

**COLORRETAL  
NEOPLASIA: A  
SYSTEMATIC REVIEW  
OF PREVENTION,  
SCREENING AND  
TREATMENT**

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**Abstract:** Colorectal cancer (CRC) is the third most common neoplasm worldwide, with a higher prevalence in developed countries. In recent years, data and epidemiological studies have shown an increase in the incidence of colorectal cancer in the population under 50 years of age. Although it is established in the literature on the influence of environmental risk factors such as lifestyle, obesity and alcohol consumption on the development of colorectal cancer, the mechanisms and factors that contribute to the development of early-onset colorectal cancer may be correlated with a combination of genetic factors, environmental exposure and early screening. The objective of this work was to carry out a literature review regarding the screening, prevention and treatment of colorectal cancer in the last 10 years (2011 to 2021), through a rigorous and critical selection of works for its composition. The methodology used was a systematic literature review. It is known that early detection and treatment significantly increase the possibility of recovery, and it is extremely important to analyze aspects related to the prevention, screening and treatment of colorectal cancer. Screening makes it possible to detect adenomatous and carcinomatous lesions in asymptomatic patients, and early treatment may be indicated. At first, all colorectal polyps must be removed (polypectomy) for histopathological study, through colonoscopy and after adequate colonic preparation, or flexible sigmoidoscopy. It has been shown that short-term minimally invasive surgical oncologic treatment offers lower perioperative morbidity and mortality and a lower incidence of postoperative complications.

**Keywords:** Colorectal cancer, Colonoscopy, Risk factors, Tracking.

## INTRODUCTION

Colorectal cancer represents the second

leading cause of death of neoplastic etiology in the US, and about 90% of these are from adenomatous polyps (most of which have the potential for malignancy) (BRAY et al., 2018; DANI, 2018).

According to data compiled by the *Global Cancer Observatory* in 2020, in Brazil, colorectal cancer cases occupy the third place in diagnosis of the pathology, as well as in most developed countries. It has an incidence of 55,102 cases, considering patients of both sexes and covering all ages, as shown in Figure 1. Although colorectal cancer mortality has decreased in the last decade, in 2020 it was responsible for 54,443 deaths in the United States (ISLAMI et al., 2021).

Colorectal cancer can occur in the following forms: hereditary, sporadic or familial (TOWSEND, 2015). In the last decade, data and epidemiological studies have shown an increase in the incidence of colorectal cancer in the population under 50 years old. (2021).

Thus, strategies related to prevention, early detection and treatment for the broad and equitable implementation of effective interventions are of utmost importance, having an impact on incidence and morbidity and mortality. Screening in the indicated population has been important in the early detection of pre-neoplastic and neoplastic lesions and their treatment - with the purpose of endoscopic or surgical removal, as indicated (BRAY et al., 2018; TOWSEND, 2015).

Primary prevention strategies such as correcting lifestyle habits, through a diet rich in natural fibers, consumption of calcium, vitamin D, folates, reduced consumption of red meat, and the fight against sedentary lifestyle have an impact on the incidence of colorectal cancer, evidenced mainly in the population over 50 years old (DANI, 2018; ISLAMI et al., 2021).

It is certain that the earlier the diagnosis and treatment, the better the survival

