Clinical and Epidemiological Profile of Colorectal Cancer in Paraná's Western Region, Brazil, 2016-2018

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Perfil Clínico-Epidemiológico do Câncer Colorretal na Região Oeste do Paraná, Brasil, 2016-2018

Perfil Clínico-Epidemiológico de lo Cáncer Colorrectal en la Región Oeste de Paraná, Brasil, 2016-2018

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ABSTRACT

Introduction: The colorectal cancer is the most frequent neoplasm of the gastrointestinal tract and the second cause of cancer related death. **Objective:** To design a clinical and epidemiological profile of the colorectal cancer at the Western Region of the Paraná State from 2016 to 2018. **Method:** Analytical cross-sectional observational study based on the evaluation of the results of anatomopathological exams, between 2016 and 2018, at a regional specialized center. Analyses were performed using descriptive statistics, chi-square test for association and Mann-Whitney U test. A significance level of 5% was adopted. **Results:** The analysis of 509 positive anatomopathological reports of colorectal cancer allowed to identify the predominance of male patients and mean age at diagnosis of 62 years. The malignancy was more incident in patients between 61 and 70 years of age (29.9%). A considerable number of cases was found in patients younger than 50 years (19.6%). The disease was predominant at the left colon, of the type moderately differentiated infiltrating adenocarcinoma according to the histological classification. Association between the tumor topography and sex was found, with predominance of females for the right colon and males for the left colon (p=0.0081). **Conclusion:** This study designed the colorectal cancer clinical and epidemiological profile at Paraná's Western Region. The disease affects more males, older than 60 years of age, mostly with moderately differentiated infiltrative adenocarcinoma at the left colon. These findings are relevant considering the possibility of applying international cancer screening protocols in this population.

Key words: colorectal neoplasms/epidemiology; adenocarcinoma; colonoscopy.

RESUMO

Introdução: O câncer colorretal é a neoplasia mais frequente do trato gastrointestinal, sendo a segunda principal causa de morte por câncer no mundo. **Objetivo:** Traçar um perfil clínico-epidemiológico do câncer colorretal na Região Oeste do Paraná (Brasil), entre 2016 e 2018. **Método:** Estudo observacional analítico do tipo transversal, construído a partir da análise de resultados de exames anatomopatológicos, realizados entre 2016 a 2018. Realizaram-se análises por estatística descritiva, teste de associação qui-quadrado e U de Mann-Whitney. Adotou-se nível de significância de 5%. **Resultados:** A análise de 509 laudos positivos para câncer colorretal permitiu identificar o predomínio de pacientes do sexo masculino e a idade média de diagnóstico de 62 anos. A malignidade mostrou-se mais incidente na faixa etária de 61 a 70 anos (29,9%), e considerável número de casos ocorreu em pacientes abaixo de 50 anos (19,6%). Houve predomínio em cólon esquerdo e do tipo histológico adenocarcinoma infiltrativo moderadamente diferenciado. Verificou-se associação entre topografia da doença e sexo, com maior predominância do sexo feminino para tumores do cólon direito e do sexo masculino para tumores do cólon esquerdo (p=0,0081). **Conclusão:** A partir deste estudo, delineia-se um perfil clínico-epidemiológico do câncer colorretal na Região Oeste do Paraná, com maior incidência da doença em homens, sexagenários, além de predomínio de tumores em cólon esquerdo e do tipo adenocarcinoma infiltrativo moderadamente diferenciado. Tais achados são relevantes considerando a possibilidade de aplicação assertiva de protocolos internacionais de rastreio do câncer nessa população.

Palavras-chave: neoplasias colorretais/epidemiologia; adenocarcinoma; colonoscopia.

