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Clinical and epidemiological evaluation of patients with sporadic colorectal cancer☆

Glaucia Maria de Mendonça Fernandes[a,b], *Cássia Veridiana Dourado Leme*[a], *Mariângela Torreglosa Ruiz-Cintra*[c], *Érika Cristina Pavarino*[d], *João Gomes Netinho*[e], *Eny Maria Goloni-Bertollo*[d,*]

[a] *Faculdade de Medicina de São José do Rio Preto (Famerp), São José do Rio Preto, SP, Brazil*
[b] *Research Unit in Genetics and Molecular Biology (UPGEM), Faculdade de Medicina de São José do Rio Preto (Famerp), São José do Rio Preto, SP, Brazil*
[c] *Department of Biological Sciences, Federal University of Triangulo Mineiro (UFTM), Uberaba, MG, Brazil*
[d] *Department of Molecular Biology, Research Unit in Genetics and Molecular Biology (UPGEM), Faculdade de Medicina de São José do Rio Preto (Famerp), São José do Rio Preto, SP, Brazil*
[e] *Coloproctology Service, Department of Surgery, Faculdade de Medicina de São José do Rio Preto (Famerp), São José do Rio Preto, SP, Brazil*

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ABSTRACT

Background: This study aims to perform a survey on clinical data, sociodemographic and risk factors from patients with sporadic colorectal cancer (SCRC) treated between 2004 and 2008 in the Coloproctology Service of a teaching hospital in the North-western region of São Paulo.

Methods: We analyzed 749 medical records. Of these, 460 were from colon cancer patients and 289 from rectal cancer patients. Most of the individuals had white skin and were aged over 62 years. The variables that were analyzed included gender, age, skin color, professional occupation, alcohol drinking and cigarette smoking, family history of cancer, and comorbidities. The identification of the clinical-sociodemographic profile and risk factors in a population with the SCRC the northwest region of São Paulo was performed to collaborate with prevention strategies.

Results: The occurrence of SCRC did not differ much between genders. The most prevalent professional occupations were those related to household chores, agricultural and commercial activities. Among the comorbidities, hypertension and cholelithiasis were the most representative. The most common diagnosis method and treatment for the majority of patients were coloscopy and surgery, respectively. On average, the time of the disease progression was eight months. The median number of lymph nodes excised ranged between 11 and 14. The most common metastasis was hepatic.

☆ The study was carried out at the Faculdade de Medicina de São José do Rio Preto (Famerp), São José do Rio Preto, SP, Brazil.

* *Corresponding author.*
E-mail: eny.goloni@famerp.br (E.M. Goloni-Bertollo).

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Conclusion: The occurrence of colorectal cancer is more frequent in men's white skin with aged over 62 years. Professional occupation seems to be more important for those exposed to carcinogenic agents. This type of tumor mostly affects the distal regions of the colon and rectum with the occurrence of liver metastasis. The affected individuals usually have low survival due to its high aggressiveness.

Avaliação clínica e epidemiológica de pacientes com câncer colorretal esporádico

Palavras-chave:
Neoplasias colorretais
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RESUMO

Experiência: O presente estudo tem como objetivo realizar um levantamento de dados clínicos e fatores sociodemográficos e de risco de pacientes com câncer colorretal esporádico (CCRE) tratados entre 2004 e 2008 no Serviço de Coloproctologia de um hospital-escola na região Noroeste de São Paulo.

Métodos: Foram analisados 749 prontuários clínicos. Destes, 460 foram de pacientes com câncer de cólon e de 289 de pacientes com câncer retal. A maioria dos indivíduos era da raça branca, com mais de 62 anos de idade. As variáveis analisadas foram gênero, idade, cor da pele, ocupação profissional, consumo de álcool e tabagismo, história familiar de câncer e co-morbidades. A identificação do perfil clínico-sociodemográfico e dos fatores de risco em uma população com CCRE na região noroeste de São Paulo foi realizada para colaborar com as estratégias de prevenção.