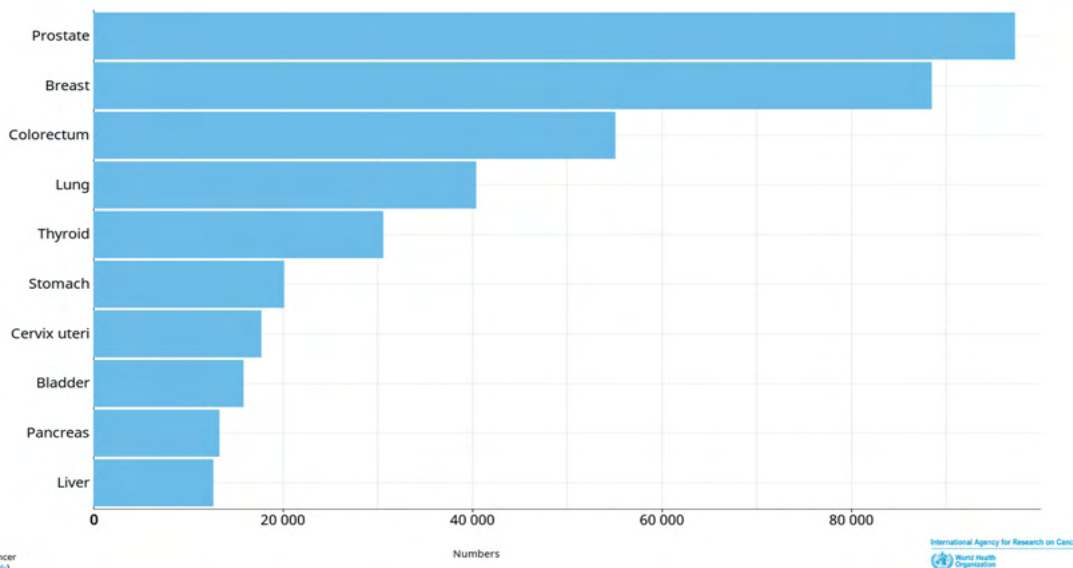


Figure 1 – Estimated number of cancer cases in Brazil for both sexes, at all ages

Source: Global Cancer Observatory (2022).

of colorectal cancer. A 5-year survival is observed in 90% of patients if the disease is localized, 68% for regional disease (lymph node involvement) and only 10% for patients with distant metastasis (ASSIS, 2011).

Therefore, the objective of this work was to carry out a literature review regarding the screening, prevention and treatment of colorectal cancer in the last 10 years (2011 to 2021), through a rigorous and critical selection of works for its composition.

## METHODOLOGY

The present work is presented as a systematic literature review. The descriptors used for the research were: (*colorectal neoplasms [DeCS/MeSH]*) AND (*prevention [DeCS/MeSH]*) OR (*tracking [DeCS/MeSH]*) OR (*treatment [DeCS/MeSH]*), in English or Portuguese, in the bases: *Scielo, MedLine and PubMed*.

The inclusion criteria were: publications (books, original articles, meta-analysis, randomized, review, case reports or clinical

protocols) presented in full, in Portuguese or English, which presented the descriptors in the title, abstract or keywords, published in the last 10 years (2011 to 2021). The period chosen was due to the scarcity of materials published in the last 5 years. Exclusion criteria were: duplicate articles, letters to the editor, *short communication*, research projects or incomplete articles.

Some materials, even if they were outside the pre-stipulated period for the search, were also considered in this study because they were considered relevant and pertinent.

## RESULTS AND DISCUSSIONS

### RESULTS

Applying the inclusion criteria, 68 articles were found. After excluding duplicate articles from the same database and between different databases, a total of 53 articles was reached for reading the abstracts. In the abstract reading stage, 21 articles were excluded because they did not present the descriptors in the title or abstract. Soon after, 4 articles were excluded

because they did not fit and/or did not fit into the proposed discussion of the topic, reaching a total of 28 articles included in the review. In addition to the articles, 2 official websites (Ministry of Health and *Global Center Observatory*) and 2 books were included because they were considered pertinent and relevant by the authors.

## DISCUSSIONS

### Colorrectal neoplasia

More than 70% of patients with the disease receive the diagnosis in an advanced stage, thus contributing to a worse prognosis (BENSON, 2007).

The colon is considered the most frequent site of primary neoplasms and most are adenocarcinomas. Its appearance may be due to genetic alterations in colonic mucosa cells, with disordered proliferation, resulting from some distinct and cumulative genetic alterations, such as mutation in the APC, K-ras, DCC and p53 gene and DNA hypomethylation. With this process, the adenomatous polyp progresses with dysplasias, which may be part of the evolution and emergence of colorectal adenocarcinoma (ASSIS, 2011; LEE et al., 2021).

