Hyperglycemia and obesity related with intestinal neoplasia. Survey in an oncology centre.

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Abstract

Background: One of the most common causes of malignant neoplams is colorectal cancer. This pathology may generate severe illness and complications leading to death. Metabolic dysfunction, including obesity and hyperglycemia, has increased exponentially and previous studies have suggested an association between those risk factors and a greater risk of colorectal cancer.

Aim: To assess the prevalence and the role of metabolic pathology in patients with intestinal cancer.

Methods: A descriptive and retrospective study conducted at a Cancer Reference Center in Sao Paulo of patients diagnosed with intestinal cancers. During the first consult, the fasting blood glucose and body mass index were verified. The Student T-test was used. The rejection standard of the null hypothesis was set at 0.05 or 5% ($\alpha \leq 0.05$).

Results: Our study analyzed 105 patients, of which 60-69 year olds were the more prevalent age group. Of those studied, 50% of the patients were found to be overweight and obese and 47.6% were found to be hyperglycemic. The prevalent weight group of patients were those classified as overweight being between 25 and 29 kg/m^2 showing an incidence of 47.4% of rectal cancer and 52.4% of colon cancer. The hyperglycemic patient group showed a prevalence of 28% with rectal cancer and 72% with colon cancer. Those showing rectal cancer consisted of 57,2% men and 28.5% women. Those showing colon cancer demonstrated a prevalence of 41.6% of men and 5.5% women. However, those patients within the hyperglycemic group had no prior diagnosis of T2DM and were unaware of their condition.

Conclusion: Our study emphasizes the importance of metabolic disorders and the necessity of effective preventive health measures in attempt to prevent the development of severe pathology with high rate of mortality.

Keywords: Intestinal cancer, Colorectal cancer, Obesity, Hyperglycemia.

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Introduction

Malignant diseases are some of the most important pathologies that can progress towards mortality. Due to multifactorial phenotypes, several elements may contribute towards the evolution of the cancer. Studies demonstrated an exponential increase of this pathology in view of some triggering factors such as industrialization and population aging [1–4].

The World Health Organization estimated that the number of malignancies may increase 20% in at least 30 years in developed countries and 100% in emerging countries [1,2]. It is important to highlight the prevalence of the risk factors that may lead to the development of malignancies in an attempt to prevent the severity and course of the disease [2]. The scientific community incessantly seeks for in-depth knowledge in the assessment of the effectiveness of adopted clinical interventions as well as the identification of risk factors and to decrease the severity of the disease.

The global prevalence of type 2 Diabetes Mellitus (T2DM) among adults is 8.3% (382 million), and already independently represents an increase in mortality [5]. In this case, T2DM and cancer have many common risk factors [6,7], however, the exact correlation between hyperglycemia and the risk

factor for cancer found in surveys was controversial and has not been studied systematically [8–13].

Recent studies have shown that the metabolic syndrome (MS) may contribute to the incidence and mortality rates of some malignant diseases [14–17]. Cowey and Hardy [18] revealed the hypothesis that individual components of MS could be related to an increased risk of cancer. The worldwide prevalence of MS ranges from 10% to 40%, which is concerning, and is accompanied by a high morbidity-mortality [19].

The risk for the development of cancer may be decreased in an attempt to eliminate, or at least minimize, the exposure to carcinogenic agents. Although, without complete identification of these related risk factors, primary prevention will become more difficult. It is estimated that more than two thirds of cancers could be prevented by appropriate changes in lifestyle [6].

Because it is necessary to improve preventative actions against malignant neoplasms, it is urgent to emphasize the importance of studies on prevalence and recognition of risk factors to decrease cellular insults as well as the recognition of unfavorable prognosis for each type of cancer [20,21]. Therefore, our intention is demonstrate the metabolic profile of patients, in order to better clinical management.

Aim

To assess the prevalence and the role of metabolic pathology in patients with intestinal cancer.

Method

A Descriptive and retrospective study, conducted at a Cancer Reference Center in Sao Paulo of patients diagnosed with intestinal malignant neoplasms according to the histopathological definitions of the International Classification of Diseases system (ICD-10). The patients in question must have obtained their defined medical diagnosis amongst terms covered in the CID C180 to C189, which are: malignant neoplasm of ascending, transverse, descending, and sigmoid colon, and without specification (respectively CIDs C182, C184, C186, C187 and C189). Patients of both genders were included in monitoring and/or treatment. The study data collection was the clinical history and laboratory tests with fasting blood glucose performed during the first consultation. As part of the criteria for inclusion, only patients who were presenting to this Institution for the first time and were previously untreated were accepted into this study.

