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Incidence and epidemiological features of synchronous and metachronous colorectal cancer

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ABSTRACT

Introduction: patients with sporadic colorectal cancer or cases associated with syndromes are at risk of having synchronous or metachronous cancer. Although it is an important subject, Brazilian data on the subject are scarce.
Objective: to evaluate the incidence and epidemiological features in patients with synchronous and metachronous colorectal cancer in a reference service of proctology in the Rio Grande do Sul. Methods: cross-sectional observational study, performed between January and July 2012, analyzing all patients admitted in the service that met the inclusion criteria. A retrospective review of records was performed, noting demographic variables, comorbidities and tumor-related variables.
Results: 150 records were analyzed, of which 53.3% were males and mean age was 63 (± 13.01) years old. The most frequently found tumor location was the sigmoid colon and high rectum (50.67%), followed by the lower rectum (36%). Adenocarcinomas were the most prevalent histological subtype (88%), followed by epidermoid tumors (1.33%). Hereditary syndromes were identified in five patients (3.33%), with four being Familial adenomatous polyposis (FAP) and one hereditary nonpolyposis colorectal cancer (HNPCC). Among the analyzed patients, four (2.67%) had synchronous and one (0.67%) had metachronous cancer.
Conclusion: the incidence of synchronous and metachronous colorectal cancer was, respectively, 2.67% and 0.67%, results that corroborate those reported in international literature.

Incidência e perfil epidemiológico do câncer colorretal sincrônico e metacrônico

Palavras-chave:
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RESUMO

Introdução: pacientes com diagnóstico de câncer colorretal esporádico ou associado a síndromes correm risco de apresentar lesões sincrônicas ou metacrônicas. Embora seja relevante, há escassez de informações sobre o tema na literatura nacional.
Objetivo: avaliar a incidência e o perfil epidemiológico dos pacientes com tumor colorretal sincrônico e metacrônico em um serviço de referência em proctologia do Rio Grande do Sul.
Método: estudo observacional transversal, realizado entre janeiro e julho de 2012, avaliando-se

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pacientes atendidos no serviço que preencheram os critérios de inclusão. Revisaram-se os prontuários, registrando-se variáveis demográficas, comorbidades e variáveis relacionadas ao tumor.

Resultados: analisaram-se 150 prontuários, sendo 53,3% do sexo masculino com média de idade de 63 (+13,01) anos. A topografia mais incidente foi cólon sigmoide e reto alto (50,67%) seguido do reto baixo (36%). O adenocarcinoma foi o subtipo histológico mais prevalente (88%) seguido pelo epidermoide (1,33%). Síndromes hereditárias foram identificadas em cinco pacientes (3,33%), sendo quatro com polipose adenomatosa familiar e um paciente com câncer colorretal hereditário não polipose. Dos 150 pacientes, quatro (2,67%) apresentaram neoplasia sincrônica e um (0,67%) lesão metacrônica. Conclusão: a incidência de tumor colorretal sincrônico e metacrônico na população avaliada foi, respectivamente, 2,67% e 0,67%, resultados que corroboram achados da literatura estrangeira.

Introduction

The presence of more than one malignant colorectal lesion is classified according to its onset period as synchronous or metachronous lesions. Synchronous cancer is defined as two or more neoplasms identified simultaneously in the same patient or a second tumor identified up to six months after the initial diagnosis. In turn, metachronous tumor is defined as a second primary lesion identified six months after the detection of the first cancer and located no more than 3 cm from the anastomosis.

Temporally, metachronous tumors are classified as early if occurring within the first three years after the primary lesion, while those occurring after three years are considered late.[1-3]

It is speculated that synchronous colon carcinomas arise from a combination of environmental and genetic factors, as well as associated predisposing diseases. Among them is ulcerative colitis, a disease that, together with familial adenomatous polyposis (FAP), corresponds to 10% of synchronic tumors[3]. In addition to FAP, another syndrome associated with multiple colorectal adenocarcinoma is Hereditary Nonpolyposis Colorectal Carcinoma (HNPCC), also known as Lynch syndrome, which corresponds to 1 to 3% of all colorectal neoplasms.[1,3]

Estimates of the incidence of synchronous colorectal carcinomas vary, according to the literature, from 2 to 9%.[2-8] However, studies of greater internal validity, due to improved scientific design, state that the true prevalence is about 4%[2,3,6]. The incidence of synchronous neoplasia is slightly lower if patients with HNPCC are excluded, decreasing the values from 4 to 2.5%.[9] In turn, few studies have evaluated the incidence of metachronous cancer, which is around 1%.[2]

This study aims to determine the prevalence of synchronous and metachronous colorectal tumor in a reference Service of Proctology in the state of Rio Grande do Sul, Brazil.