RESUMEN

Introducción: El cáncer colorrectal es la neoplasia más frecuente del tracto gastrointestinal y la segunda causa de muerte por cáncer a nivel mundial. **Objetivo:** Trazar un perfil clínico-epidemiológico del cáncer colorrectal en el Oeste de Paraná (Brasil), entre 2016 y 2018. **Método:** Estudio observacional analítico transversal realizado con los análisis de resultados de exámenes anatomopatológicos entre 2016 a 2018. Se realizaron análisis mediante estadísticas descriptivas, prueba de asociación chi-cuadrado y U de Mann-Whitney. Se adoptó nivel de significación del 5%. **Resultados:** Entre los 509 informes positivos para cáncer colorrectal, el 52,8% de los pacientes eran del sexo masculino y tenían promedio de edad de diagnóstico de 62 años. El cáncer fue más frecuente en el grupo de 61 a 70 años (29,9%) y un número significativo de casos se presentó en pacientes menores de 50 años (19,6%). Predominó la enfermedad de colon izquierdo y del tipo histológico de adenocarcinoma infiltrante moderadamente diferenciado. Fue encontrado asociación entre la topografía y el sexo, con mayor predominio del sexo femenino para los tumores de colon derecho y del sexo masculino para los tumores de colon izquierdo (p=0,0081). **Conclusión:** Se elabora un perfil clínico-epidemiológico del cáncer colorrectal en la región Oeste de Paraná, con mayor incidencia en el sexo masculino, edad de 60 años, predominio de tumores en el colon izquierdo y del tipo adenocarcinoma infiltrante moderadamente diferenciado. Estos puntos son relevantes considerando la posibilidad de aplicación asertiva de protocolos internacionales de rastreo del cáncer en esta población.

Palabras clave: neoplasias colorrectales/epidemiología; adenocarcinoma; colonoscopia.

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INTRODUCTION

Colorectal cancer refers to all malignant neoplasms that affect the large intestine (cecum, ascending, transverse, descending and sigmoid) and rectum. It is the most frequent of the gastrointestinal tract, the third most incident worldwide and the second main cause of death by cancer, responsible for more than 880 thousand deaths in 2018, according to GLOBOCAN[1-3].

The National Cancer Institute (INCA) estimated 21,970 new cases of colorectal malignant neoplasm in men and 23,600 in women for the triennium 2023-2025, corresponding to the second most incident cancer for these populations[4]. The rates of incidence and mortality of colorectal cancer vary in the whole word, with recent increases in Latin America, East Europe and Asia, with similar tendency being observed in Brazil's South and Southeast regions[5-8]. Menezes et al.[9] estimated that 16,282 Brazilians died by colorectal cancer in 2014 (7.98/100 thousand inhabitants) and for 2017 and 2018, the rate of mortality was 8.59/100 thousand inhabitants according to data available at INCA's[4,9] *Atlas On-line de Mortalidade* (Online Mortality Atlas).

The main risk factors for the development of colorectal cancer are advanced age, family history, male sex, Black race, life habits (tobacco use, sedentarism, poor fiber intake, use of large quantities of red meat, processed food and alcohol beverages), obesity, inflammatory bowel diseases and hereditary cancer syndromes[1,2,10,11].

Individuals older than 50 years of age are the main group of risk of developing the disease, the highest prevalence is in the age range of 60-80 years[12,13]. A significant amount of patients are diagnosed with less than 40 years at more advanced stages and frequently with worst diagnosis[13,14].

Colorectal cancer precursor lesions appear mostly like polyps – mucosa and/or submucosa protrusions into the lumen[14]. Most common pre-neoplastic polyps (2/3 to 3/4 of colonic polyps) are adenomas with great potential of differentiation of cancer from the sequence adenoma-adenocarcinoma. This is a well-established malignant transformation process in the literature whose evolution occurs in average in five to ten years. Adenocarcinomas are the most prevalent histological type of colorectal cancer, representing 96% to 98% of all the malignant neoplasms of this portion of the gastrointestinal tract[1,15-18].