The criteria for diagnosis of T2DM was based on the International Diabetes Federation's guidelines (IDF), and these patients were in use of oral hypoglycemic [22]. Classification of obesity, according to World Health Organization, with Body Mass Index (BMI) 18.5–24.9 Kg/m^2 normal, 25.0–29.9 Kg/m^2 overweight, >=30 Kg/m^2 obesity [23]. Statistical analysis was performed in descriptive analysis with categorical variables expressed as absolute frequencies, and percentages were compared with the chi-square test. Continuous variables were expressed as mean and standard deviation and compared using the Student T-test. The rejection standard of the null hypothesis was set at 0.05 or 5% ($\alpha \leq 0.05$), noting with an asterisk (*) the significant values.

Results

Our study analyzed 105 patients diagnosed with intestinal cancer, of which 67 presented colon cancer and 38 having rectal cancer. We demonstrated a predominance of rectal cancer in women and colon cancer in men. Regarding cancer site and related obesity, our study showed a prevalence of 50% of the patients classified as overweight.

The Glycemic profile was analyzed demonstrating 47.6% of the patients presenting hyperglycemia (Table 1) Patients between 60-69 years old were the more prevalent age group (Table 2). We separated the obesity and cancer related patients as according to their BMI. Patients classified as overweight, being between 25 and 29 kg/m^2 were more the prevalent weight group, with 47.4% of the patients showing rectal cancer and 52.4% showing colon cancer (Table 3). The hyperglycemic patient group showed a prevalence of 28% with rectal cancer and 72% with colon cancer. Those showing rectal cancer consisted of 57.2% being men and 28.5% being women. Those showing colon cancer demonstrated a prevalence of 41.6% of men and 5.5% of women. However, those patients within the hyperglycemic group had no prior diagnosis of T2DM and were unaware of their condition (Table 4).

Table 1. *Basal characteristics of cancer and metabolic dysfunction.*

	Cancer	Rectal	Colon	p
Total	105	38	67	-
Women	61	27	34	-
Men	44	11	33	-
Overweight	50%	20	43	*
Hyperglicemia	47.60%	14	36	*

p: *significance statistical p<0.05

Table 2. *Description of neoplasm site related with age of patients.*

Age	W% (n)	M% (n)	Total% (n)	W% (n)	M% (n)	Total% (n)
	Rectal	rectal	Rectal	Colon	Colon	Colon
20-39 years	100% (1)		2,6% (1)	66.6% (2)	33.3% (1)	4,6% (3)
40-49 years	80% (4)	20% (1)	13.1% (5)	7.81% (5)	7.81% (5)	14.6% (10)
50-59 years	50% (4)	50% (4)	21.1% (8)	62.5% (10)	36.5% (6)	25% (16)
60-69 years	68.3% (13)	31.5% (6)	50% (19)	40% (6)	60% (9)	23.4% (15)
70-79 years	100% (5)		13,1% (5)	45% (9)	55% (11)	31.2% (20)
80 years/>				66.6% (2)	33.3% (1)	4.6% (3)

W: Women, M: Men, n: Number of patients

Table 3. *Distribution of groups according to BMI and neoplasm site.*

BMI	W% (n)	M% (n)	Total% (n)	W% (n)	M% (n)	Total% (n)
kg/m²	Rectal	Rectal	Rectal	Colon	Colon	Colon
<25 kg/m²	56.3% (9)	43.7% (7)	42.1% (16)	58.3% (14)	41.6% (10)	35.8% (24)
25 to 29	50% (9)	50% (9)	47.4% (18)	48.7% (17)	51.4% (18)	52.4% (35)
=>30	75% (3)	25% (1)	10.5% (4)	40% (2)	60% (3)	11.8% (8)

W: Women, M: Men, n: Number of patients

Table 4. *Analysis of glycemic profile related to neoplasm site.*

Neoplasm	W% (n)	W% (n)	M% (n)	M% (n)	Total% (n)
	T2DM	Hyp.	T2DM	Hyp.	
Rectum		28.5% (4)	14.3% (2)	57.2% (8)	28% (14)
Colon	22.4% (8)	5.5% (2)	30.5% (11)	41.6% (15)	72% (36)

W: Women, M: Men, n: Number of patients, T2DM: Diabetes mellitus type 2, Hyp: Hyperglycemia

Discussion

Epidemiological studies found a higher prevalence of cancer in individuals over 60 years of age, as was also demonstrated in our study. An increase in the life expectancy, as well as a higher prevalence of T2DM in older individuals was also revealed [24]. In addition, modernization and an industrialized diet may have contributed to the exponential growth in obesity. Although these pathologies reveal a high morbidity and mortality when isolated, could the advent of the metabolic dysfunction, also present, currently trigger the onset of cancer or is it merely due to the increase in the expectancy of life? Studies still remain controversial in answering this important question.