Resultados: A ocorrência de CCRE não diferiu muito entre gêneros. As ocupações profissionais mais prevalentes foram as relacionadas aos afazeres domésticos, atividades agrícolas e comerciais. Entre as comorbidades, hipertensão e colelitíase foram as mais representativas. O método de diagnóstico e de tratamento mais comum para a maioria dos pacientes foi colonoscopia e cirurgia, respectivamente. Em média, o tempo de progressão da doença foi de oito meses. O número mediano de linfonodos extirpados variou entre 11 e 14. A metástase mais comum foi a hepática.

Conclusão: A ocorrência de câncer colorretal é mais frequente em homens de pele branca com idade superior a 62 anos. A ocupação profissional parece ser mais importante para as pessoas expostas a agentes cancerígenos. Este tipo de tumor afeta principalmente as regiões distais do cólon e do reto, com a ocorrência de metástases no fígado. Geralmente, os indivíduos afetados exibem baixa sobrevida, devido à alta agressividade dessa neoplasia.

Background

Sporadic colorectal cancer (SCRC) is a term for malignant neoplasms that are not a familial or inherited disease, which occur in the large intestine (colon) and rectum.[1] It often develops initially as an adenomatous polyp.[2–6]

This type of cancer is the second most common in Western countries.[3,7] In 2012, a study conducted by the Brazilian National Cancer Institute (BNCI) reported an estimated 518,510 new cases of cancer in the country. Of these, approximately 30,000 were colorectal cancer. It ranks fifth as the most frequent cause of death in Brazil. Approximately 14,180 cases in men and 15,960 cases in women are newly diagnosed each year.[1]

The carcinogenesis of colorectal and rectum cancers involve the interaction between environmental and genetic factors.[8,9] Some risk factors are well-established, such as age over 50 years,[1,9–12] lifestyle habits, such as highly saturated fatty acid diet and red meat,[1,3,7,8,10] alcohol consumption, and smoking,[2,8,9,11] besides comorbidities, such as cholelithiasis, metabolic syndrome, and diabetes.

Signs and symptoms of colorectal cancer occur according to the anatomical region affected. SCRC also depends on its physiology and clinical parameters such as size, extent, and spread of the neoplasia. It is a characteristic of this tumor to present intestinal obstruction, bleeding (hematochezia, enterorrhagia), change in bowel habits, and systemic settings such as significant weight loss.[1,3,12,13]

The prevention of sporadic SCRC involves three phases of action in health as follows: the primary phase aims to prevent the development of the disease, such as eating an adequate diet, physical exercise training, and absence of tobacco and alcohol consumption[5,12]; the secondary phase

is the prevention through an early diagnosis by means of a physical examination performed by a proctologist, laboratory tests (fecal occult blood test, carcinoembryonic antigen CEA test), and imaging screenings (colonoscopy, proctosigmoidoscopy)[1,3]; and the tertiary phase is the prevention of sporadic SCRC with relief of the symptoms and prevention of consequences.[7]

In Brazil there is a shortage of detailed population data in SCRC. Therefore the present study aims establish the clinical–sociodemographic profile and risk factors in a population with the SCRC the northwest region of São Paulo to collaborate with prevention strategies.

Methods

The study was approved by the Local Ethics Committee (CEP) – São José do Rio Preto Medical School – FAMERP (n°216/2009).

Were included in the study, the clinical reports of all patients who had a clinical diagnosis and/or histopathological of colon cancer by the physician in Coloproctology Service of a university hospital in the region northwest of São Paulo. Were excluded patients having family members diagnosed with cancer or cases of hereditary colorectal cancer, according to evaluation of Coloproctology service.

The variables that were analyzed included gender, age, skin color, professional occupation, alcohol drinking and cigarette smoking and comorbidities. Skin color was classified as white or non-white; we considered individuals whose skin color was non-white as Grayish-browns, Blacks and Yellows.