In non-polypoid colorectal cancer, colorectal cancer may develop rapidly, being preceded by few or no polyps and may occur at a younger age (adults under 50 years), in a more proximal location of the colon or in multiple locations (synchronous tumors). at diagnosis or during follow-up (metachronic tumors) (DA SILVA et al., 2017).

### Prevention

Most cases of colorectal cancer are associated with modifiable environmental risk factors such as obesity, physical inactivity, poor diet, alcoholism and smoking. Consequently, middle to low-income countries account for the vast majority of cases. In addition, in recent years, the growth of cases in people under 50

years of age is an emerging trend (WITOLD et al., 2018; KEUM; GIOVANNUCCI, 2019).

Stoffel and Murphy (2020) reported that approximately 1 in 10 cases of new colorectal cancer diagnoses are found in people younger than 50 years. On closer analysis, the authors determined that three out of four patients who had early-stage cancer had no family history of the disease; that is, the increase observed in this portion of the population is connected with factors such as diet, environmental factors and lifestyle.

The 2017 report from the *World Cancer Research Fund (WCRF)* comparing to *American Institute of Cancer Research (AICR)* concluded after a systematic review that factors such as obesity; the low frequency of physical activity; diets high in red and processed meat, low in fiber and low in calcium; and the use of alcohol and cigarettes increase the risk of developing colorectal cancer. In Figure 2, present in the research by Keum and Giovannucci (2019), it is possible to observe the factors that have a high risk level for colorectal cancer, indicated in the column: *Level of evidence*.

According to several results, physical activity is a protective factor with regard to the development of adenomas and colorectal cancer. As a lifestyle with physical activity normally implies a more balanced diet and reduced weight gain, this type of prevention has a synergistic effect in relation to preventing the incidence of colorectal cancer. et al., 2012; WITOLD et al., 2018; KUEM; GIOVANNUCCI, 2019).

Regarding alcohol consumption, Choi, Myung, and Lee (2018) concluded that even a reduced amount of alcohol (one alcoholic drink or less per day) still presents an increased risk for colorectal cancer compared to occasional consumption or no consumption. of alcohol.

In addition to the above, Witold et al. (2018) warn that environmental factors such

Aetiological factors	Level of evidence <sup>a</sup>	Unit increase	Colorectal cancer RR (95% CI)	Colon cancer RR (95% CI)	Rectal cancer RR (95% CI)
Obesity	↑↑	5 kg/m <sup>2</sup> in BMI	1.05 (1.03–1.07)	1.07 (1.05–1.09)	1.01 (1.01–1.04)
	↑↑	10 cm in WC	1.02 (1.01–1.03)	1.04 (1.02–1.06)	1.02 (1.00–1.03)
Total physical activity	↓↓	5 MET-hours per week	0.97 (0.94–0.99)	0.92 (0.86–0.99)	1.02 (0.95–1.10)
Western dietary pattern	↑↑	Highest versus lowest	1.12 (1.01–1.24)	1.30 (1.04–1.63)	1.09 (0.91–1.29)
Prudent dietary pattern	↓↓	Highest versus lowest	0.89 (0.84–0.95)	0.89 (0.80–0.99)	0.96 (0.83–1.10)
Processed meat	↑↑	50 g per day	1.16 (1.08–1.26)	1.23 (1.11–1.35)	1.08 (1.00–1.18)
Red meat	↑	100 g per day	1.12 (1.00–1.25)	1.22 (1.06–1.39)	1.13 (0.96–1.34)
Total fibre	↓	10 g per day	0.93 (0.87–1.00)	0.91 (0.84–1.00)	0.93 (0.85–1.01)
Whole grain	↓	90 g per day	0.83 (0.79–0.89)	0.82 (0.73–0.92)	0.82 (0.57–1.16)
Alcohol (as ethanol)	↑↑	10 g per day	1.07 (1.05–1.09)	1.07 (1.05–1.09)	1.08 (1.07–1.10)
Smoking <sup>b</sup>	↑	Current versus never smokers	1.15 (1.00–1.32)	1.10 (0.89–1.36)	1.19 (0.94–1.54)
Aspirin <sup>b</sup>	↑↑	75–1200 mg per day versus control	0.76 (0.63–0.94)	0.76 (0.60–0.96)	0.90 (0.63–1.30)
Total calcium <sup>b</sup>	↓	300 mg per day	0.92 (0.89–0.95)	0.91 (0.87–0.96)	0.95 (0.83–1.08)

