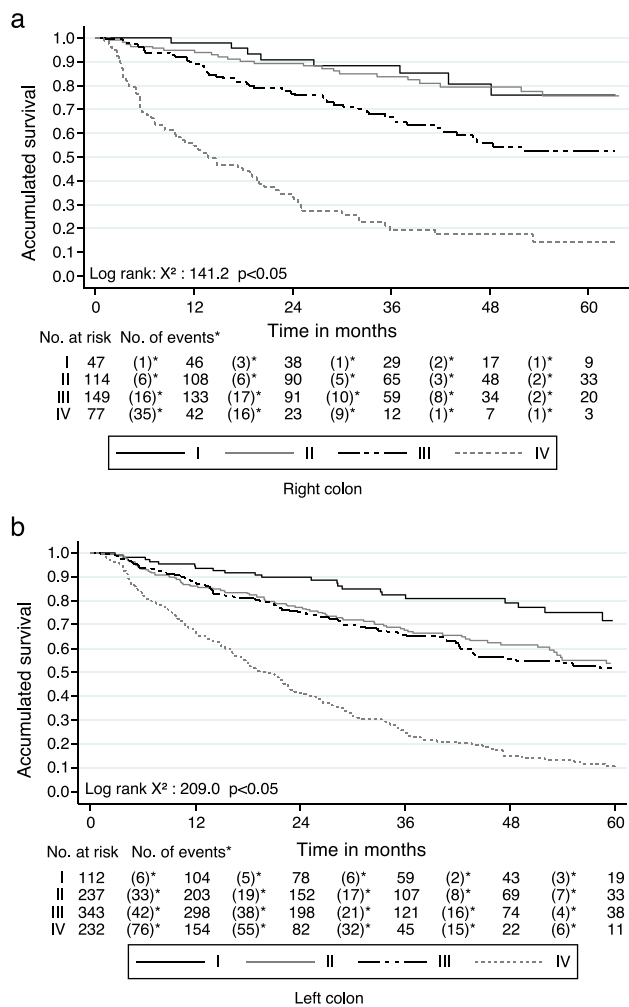
The mean age of our study patients at diagnosis (63.3 years) corresponded to that of the majority of patients in other parts of Colombia and the world.<sup>3,6-9,18,19</sup> Contrary to that reported in the majority of studies from developed countries, in which incidence is higher in men,<sup>3,20,21</sup> we observed a predominance in women, which has been



**Figure 5** Disease-free survival by stage in colon cancer (a) and rectal cancer (b).

described in other national studies.<sup>7-9</sup> The hypotheses for predominance in men have been their greater exposure to risk factors and female hormones as protective factors in women.

The most important risk factors in our study were smoking and alcohol consumption. They have consistently been described as carcinogens associated with numerous neoplasias,<sup>22</sup> including colorectal cancer. Their frequencies vary among the different studies, but they are more consistent in relation to smoking, which has reached 52% in some reports.<sup>6,7,9,23</sup> Another relevant risk factor we found was diabetes mellitus, which concurs with the data from different analyses worldwide that have also reported a higher mortality rate in those patients.<sup>6,24-26</sup> Despite the clear association that has been shown between a family history of colon cancer and the incidence of colorectal cancer and a 2 times increased risk, or higher, for colorectal cancer if at least one first-degree relative presents with the disease, a family history of colon cancer was infrequent in our study, as well as in others.<sup>6,7,20,23,27</sup> Most of our patients were normal weight, followed by overweight, and a smaller percentage were obese, which is congruent with findings from other Colombian studies.<sup>8,9,23</sup> Obesity has been identified as a risk