We considered smokers those patients who smoked over a 100 cigarettes and alcoholics those patients who drank more than four drinks per week for six months or longer.[8]

By analysing the medical records, we obtained the following clinical data: symptomatology, comorbidities, primary site of tumor, location of the tumor that were classified in the large intestine as either proximal (cecum, ascending or transverse colon) or distal (descending colon, sigmoid, rectosigmoid junction or rectum), clinical stage, level of histologic differentiation, and patient survival. Staging of Dukes is classified in Stage A (growth limited to the wall of the rectum without extension to outside the rectal tissues and without lymph nodes metastasis), Stage B (growth extends through the wall in the outside the rectal tissues, but the lymph nodes are free of metastasis), Stage C (lymph nodes involved with tumor) and stage D (distant metastasis).[14]

Astler-Coller considers staging in Stage B1 and B2 (respectively, incomplete and complete penetration of the muscularis propria), B3 (complete penetration of the distal muscularis propria), Stages C1 (absence of lymph nodes), C2 (presence of lymph nodes), C3 (presence of lymph nodes affected in the ligation point proximal vascular) and stage D (distant metastasis).[14]

Currently the classification adopted in accordance with the International Union Control Cancer (UICC), issued in 2002, the clinical staging (TNM), used to analyze the aggressiveness of tumors, is divided into stages I through IV. Tumors were classified according to the TNM following three criteria: tumor extent (T), presence of lymph node involvement regional (N) and presence of distant metastasis (M).[14,15]

The data were analyzed by descriptive statistics, using the Excel software (version 2007).

Table 1 – Percent distribution of occupational activities.

Occupation	Frequency (*n*)	Percentage (%)
Domestic services	279	37.24
Agricultural	130	17.35
Commercial	94	12.55
Metallurgy	55	7.34
Construction civil	45	6.00
Administrative	43	5.74
Driver	40	5.34
Divers	28	3.73
No information	35	4.67
Total	749	100 (99.96)

Results

We analyzed the medical records of 749 patients. Of these, 460 were affected by colon cancer (Group I) and 289 by rectal cancer (Group II).

Group I was composed of 212 women (46.08%) and 248 men (53.91%). Group II included 135 women (46.71%) and 154 men (53.28%). The mean age at diagnosis for colon cancer patients and rectal cancer patients was 63 years (±14.7) and 62.6 (±14.5) years, respectively.

Regarding skin color, the group of colon cancer patients included 181 white individuals (91.87%), while in the group of rectal cancer patients, only 54.63% were white.

The assessment of the patients' professional occupation showed a higher frequency of individuals whose working activities related to household chores (37.24%), agricultural (17.35%) and commercial activities (12.55%). The percentages allocated to the occupation activities are shown in Table 1.

Smoking habit was observed in 26.90% and 26.82% of the patients in Groups I and II, respectively. Alcohol addiction corresponded to 20.81% in the first and 20.48% in the second group.

The most common symptoms presented by patients with colon cancer were intestinal obstruction (10%), bleeding (8.91%), and abdominal pain (8.26%). Among those who presented neoplasia in the rectum, bleeding (32.17%), diarrhea (14.53%), and weight loss (8.99%) where predominant (Table 2).

The most prevalent comorbidities are shown in Table 3. In which the most frequent was the systemic hypertension present in patients with colon cancer (17.82%) and in patients with rectal cancer (26.29%) followed by cholelithiasis, 9.78% and 21.79%, in patients with cancer of the colon and rectum, respectively.

The occurrence of cancer according to the primary tumor site was predominant in the rectum (41.70%). Signs and symptoms vary according to the anatomical region.

Regarding diagnosis, colonoscopy was the most method used in 54.31% of the colon cancer patients, the remaining patients received a diagnosis by rectosigmoidoscopy or an emergency surgical procedure. Among the patients diagnosed

Table 2 – Signs and symptoms reported in the first consultation, in accordance with the anatomical groups.

Signs and symptoms	Colon		Rectum	
	Frequency (*n*)	Percentage (%)	Frequency (*n*)	Percentage (%)
Bleeding	41	8.91	93	32.17
Abdominal pain	38	8.26	10	3.46
Diarrhea	22	4.78	42	14.53
AA Obstructive	46	10	13	4.49
Weight loss	21	4.56	26	8.99
Stools tape	6	1.30	6	2.07
AA Inflammatory	6	1.30	0	0
Anemia	7	1.52	0	0

AA, acute abdomen.

with colon cancer, 75.70% had neoplasms in stage III and IV equally distributed by gender of which about one third died. For individuals with rectum cancer, colonoscopy was the method of diagnosis of 52.68% of patients. Of these, 62.96% had tumors in stages I and II equally distributed by gender of which 44.11% of the patients died.