According to the guidelines of the American Cancer Society (ACS) published in 2018[10], there is consensus for screening individuals aged 50-75 years in good health conditions and more than 10-year life expectancy. Screening since 45 years of age is feasible but risks and benefits inherent to the procedures and particularities of the patient's clinical context should be considered[10]. Kuipers et al.[1] detail that colonoscopy is the gold-standard method to the colorectal cancer screening as it allows simultaneously the diagnostic suspicion and treatment[1]. As ratified by ACS[10] and other authors[2,12,19], regular screening and excision of pre-cancer lesions are effective strategies to reduce the incidence and mortality of colorectal cancer, especially after excision and anatomopathological analysis to follow up and classify the polyps.

Considering the above, this malignancy is important in the context of public health. The literature is scarce about the incidence and prevalence of this disease in Brazil's South Region, especially in Paraná's West Region. The main objective of this study is to design a clinical and epidemiologic profile of colorectal cancer in adult patients of this region of the State between 2016 and 2018.

METHOD

Observational, analytical, cross-sectional study elaborated from the analysis of colorectal cancer diagnosed between January 2nd, 2016 and December 31st, 2018 and results of anatomopathological exams performed at a specialized laboratory in the city of *Cascavel* (Paraná). The sample consisted in medical reports with diagnosis compatible with colorectal cancer (anatomically located between the ileocecal valve and the rectum, including this) from the municipalities of *Cascavel* and *Toledo* both located in Paraná's Western Region.

The main variables collected were: date of the exam, sex, date of birth, city or municipality, origin of the sample (biopsy or surgical piece from colectomy), anatomopathological diagnosis (histological type and grade of differentiation) and anatomic location (topography). Other epidemiological variables as occupation, education, race, religion, life habits and family history were unavailable. The data were entered in Microsoft Excel 2016® spreadsheets.

The tumors found from the ileocecal valve up to the end of the transverse colon were grouped as right-side colon and those between the splenic flexure up to the inferior rectum as left-side colon according to the literature-based embryologic origin of the tissues[20-22]. Later, groups were subdivided per age (years of life stratified in decades), sex and histological type.

The qualitative variables sex, city and municipality, origin of the sample, anatomopathological diagnosis and topography were quantified in tables and graphs. Mean, median, standard deviation were calculated for the variable age, stratified in life decades to check absolute and relative frequency. Later, these data were organized in column graphs. Chi-square test was applied to investigate

possible associations between sex and topography of the lesion. Analyzes and stratifications were run at Microsoft Excel 2016®. The Shapiro-Wilk test of normality of the distribution of the variable age was applied with the software RStudio® version 1.2.1335 and concluded that the distribution was not normal. Consequently, the Mann-Whitney U test was applied to evaluate differences of age between the groups analyzed. The value of p = 0.05 and confidence interval of 95% (CI 95%) were adopted.

The data collection started upon approval by the Institutional Review Board of "*Universidade Federal do Paraná*" number 5,012,545 (CAAE (submission for ethical review) 20173419.7.0000.0102). The Informed Consent Form was waived because only deidentified data from anatomopathological exams found in medical reports and stored at the laboratory system were utilized.

RESULTS

11,253 medical reports of anatomopathological exams were analyzed and, among them, 509 positive results of colorectal cancer which met the inclusion criteria were selected. Of these, 261 exams were run with samples of colon biopsies and 248 surgical pieces from colectomies. To reduce the duplicity of information from the same patient whose biopsy preceded a surgery to collect new sample, the data were analyzed and compared. Analyzes of the same tumor were excluded, remaining those with details pertinent to the present study and duplicate medical reports were rejected as well.

Colorectal cancer was the most incident in men, corresponding to 52.8% of the cases and 47.2% in females as shown in Table 1 with an overview of the data collected. The mean age was 62 years [±13.5; CI 95% (58.14-65.58)] and the median age at diagnosis was 63 years. The mean age at diagnosis was lower in women than in men, respectively 60 [±14.2; CI 95% (58.49-62.10)] and 63 years [(±12.7; CI 95% (61.73-64.78)], statistically relevant according to the Mann Whitney U test (value of p = 0.0266).