Method

The present is a cross-sectional study carried out between January and July 2012, involving all patients treated at the Proctology Service of Hospital Geral de Caxias do Sul in the period between January 2010 and March 2012.

Inclusion criteria consisted of patients who underwent surgical resection, preoperative histopathological diagnosis, and postoperative anatomopathological tumor analysis and adequately prepared colonoscopy before surgery.

Variables such as age, gender, comorbidities, tumor location, presence of synchronous or metachronous tumor, presence of hereditary syndrome and histological subtype were assessed using a data collection instrument obtained by patients' charts review.

Assessed comorbidities were systemic arterial hypertension (SAH), diabetes mellitus (DM), obesity classified according to body mass index (BMI), dyslipidemia, smoking, alcoholism, lung disease, liver disease, kidney disease, thyroid disease and depression. Tumor location was defined as cecum and ileocecal valve, right colon, hepatic flexure, transverse colon, splenic flexure, left colon, sigmoid colon and high and low rectum. The presence of hereditary syndrome was evaluated and the syndromes included were FAP and HNPCC. Histologically, the tumors were classified as adenocarcinoma, epidermoid tumor, undifferentiated and polypoid lipoma.

Data were stored in Microsoft Excel 2007 spreadsheets and statistical analyses were performed using SPSS software, release 17.0®.

Results

From January to July 2012, medical records of all patients with colorectal cancer treated at the Proctology Service from January 2010 to March 2012 were retrospectively reviewed. A total of 150 records were analyzed, of which 53.3% were males with a mean age of 63 (± 13.01) years old. Among the comorbidities assessed, the most prevalent was hypertension, seen in 24.6% of patients, followed by diabetes mellitus, lung and heart disease (Table 1).

Regarding tumor location, the most affected portion was the sigmoid colon and high rectum (50.67%) followed by the low rectum (36%). Adenocarcinoma was the most prevalent histological subtype, corresponding to 89.3% of cases, followed by epidermoid tumors (1.33%) and undifferentiated and polypoid lipomas, both with an incidence of 0.67% (Table 2).

Table 1 – General sample characteristics.

	Absolute value	Percentage value (%)
Gender		
Male	80	53.3
Female	70	46.7
Total	150	100
Comorbidities		
SAH	37	24.6
DM	9	6
Pneumopathy	6	4
Cardiopathy	4	2.67
Smoking	3	2
Obesity	2	1.33
Hepatopathy	2	1.33
Thyroidopathy	2	1.33
Breast cancer	1	0.67
Mood disorder	1	0.67
Parkinson's disease	1	0.67
No comorbidities	82	54.67
Total	150	100

SAH, systemic arterial hypertension; DM, diabetes mellitus.

Hereditary syndromes were identified in five patients (3.33%), all with adenocarcinoma histology. Of these, four patients had FAP and 1 had HNPCC.

From 150 patients, only four (2.67%) had synchronous neoplasia. The incidence of metachronous tumor was 0,67% (one patient), whose tumor location was in the cecum (Table 3). The mean age of patients with synchronous tumors was 61.5 (± 13.02) years old, of which three were females. The adenocarcinoma histological subtype was seen in four patients and only one patient was diagnosed with a hereditary syndrome (FAP).

When analyzing tumor characteristics of the four patients with synchronous lesions, it was demonstrated that two patients were classified as C according to Dukes' criteria; the tumors did not have a predominant topography and total colectomy was indicated in three patients, with proctocolectomy being indicated for the fourth case (Table 4).

Discussion

Colon cancer is the third most common malignancy in Brazil[10] and the second most common cause of death from malignancy in the western world. The risk of developing a tumor throughout the lifetime in the general population is approximately 5%. United States data estimated that 141,210 new colorectal cancer cases were diagnosed in the US in 2011.[11]

Patients with sporadic colorectal cancer or cases associated with genetic syndromes are at risk of developing synchronous tumors at diagnosis, as well as metachronous lesions in the follow-up.[6] Due to the possibility of the existence of synchronous tumors, all patients with a diagnosis of this type of tumor should have their colon thoroughly analyzed preoperatively to investigate the presence of a second or third lesion, which can modify the extent of the surgical procedure.[12]

Although colonoscopy is the test of choice in the preoperative investigation, it is not, even when associated with double-contrast barium enema, enough to detect all synchronous lesions, with a sensitivity of 66%.[13] Therefore, the palpation of the entire colon and rectum is recommended during surgery to detect synchronous tumors not identified at the preoperative evaluation.[2,13]

Table 2 – Tumor-related characteristics.