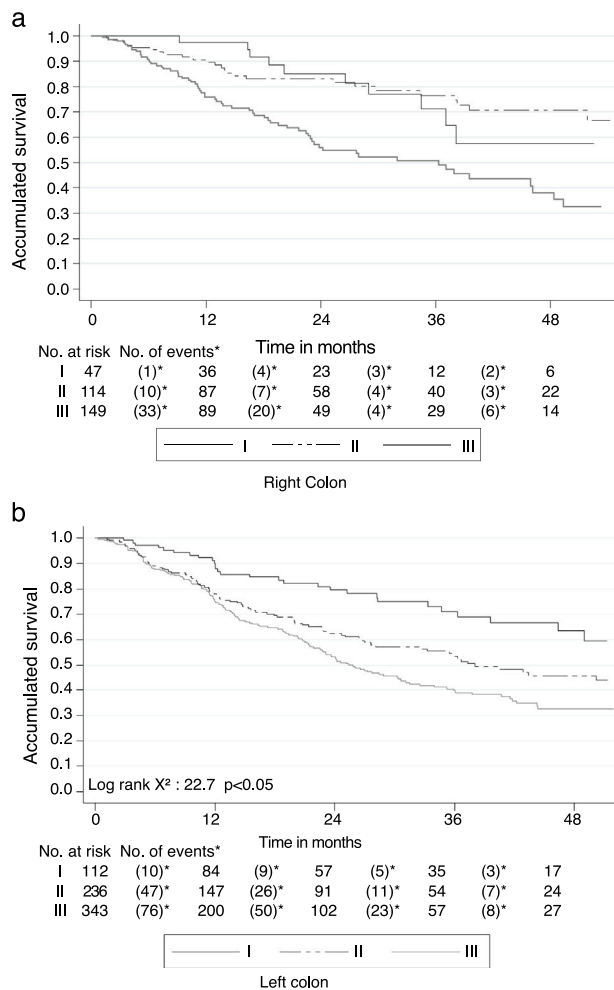


**Figure 6** Overall survival by stage in the right colon (a) and the left colon (b).

factor <sup>28-30</sup> and should be taken into account in Colombia, given its increasing prevalence.

The main symptoms in our patients were rectal bleeding and abdominal pain, results that are similar to those reported in the national and international literature, in which positive predictive values reached 12.9 and 13.5, respectively, in some meta-analyses.<sup>31,32</sup> The main symptoms in our patients were followed by changes in bowel habit, diarrhea, constipation, weight loss, and anemia, findings that also concur with those of other studies.<sup>6-8,23</sup> Only 0.8% of patients were asymptomatic at diagnosis, suggesting that educating patients to recognize disease symptoms could impact their outcomes. Initial presentation as obstruction or perforation, with a reported frequency of 3 to 40% in the literature, more common in the colon than in the rectum (21.7 and 5.9%, respectively) and with a higher mortality rate, was not found in our study.<sup>33,34</sup>

The most frequent stage at diagnosis was stage III, followed by stage II and stage IV. Percentages were similar for stages II and IV and very few patients presented with *in situ* tumors. Almost all the tumors (98.1%) were adenocarcinomas, nearly half of which were well-differentiated. Close to half of the tumors were located in the rectum, almost



**Figure 7** Disease-free survival by stage in the right colon (a) and the left colon (b).

one-fourth in the descending colon, and one-fourth in the ascending colon. Very similar results were also found in other studies from Colombia<sup>6,9,23,35</sup> and other locations,<sup>18,36</sup> with a few exceptions, such as the Danish cohort<sup>19</sup> and one of the case series from Cali.<sup>8</sup> Carcinoembryonic antigen testing was positive at diagnosis in half of our patients (that datum was obtained in 32.9% because not all the patients were initially evaluated at the IDC), showing its low sensitivity for diagnosis, especially at early disease stages. That antigen is positive in advanced disease in a higher number of patients and an effort has been made to identify other markers, but with little success.<sup>7,37-39</sup>

Less than 10% of our patients presented with metastases at diagnosis and 7.3% presented with them during follow-up, for a total of 15.5%. The majority were metachronous distant metastases, and the liver, lung, and peritoneum were the most affected locations. Those percentages were lower than results reported in other parts of the world, but the metastasis sites and synchronicity were very similar.<sup>33,40-43</sup>