Colorectal cancer is more prevalent in the age-range of 61-70 years with 29.9% of the diagnosis, followed by 22.4% in the age-range of 51-60 years and 21.8%, in 71-80 years. Patients with 50 years or less accounted for 19.6% of the cases, 12.5% in 41-50 years old patients, 4.7%, in 31-40 years and 2.4% in less than 30 years. The distribution of cases by sex and age (stratified in decades of life) is shown in Figure 1.

Malignant left colon neoplasm was the predominant topography 72.7% (n=370), of these, 176 in the rectum and 89 cases in sigmoid. Right colon presented 26.1% of the cases (n=133), 36, transverse and 35, cecum. Colorectal cancer cases distributed by anatomic location are shown in Figure 2.

Grouping the cases per topography (right and left colon) and excluding those with undetermined location, there was predominance of right colon disease in female patients; for men, left colon tumors were more frequent as depicted in Table 2. This finding was statistically significant as revealed by the chi-square test (value of p =

Table 1. Overview of the data collected on colorectal cancer at Paraná's Western Region, 2016-2018

Variable		Municipality		TOTAL
		Cascavel	Toledo	
Origin of the sample	Biopsy	182	79	261
	Surgical piece	194	54	248
Sex	Female	178	62	240
	Male	198	71	269
Age	≤30 years	11	1	12
	31-40 years	16	8	24
	41-50 years	48	16	64
	51-60 years	90	24	114
	61-70 years	106	46	152
	71-80 years	78	33	111
	>80 years	27	5	32
Topography	Right colon	98	35	133
	Left colon	274	96	370
	Unspecified	4	2	6

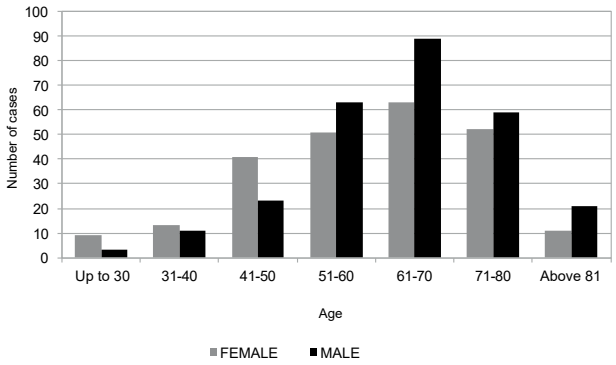

Figure 1. Distribution of colorectal malignant neoplasms by age and sex

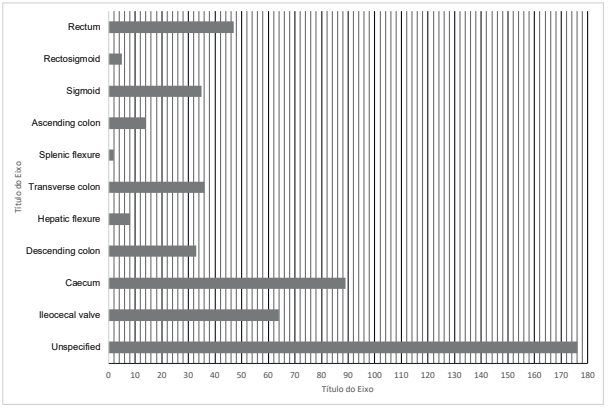

Figure 2. Distribution of colorectal cancer per anatomic location

0.0081). The mean age for left colon cancer is lower than right colon, 61 years [±13.8; CI95% (59.21-62.03)] and 66 years [±11.8; CI 95% (63.51-67.54)], respectively, a relevant difference according to the U Mann-Whitney test (value of p = 0.0003).