↑↑, convincing risk factor; ↑, probable risk factor; ↓↓, convincing protective factor; ↓, probable protective factor; BMI, body mass index; CI, confidence interval; CRC, colorectal cancer; MET, metabolic equivalent of task; RR, relative risk; WC, waist circumference. <sup>a</sup>Level of evidence as indicated by WCRF–AICR summary report for CRC<sup>3</sup>, except for smoking and aspirin (based on evidence from observational studies and randomized controlled trials).<sup>b</sup>Long latency was required to observe an effect on CRC.

Figure 2 – Summary of associations between protective or risk factors and colorectal cancer by anatomical factors.

Source: Kuem; Giovannucci (2019)

as lifestyle and nutrition are relevant to result in the development of colorectal cancer when combined with genetic factors. Therefore, the surveillance of families with genetic potential and the promotion of a healthy lifestyle, with an emphasis on the population under 50 years of age, is essential to reduce the risks that colorectal cancer would provide.

### Tracking

For Townsend (2015), screening for cancer is the cornerstone of secondary prevention, since, according to the author, colorectal cancer is predictive. Thus, the detection of precursor lesions in screening tests and their resection substantially reduces the incidence and mortality from colorectal neoplasms.

In general, symptoms such as hemorrhage, change in bowel habits, abdominal pain, weight loss and anemia can occur at an advanced stage of colorectal cancer, which is why the traceability of lesions or adenomatous polyps is so necessary (DIAS, et al, 2007).

Towsend (2015), considers the choice of screening method to be controversial, because

prevention methods have changed over the years and patients are classified into medium and high risk groups. To *American college of Gastroenterologists*: Patients with a first-degree relative with colorectal cancer diagnosed after age 60 are twice as likely to be at risk for developing this cancer. For Townsend, the possibility of these patients developing cancer around the age of 40 is the same as the general population over 50 years of age. Therefore, according to the author, patients at moderately increased risk are considered, and screening must begin at age 40. Patients at high risk are those with hereditary cancer syndrome, such as Familial Adenomatous Polyposis (FAP) or Hereditary Non-Polyposis Colorectal Cancer (NCCPH), as well as those with Crohn's Disease.

It is estimated that the appearance of an adenoma, its growth and transformation into a tumor takes more than ten years, a period that is sufficiently long to allow its identification, resection and, therefore, prevention. The high incidence of colorectal cancer and the

difference in the results of treatment of an established neoplasm, according to the stage of the disease, justify efforts for early detection and screening in the population considered at risk for the disease (MANZIONE, 2004).

The Brazilian Association for the Prevention of Intestinal Cancer recommends screening for colorectal cancer according to the estimated risk for neoplasia presented individually through epidemiological and molecular genetic assessments. Such criteria defined in the population three distinct risk groups: low, moderate and high risk (DIAS et al., 2007).

The American College of Gastroenterology recommends the use of one of four screening tests for colorectal cancer: barium enema, fecal occult blood test, sigmoidoscopy, and colonoscopy. In addition, they point out that it is necessary to carry out a fecal occult blood test and/or sigmoidoscopy. According to the American College, colonoscopy must be reserved for individuals with positive results from initial screening tests or for those individuals at high risk of developing colorectal cancer (MENEZES, 2016).

Colonoscopy is considered the gold standard for screening. It has the advantage of providing a way to intervene in the natural history of colorectal cancer, facilitating endoscopic polypectomy. The disadvantages of this method are that it is more invasive, which can cause colonic perforation or bleeding. Even though it is considered the gold standard, improvements are needed in this type of screening, as there are 15% failures in the diagnosis of polyps, especially for those smaller than 1.0 cm (TOWSEND, 2015).