The mean age of the patients at death was 67.8 years (±15.21) and 68 years (±15.34) in Groups I and II, respectively. The time between diagnosis and death was correspondingly 4 and 5 months (±8.31) and 9.8 months (±12.25) in Groups I and II, respectively.

The coexistence of cancer and adenoma was identified in 46 and 27 patients in Groups I and II, respectively. The predominant histological type was the adenocarcinoma, which represented 88.83% of colon cancers and 93.65% of rectal cancers. In some cases, histological identification was not possible.

Regarding the treatment, surgery was performed in 77.15% of patients in the first group and 65.85% in the second group. In addition, chemotherapy was performed using 5-fluorouracil in combination with folinic acid in 47.20% and 55.12% of patients in Groups I and II, respectively.

The initial clinicopathological stages (TNM) of colon and rectal cancers are shown in Table 4. The median number of lymph nodes parched during surgery for histopathological analysis was 14 and 11 in colon and rectal surgery, respectively.

The main sites of dissemination of patients who presented metastatic colon cancer were liver (64.51%), peritoneum (19.35%), and lung (9.67%); among the metastases observed in rectal cancer patients, the liver was also the most affected organ (54.11%), followed by the peritoneum (12.94%), lung (11.76%), bone (8.23%), central nervous system (5.88%), and urinary system (7.05%).

Discussion

Our findings showed that the occurrence of SCRC did not differ between gender, which corroborates other studies that also report a similar distribution between men and women[1,5,6,16]; although Santos et al.[5] observed a higher incidence of colon cancer in women and rectal cancer in men.[5]

Steele et al.[16] reported a predominance of occurrence of SCRC in white-skinned individuals with percentage raging up to 80%. Our study found similar results in relation to colon cancer (91.87%) and showed a smaller percentage (54.63%) in rectal cancer. Other studies have shown a higher incidence and survival of sporadic SCRC among African-Americans.[16,17] It is worth mentioning that the Brazilian population, which is representative of our study, has an ethnic composition with great confluence of several other ethnic groups, making it difficult to analyze the influence of this variable.

It is established in the literature the age of 50 years as risk factor for developing sporadic SCRC.[1,5,9,10,12,18] Corroborated with the literature, in our study, the mean age at diagnosis was 63 years (±14.7) for patients with colon cancer and 62.6 years (±14.5) for patients with rectal cancer.

Regarding the professional occupation, our data showed a predominance of SCRC in those who perform activities related to household chores, agricultural and commercial activities. In fact, the exposure to some carcinogenic agents used in agriculture, and in some industries is

Table 3 – Comorbidities in patients with cancer of the colon and rectum.

Comorbidities	Colon		Rectum	
	Frequency (*n*)	Percentage (%)	Frequency (*n*)	Percentage (%)
HAS	82	17.82	76	26.29
DM-2	30	6.52	17	5.88
Cholelithiasis	45	9.78	63	21.79
Diverticular disease	38	8.26	32	11.07
Renal cyst	33	7.1	25	8.65
Hepatic steatosis	28	6.08	37	12.80

HAS, hypertension arterial systemic; DM-2, diabetes mellitus.

Table 4 – Adenocarcinoma of colon and rectum and clinicopathological staging.

Variable		Colon		Rectum	
		N	%	N	%
TNM					
T	Is	3	0.65	0	
	1	17	3.69	14	4.84
	2	57	12.39	40	13.84
	3	210	45.65	79	27.33
	4	28	6.08	7	2.42
	NI	145	31.52	149	51.55
N	0	197	42.82	92	31.83
	1	95	20.65	28	9.68
	2	57	12.39	21	7.26
	NI	111	24.13	148	51.21
M	0	224	48.69	98	33.91
	1	146	31.73	72	24.91
	NI	90	19.56	119	41.17
Duke					
	A	18	3.91	42	14.53
	B	123	26.73	28	9.68
	C	87	18.91	27	9.34
	D	147	31.95	70	24.22
	NI	85	18.47	122	42.21
Astler-Coller					
	A	13	2.82	13	4.49
	B1	41	8.91	29	10.03
	B2	82	17.82	28	9.68
	B3	2	0.43	0	0
	C1	20	4.34	6	2.07
	C2	62	13.47	20	6.92
	C3	7	1.52	0	0
	D	146	31.73	71	24.56
	NI	87	18.91	122	42.21