The most frequent histological type of the sample was infiltrative adenocarcinoma followed by mucinous carcinoma, squamous cells carcinoma and neuroendocrine tumor. The distribution of colorectal cancer cases according to the histological type is presented in Table 3. The cases of mucinous carcinoma were evenly distributed between men and women, with mean age of 65 years [±11.9; CI 95% (57.97-71.52)] and seven cases located in the left colon. All the squamous cell carcinoma occurred in females, mean age of 52 years [±19.4; CI 95% (39.77-63.83)]. Four cases of neuroendocrine tumors were identified in men and five cases in women with mean age of 48 years [±14.5; CI 95% (38.98-57.90)]. All the cases of squamous cell carcinoma and neuroendocrine carcinomas were found at the left colon .

For being the predominant histologic type of the casuistic (90.8%), the statistics for infiltrative adenocarcinoma tumors concur with the findings of the present study. Thus, adenocarcinomas are more incident in males at the left colon, with mean age at the diagnosis of 63 years [±12.8; CI 95% (61.40-63.75)].

The sample investigated presented 432 adenocarcinomas histologically classified as pure and 28, mixed as shown in Table 3. According to the grade of differentiation, 417 were defined as moderately differentiated, 22, well-differentiated, 21, little differentiated and for two of them, no evaluation was possible at the diagnosis.

DISCUSSION

The incidence of colorectal cancer in men (52.8%) from Paraná's Western Region was slightly higher, compatible with Brazil and Southern Regions' data[5,7,23,24], besides international estimates whose difference of incidence among sexes is more evident[1,11]. However, it differs from studies conducted in the States of Sergipe[25] and Minas Gerais[26,27], with higher incidence in females. The quantitative discrepancies among Brazilian States is anticipated and reported by INCA[4,24]. The mean age at diagnosis of colorectal cancer was 62 years, mostly in patients aged 51-80 years (74.1%), peaking in sexagenarian, consistent with vast literature[12,23,25-28].

The incidence in patients younger than 50 years (19.6%), mostly those from 41 to 59 years (12.6%) stands out. A single analysis of the group revealed that colorectal cancer was predominant at the left colon (84.0%) affecting more women (63.0%) with mean age of 42 years, similar to the results of Patel and Ahnen[29] who reported increase

Table 2. Association between sex and topography of colorectal cancer

Topography	Sex		TOTAL	*p* value
	Female	Male		
Right	76	57	133 (26.44%)	0.0081
Left	162	210	370 (73.56%)	
Total	238	265	503 (100%)	

Table 3. Distribution of colorectal cancer according to histology

Origin	Histological type			Fi	Fri
Primary tumor	Infiltrative adenocarcinoma	Usual pure		432	84.87%
		Usual mixed	With mucinous areas	4.91%	4.91%
			With signet ring cells	0.39%	0.39%
			With neuroendocrine foci	0.20%	0.20%
	Signet ring cells carcinoma			5	0,98%
	Squamous cell carcinoma			10	1.96%
	Micropapillary carcinoma			1	0.20%
	Mucinous carcinoma			12	2.36%
	Serous carcinoma			1	0.20%
	Mucosa associated lymphoid tumor (MALT)			1	0.20%
	Large cells malignant neoplasm			2	0.39%
	Infiltrative sarcoma			1	0.20%
	Gastrointestinal stromal tumor			1	0.20%
	Neuroendocrine tumor			8	1.57%
Metastasis	Infiltrative adenocarcinoma			2	0.39%
	Squamous cell carcinoma			1	0.20%
	Non-Hodgkin's lymphoma			1	0.20%
	Large cells malignant neoplasm			1	0.20%
	Malignant mixed Müllerian tumor			1	0.20%
	Neuroendrocrine tumor			1	0.20%
Total				509	100.00%

Captions: Fi = absolute frequency; Fri = relative frequency.

of incidence in younger than 50 years in the last decade in the United States of America, ratified by Macrae[11]. The two authors[29] described that 75.2% of colorectal malignancies of this population (investigated only for patients younger than 50 years) occur in the age range of 40-49 years at the left colon, mostly.