	Absolute value	Percentage value (%)
Tumor location		
Sigmoid colon and high rectum	76	50.67
Low rectum	54	36
Cecum and ileocecal valve	3	2
Transverse colon	2	1.33
Splenic flexure	2	1.33
Hepatic angle	1	0.67
Left colon	1	0.67
Right colon	1	0.67
Not specified	10	6.67
Total	150	100
Histological subtype		
Adenocarcinoma	134	89.3
Epidermoid	2	1.33
Undifferentiated	1	0.67
Polypoid lipoma	1	0.67
Not specified	12	8
Total	150	100
Hereditary syndrome		
FAP	4	2.67
HNPCC	1	0.67
No syndrome	145	96.67
Total	150	100

FAP, familial adenomatous polyposis; HNPCC, nonpolyposis colorectal cancer.

The preoperative detection of synchronous tumors not only allows establishing the appropriate surgical strategy, but also facilitates the follow-up plan after surgery. It is believed that the presence of synchronous lesions require a modification in surgical extension in 34.4% of patients, as they indicate lesions in surgically distinct colonic segments.[2,6]

Estimates of the incidence of synchronous colorectal adenocarcinoma vary, according to the literature, from 2 to 9%.[2-8] The results of the present study are consistent with the literature, as the incidence in this population was 2.8%. We believe that the incidence found was lower than that reported in other studies due to the smaller number of patients. However, if we evaluate that only 4.5% of our sample had a

Table 3 – Incidence of synchronous and metachronous tumors.

	Absolute value	Percentage value (%)
Synchronous tumor	4	2.67
Metachronous tumor	1	0.67
Single tumor	145	96.67
Total	150	100

Table 4 – Characteristics of patients with synchronous colorectal cancer.

Patient	TNM	Dukes classification	Topography 1	Topography 2	Surgery
Case 1	pT4N2M0	C	Transversal	Low rectum	Total colectomy
Case 2	pT1N0M0	A	Splenic flexure	Cecum and Ileocecal valve	Total colectomy
Case 3	pT1N0M0	A	Transversal	Right colon	Total colectomy
Case 4	pT3n1m0	C	Low rectum	Left colon	Proctocolectomy

diagnosis of hereditary adenocarcinoma and only one of these cases had synchronous tumors, we observe that the results of the present study are very similar to those described by other authors. According to Fante et al., the incidence of synchronous neoplasia is slightly lower if patients with hereditary pathologies are excluded, decreasing from 4 to 2.5%.[9]

Of the four cases of synchronous tumors, two affected the rectal segment, whereas the remaining lesions were distributed between the cecum and sigmoid colon. This finding corroborates previous descriptions that suggest a higher prevalence of synchronous adenocarcinoma in cancers arising in the colon, when compared to rectal tumors.[6]

Risk factors for synchronous tumors include male sex, family history, advanced age and the presence of synchronous adenomas. In our sample, 75% were females. However, this finding has no statistical significance due to the small number of patients evaluated.

Age is a controversial subject, as several studies have indicated that synchronous tumors occur in older patients,[13] while other studies have shown that the patients were younger. Moreover, there are studies that showed no significant difference regarding age of patients with a solitary tumor in comparison to those with synchronous tumors.[2,3] The divergence regarding the results is possibly due to the fact that synchronous tumors were not stratified by location or genetic predisposition.

This fact is demonstrated by the study of Fukatsu et al., in which there was no difference in age between the groups with isolated and synchronous tumors; however, when these were analyzed for tumor location, it was shown that the presence of both lesions in the right colon occurs in older patients, whereas both lesions in the left colon occur in younger patients[4]. This finding supports the theory that tumors of the right colon and left colon have distinct molecular biology features and different risk factors, as right colon tumors are more prevalent in the elderly and in females, while tumors of the left colon are more prevalent in younger males.

Moreover, few studies have evaluated the incidence of metachronous tumors. According to Chen et al., the incidence is approximately 1% (2), similar to that found in this study, of which incidence was 0.67%.

Conclusion

The incidence of synchronous colorectal tumors in this population was 2.67%, which is consistent with values previously reported in the literature, especially when cases of hereditary tumors were excluded. Moreover, the incidence of metachronous tumor was 0.67%, which also corroborates the literature findings, although few authors have addressed this issue in particular.

Conflict of interest

The authors declare no conflicts of interest.

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