Is, in situ; NI, no information.

related to the SCRC, such as dichlorodiphenyltrichloroethane (DDT), dichlorodiphenyldichloroethylene (p,p′-DDE), and polychlorinated biphenyl (PCB).[19] In our study, however, the investigation of such exposures was not possible.

Several etiological factors resulting from the interaction of environmental and genetic factors are involved in the development of colon and rectal cancers. Among them we can mention family history, alcohol drinking and smoking,[3,8,9] a highly saturated fat diet and red meat,[1,6,20] and the presence of comorbidities, such as cholelithiasis,[20–22] metabolic syndrome,[23] type II diabetes,[20,24,25] and obesity.[26,27]

Smoking habit is a risk factor for SCRC,[28,29] and its occurrence seems to reflect more on the building up of the amount of yearly exposure than on the time of exposure,[29–31] especially in rectal cancer.[31] Alcohol drinking increases the risk of developing SCRC in individuals who drink 30–45 g/day, and especially those who ingest more than 45 g/day.[32] An increased risk of those who drink more than 100 g/week[33] has also been demonstrated. Genetic polymorphisms of enzymes that act on the metabolism of ethanol, folate, and DNA repair together, these factors may determine a genotoxic effect and also act as a solvent to tobacco carcinogens and also, which might induce the production of free radicals[34] and decrease the absorption of folate in alcoholics;[32] also, they would stimulate the production of free radicals[34] and decrease the absorption of folate in alcoholics.[32] Smoking and drinking were observed in our study; however, it was not possible to determine the amount of exposure due to the retrospective nature of the study.

Regarding the diet, although studies are still controversial, it is notoriously known that fruits, leguminous plants, green vegetables, and dairy products play a protective role against cancer of the alimentary system. On the other hand, excessive intake of meat and animal fat is not recommended.[1,7,9] We did not evaluated the food habits in our study. As it is a review of medical records, these do not show this information.

Among other comorbidities associated with the development of sporadic SCRC are hyperinsulinemia, obesity,[24,25] and metabolic syndrome.[23] The latter is also related to a higher incidence of liver metastasis and tumor recurrence. It also is a probable independent factor of worse prognosis in survival of patients with this type of neoplasm.[35]

In our study, cholelithiasis was one of the most prevalent comorbidities; however, the association between cholecystectomy and SCRC is contradictory in the literature. Goldacre and colleagues[22] did not observe this association, while other studies have found it,[20,22] especially in women.[20] It was not possible to identify the relationship with cholelithiasis in the researched literature.

The weight gain in both gender has been associated with an increased risk of SCRC, although the body mass index increment does not seem to contribute to the development of this neoplasia.[21,27] Thus, it becomes important to identify individuals with metabolic syndrome. They may represent a population susceptible to the development of SCRC. In our study, we were unable to assess the frequency of metabolic syndrome among those who developed this type of neoplasia.

Regarding the most affected anatomical region, our study found a higher incidence of SCRC in the rectum, which is consistent with the findings of other studies.[5,6] As each anatomical region presents distinct embryological development and physiology when exposed to carcinogens, the mechanism of development of neoplasia as well as the symptoms presented by the patient in each anatomical segment is peculiar to their location. Thus, the correct identification of the primary site of tumor development is of vital importance to assist in the choice of treatment among the different therapeutic approaches.[36]

Symptoms of SCRC are expressed according to tumor location in association with the anatomy and physiology of the affected region, such as an obstruction, bleeding (hematochezia, enterorrhagia), change in bowel habits, and significant weight loss,[1,3,12,13,37] and these symptoms may help in the early detection of this neoplasm.[38] In this study, as found in the literature, the most common symptoms presented by patients with colon cancer were intestinal obstruction, rectal bleeding, and abdominal pain.[1,37,38]