The population of young adults diagnosed with early-onset colorectal cancer is drawing attention of the scientific community. The incidence of this cancer has been diminishing progressively in 50 years or older patients and increasing in younger patients[13,29]. This fact can be justified by the efficacy of screening and early treatment in the first group. In addition, the initial symptoms are underestimated in the second group (eventually with late diagnosis, as it is unusual the populational screening at this age range) and more prevalence of hereditary cancer syndromes and life habits, responsible for increased risk of developing the disease[6,13,29,30].

Macrae[11] emphasizes progressive increase of colorectal cancer in young adults, predominantly at the left colon, similar to the present study with mean age at the diagnosis of left colon malignant neoplasms lower than right colon, 61 and 66 years, respectively (Mann-Whitney U test, value of $p = 0.0003$).

Similar to former studies[25,26,28], the predominant topography was left colon compared with right colon, regardless of the age group investigated and the most affected anatomic regions were rectum (34.6%), sigmoid (17.5%) and rectosigmoid (12.6%). Possible association of higher incidence of the disease at the right colon in women and left colon in men was found (chi-square test, value of $p = 0.0081$). The analysis by Baran et al.[20] elucidated the differences between right and left colon, corroborating the present findings regarding sex and mean age of the patients for each topography according to separate evaluation of the groups. Because of distinct embryologic origins of these regions, disparities of the genic expression and epidemiology of the tumors of each anatomic site were investigated, which influenced the prognosis and treatment of the neoplasms[20].

The sample's most prevalent histological type was the infiltrative adenocarcinoma (90.8%) with moderately

differentiated histologic grade, a finding consistent with former studies[25-28] where most of the adenocarcinomas originate from adenomatous polyps. Typically, these pre-malignant lesions follow the sequence adenoma-adenocarcinoma for differentiation from malignant neoplasms, a process which usually lasts ten years in average. This characteristic reiterates the importance of screening tests as colonoscopy because they facilitate the diagnosis at initial stages or in pre-malignant phases, which may improve the quality-of-life and lower treatment costs[10,12,16,19].

CONCLUSION

It was possible to design the clinical-epidemiologic profile of colorectal cancer at Paraná's West Region consistent with the literature. This cancer is more incident in male-sexagenarian patients with mean age of 62 years. The most common anatomic location is the left colon, particularly the rectum and moderately differentiated infiltrative adenocarcinoma was the histological type predominantly found in the sample.

Nearly 1/5 of the casuistic is formed by younger patients with less than 50 years, corroborating the importance of clinical suspicion in this age range, especially women with changes of intestinal routine and other symptoms suggestive of colorectal neoplasm. These are unspecified clinical findings and sometimes, colorectal cancer is not considered among the diagnostic hypotheses, eventually leading to diagnostic and therapeutic delay. For the population investigated, left colon colorectal cancer was predominant, which prompts the diagnostic investigation by sigmoidoscopy, lest costly and broader populational reach. The clinical suspicion is pertinent not only in symptomatic patients but in asymptomatic as well with positive family history and other risk factors for the development of the pathology.

International guidelines and protocols of colorectal screening are necessary to be adopted for early prevention, diagnosis and treatment and potential better clinical outcomes further to preservation of the quality-of-life and life expectancy of the patients.

The unavailability of epidemiological data as occupation, education, race, religion, life habits and family history are limitations of the analysis that could possibly contribute for a thorough epidemiological profile of colorectal cancer in that region. Despite the collection of data was performed at a reference anatomopathological laboratory of Paraná's West Region with large annual volume of exams, there are other local laboratories which were not included in the analysis of the casuistic.

CONTRIBUTIONS

All the authors contributed substantially to the study design, acquisition, analysis and/or interpretation of the data, wording and/or critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

The author Carolina Kosako Tanzawa has potential competing interests because she is pathologist-physician of the pathological anatomy laboratory whose database was utilized for this article. The other authors have no conflict of interests.

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