Our research showed results similar to most studies demonstrating a high prevalence of hyperglycemia and obesity in patients who were newly diagnosed with intestinal cancer [16]. A particularity of our research, however, demonstrated a considerable percentage of individuals with unknown hyperglycemia. Yet, it is important to emphasize that other studies using an approach different from ours revealed a relationship between cancer and T2DM and an increased mortality with a worse prognosis [25,26].

Several studies have shown that T2DM plays an important role in neoplasias [16,20]. Our study clearly revealed the association between hyperglycemia and intestinal neoplasia in the initial stages of a cancer diagnosis. It also implicated that the hyperglycemia was unknown and was therefore being untreated. Steeland et al. [27] however, demonstrated different results from ours, with no significant association between cancer and T2DM.

Obesity was the other major focus of our study. It was demonstrated in other studies that patients with a BMI >= 30 kg/m^2 increased by at least 40% the risk for colorectal cancer compared with patients with a BMI<25 kg/m^2 [28]. This data is estimated based upon obesity only with no particular associated comorbidity. Our study demonstrated a higher prevalence of overweight more so than obesity, and with the majority of cases correlating with hyperglycemia in patients with cancer. Nevertheless, because of a strong association between pathologies, we can conclude that the inflammatory environment of this situation may lead to the mutation and proliferation of cells. Trevisan et al. [29] and Colangelo et al. [30] demonstrated that components associated with MS increases the risk for the development of colon cancer when compared with individual components of MS. In accordance with this viewpoint, we studied two components of MS, hyperglycemia and obesity, of which we found that the prevalence of both components were almost equal and the pathologies were associated.

Several studies reinforced the possibility of hyperglycemia developing into cancer. In addition to hyperglycemia triggering a state of chronic inflammation with the release of inflammatory mediators, there are theories relating to insulin resistance with mutagenic and anti-apoptotic factors [6,20]. The capacity to generate ROS which then leads to increased hormone production (such as estrogen, adipokines, IGF-1 and insulin), and then triggers an energy-rich environment, is another possible mechanism visualized in insulin resistance and obesity [31]. According to Cowey, hormone variability, the redox system, and energy availability proceed to cell modification, proliferation and angiogenesis, as well as the inhibition of apoptosis, which is also, can be considered yet another possible mechanism for cancer development [18]. Also, hyperglycemia and the prolonged exposure time of intestinal mucosa to fecal bile acids develops constipation and may play an important role in colorectal carcinogenesis as well [32]. Furthermore, Li et al. [33] demonstrated that over presence of beta-catenin was considered a trigger to cellular proliferation in the colorectal epithelium of T2DM.

Nevertheless, in trying to answer the query, it has been found that although some studies are contradictory, yet most of them reinforce our results. Hyperglycemia and obesity are found present in the early diagnosis of intestinal cancer, however, we took a differing approach in our study by separating the analysis into two categories, that being colon malignancies versus rectal malignancies. It is important to consider this correlation and work towards preventing metabolic dysfunctions in an attempt to prevent the development of one of the most common cancers that also holds a high mortality rate.

Conclusion

Our study demonstrates the high prevalence of metabolic dysfunctions, hyperglycemia and obesity, in new patients diagnosed with intestinal cancer. Since cancer is consider one of the pathologies with a higher rate of mortality, it is of great importance the production of studies attempting to correlate the possible risk factors that may be involved in the development of this pathology. It is important to highlight that in our study most of the patients with hyperglycemia were completely unaware of their situation. Considering that hyperglycemia and overweight may be a risk factor for cancer, more studies are still required, as well as effective health policies in the attempt to prevent the evolution towards metabolic disorders.

Limitations of Study

A small percentage of patients were used in this study. Although the institution is a Reference Center for Oncology, patients only in the initial stage of cancer diagnosis were recruited. More studies are required to strengthen this thesis; nevertheless, significant relevance was demonstrated in our results.

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