Colonoscopy is an important additional test for the detection of SCRC and as well as of its precursor lesion, the adenoma. When identified at an early stage, a five-year survival appears to be greater than 90%.[37,39,40] Some protocols, such as the EPAGEII, which was developed in Europe, determine the screening method to be performed. It is based on the symptomatology as well as on the presence of risk factors and age of the patient.[39] Thus, coloscopy, the gold standard for detection of SCRC, acts at the secondary prevention level of cancer,[39,40] and it represents an important tool used in public health programs. In this study, 54.31% of patients with colon cancer and 52.68% of patients with rectal cancer were subjected to this test. This percentage reflects the fact that the majority (75.70%) of them was referred to the Coloproctology Service in an advanced stage of the neoplastic process (T3 and T4).

The predominant histological malignant neoplasm type in our study was the adenocarcinoma (88.83% of colon cancers and 93.65% of rectal cancers). It is responsible for more than 90% of the cases reported in the literature.[2,3] Because the adenoma is typically a premalignant lesion,[36] its early detection is of utmost importance, since it is an independent risk predictor for the SCRC.[41] Other histological malignant neoplasm types, including mucinous adenocarcinoma (17%), of which 2–4% are squamoussignet-ring cell carcinoma, squamous cell carcinoma, and undifferentiated carcinoma.[3]

Among the therapeutic options available for colorectal cancer, chemotherapy stands out, whose toxicity is variable according to the agent applied and that can decrease the quality of life of patients in relation to psychological and physical activity.[42,43] Currently, the public health network uses an association between 5-fluorouracil and folinic acid-leucovorin.[38] This drug therapy has been associated with improved survival and decreased tumor recurrence in patients undergoing this therapeutic regimen.[36,43,44] Although there are other drugs that have shown a significant improvement in these patients' survival, such as the bevacizumab.[36,42,43] In our study, 47.20% of the colon cancer patients and 55.12% of the rectal cancer patients underwent chemotherapy using mainly 5-fluorouracil and folinic acid.

Another therapeutic method used is the surgical resection of the tumor associated with the removal of lymph nodes for adequate staging.[40] International consensus and scientific papers recommend an evaluation of at least 12 regional lymph nodes in the anatomical sample during the curative treatment by surgery, in order to obtain more reliable data for the appropriate clinical staging.[18,45] In our study, we observed that the procedure performed at our institution is in accordance with that established in the literature, since the median number of lymph nodes resected was 14 in colon surgery and 11 in rectal surgery.

Regarding the systemic dissemination of colon and rectal cancers, the literature indicates that the main mechanism of tumor spread occurs via a hematogenous pathway and, to a lesser extent, by the lymphatic route with possible implantation of tumor cells in organs such as liver, lungs, bones, cerebrum, ovaries, and skin.[2,18] Additionally, the dissemination of neoplastic cells can occur by continuity, which happens through the wall of the organs.[2,12,19] In this study, we found a higher incidence of liver metastases, followed by those affecting the peritoneum, lung, bones, central nervous system, and urinary system.

In 2004, Tucunduva et al.[46] conducted a study with non-oncologists physicians at a health service in order to assess their knowledge and attitude toward preventive measures for the most common cancers. It was highlighted that these physicians showed interest in the prevention of various cancers, but they had difficulty in carrying out the counseling recommended by the consensus.[47] Thus, the study of colorectal cancer is relevant because a better knowledge of preventive measures, risk factors, associated signs and symptoms, research methods, and appropriate time for referral to specialists, including general practitioners contribute to the reduction of survival morbidity and improve public health and quality of life.

Conclusion

Malignant tumors SCRC treated in the Coloproctology Service at a university hospital in the northwest of São Paulo occur more frequently among individuals over 62 years of age, especially in men with white skin and with professional activities of agricultural, commercial and domestic. The most frequent comorbidities were hypertension and cholelithiasis. The distal regions of the colon and rectum were the most affected, with prevalence of hepatic metastasis. The high rate of patients with stages III and IV indicated late demand in treatment centers, which reflects the need for preventive education campaigns in order to achieve early diagnosis of the disease.

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Conflict of interest

The authors declare no conflicts of interest.

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