Most of the patients were treated with surgical intervention and, depending on the location, neoadjuvant and adjuvant therapy with chemotherapy and radiotherapy, as well as palliative therapy, were applied as required. A



percentage of patients did not undergo treatment, either because they died before treatment could be started, they refused it, or they were lost to follow-up. Such a situation is also reported in the international literature, demonstrating that surgery is the cornerstone of curative management of colorectal cancer that is not metastatic at diagnosis. In addition, chemotherapy and radiotherapy play an important role in treatment for aiding in improving the survival rate of those patients.<sup>44–47</sup>

Five-year OS was 45.5%, which is lower than that reported in other countries,<sup>3,4</sup> and 2-year OS was 68.4%, higher than that described by Pardo and de Vries in a Colombian study.<sup>47</sup> We also found a lower survival rate for rectal cancer, compared with colon cancer, and that difference began to be established at approximately 11 months from diagnosis. Survival was also lower in cases with the most advanced disease stages in both the colon and the rectum, but there continued to be a difference between the two cancers, with poorer outcome in the cases of rectal cancer. The mortality rate was slightly higher in cases of rectal cancer, compared with colon cancer, contrasting with results from studies in the United States, in which rectal cancer is diagnosed at more localized stages (43 vs. 38%), most likely because patients present with symptoms.<sup>3</sup>

In our case series, the patients with right colon cancer had higher OS and DFS than those with left colon cancer, contrary to that reported in studies in which right colon cancer has a worse prognosis than left colon cancer. That is surmised to be due to that fact that patients with right colon cancer are elderly, the disease is diagnosed at more advanced stages, the histologic patterns possibly have a worse prognosis, such as mucinous disease and poorly differentiated or undifferentiated adenocarcinomas, and a possibly higher number of KRAS and BRAF mutations and microsatellite instability. That difference in behavior according to cancer location has been related to certain biologic particularities of each laterality, such as the different embryologic origins that impact cellular migration and differentiation, as well as genetic expression. It has also been related to a microbiota with the formation of biofilms in the right colon with procarcinogenic responses of epithelial cells and higher levels of bile acids in the right colon that have the potential to damage DNA.<sup>21,29,34,48–53</sup> All those assertions from other case series that attempt to explain the lower survival rate in cases of cancer in the right colon are speculative, and given that the majority of those aspects were not evaluated in our study, the difference between our results and those previously published cannot be explained.

With respect to the differences stated above in the outcome of patients according to tumor laterality, some authors have suggested that colorectal cancer should be divided into right cancer (from the ascending colon to the splenic flexure) and left cancer (from the splenic flexure to the rectum). Based on that classification, the 2-year OS was higher than that found for cancer of the colon and rectum, but the 5-year OS was similar. Our findings were different from those of other international studies in which OS of patients with cancer of the right colon was lower,<sup>50,53–56</sup> which has also been debated in light of findings in other cohorts<sup>57–60</sup> that, like our study, reported the same OS for the tumors on both sides and even a better survival rate for tumors on the left side.

The main strength of the present study was its sizable number of patients, being the second largest Colombian case series after the study by Bohórquez et al.,<sup>9</sup> and its main weakness was the fact that certain data were not reported in the medical records, a common failing in descriptive studies. We were able to show that the patients were similar to those evaluated in both national and international studies, that their management followed the guidelines established by different medical societies, and that patient survival was lower than that observed in developed countries, most likely because Colombia is a country lacking in resources and therefore access to healthcare services is difficult in some cases. It was concluded that screening strategies as stipulated in the different guidelines, as well as the Colombian ones,<sup>61</sup> must be strengthened, given their beneficial impact in relation to colorectal cancer deaths. Detection at earlier stages of the disease will result in lower recurrence and mortality rates.<sup>62</sup>

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## 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 declare that no patient data appear in this article.

## Conflict of interest

The authors declare that there is no conflict of interest.

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