A potential area related to diagnostic improvement in imaging exams of the gastrointestinal region, such as colonoscopy and endoscopy, has been explored by different authors in recent years (KUDO et al., 2020; YANG et al., 2020). This being related to

the use of technologies and the creation of models, through the joining of thousands of images, in order to create more effective and simplified diagnostic analysis methods, with the possibility of being used by non-specialist professionals with a level of precision sufficient to detect cases of colorectal neoplasia (DANI, 2018).

Kudo et al. (2020) created the ENDO-Brain system, based on artificial intelligence, to facilitate the identification of neoplasms by professionals who are not specialists in imaging exams. The system was fed with around 69,000 images of patients who had colorectal polyps and, to assess their level of accuracy, the diagnoses were compared with the analysis of 30 professionals in 100 cases. The system differentiated neoplastic from non-neoplastic lesions with 96% accuracy, with 96.9% positive predictive value and 94.3% negative predictive value, values significantly higher than those obtained by professionals in their diagnoses. Therefore, the technology presented represents an advance in the detection of neoplastic lesions and is already authorized for use by the Japanese regulatory agency in generalized clinical settings.

Yang et al. (2020) proposed a breakthrough in the detection of colonoscopy images by testing an artificial intelligence system that classifies the results obtained into four different categories: advanced colorectal cancer, high-grade dysplasia and early colorectal cancer, tubular adenoma and non-neoplasms. The diagnoses were based on 3,838 images from 1,339 patients. The system demonstrated an accuracy of 67.3% in internal validation and 79.2% in external validation. The authors concluded that a model showed promising performance in the classification of neoplastic lesions and can help professionals to build ideal treatment strategies for each case.

Thus, the start of screening is differentiated according to the risk for developing colorectal

cancer - medium or high risk. According to the latest guidelines, studies and guidelines of the *US Preventive Services Task Force (USPSTF)*, *American College of Gastroenterology (ACG)* and *American Cancer Society (ACS)* screening for colorectal cancer is recommended in the medium-risk population, from 45 years to 75 years (as long as life expectancy is 10 years or more), with colonoscopy (gold standard exam) every 10 years or flexible sigmoidoscopy every 5 years or annual fecal immunochemical test or annual fecal occult blood test (DAVIDSON et al., 2021; SHAUKAT et al., 2021; WOLF et al., 2018).

In Brazil, the Primary Care Notebook issued by the Ministry of Health (MS) recommends that the beginning of screening for colorectal cancer in adults, be done between 50 and 75 years of age, through the fecal occult blood test (BRASIL, 2010).

According to *Canadian Task Force on Preventive Health Care – CTFPHC* e o *European Council* initiation of screening at age 50 is recommended for medium-risk adults. In the guidelines of *American college of Gastroenterologists (ACG)*, for individuals at increased risk for developing colorectal cancer, colonoscopy is recommended every 5 years (in some cases every 2-3 years) starting at age 40 or 10 years before the case diagnosed in a first-degree relative in cases where there are associated genetic factors (CANADIAN TASK FORCE ON PREVENTIVE HEALTH CARE et al., 2016; LANSDORP-VOGELAAR; VON KARSA, 2016; SHAUKAT, 2021).

### **Treatment**

The size, location, extension of the tumor and the patient's general health will directly influence the treatment to be indicated, in addition to its micro and macro characteristics (BARBOSA et al., 2019; MATHEWS; DRAGANOV; YANG, 2021). The unique anatomy of the rectum makes surgical access difficult, and because of its

anatomical distance from the small intestine and retroperitoneal pelvic location, it provides an opportunity for radiotherapy treatment not feasible in colon tumors. The treatment has changed significantly in the last 25 years, with controversies about surgery, radiotherapy or chemotherapy, in addition to controversies and divergences regarding the ideal time for each modality (TOWSEND, 2015).

There are several therapeutic modalities for the treatment of colorectal cancer such as surgery (curative or palliative), chemotherapy, and radiotherapy, which can be used alone or in combination (DA SILVA, 2017).

One of the main lines of treatment for the management of polyps is endoscopic resection, which is consolidated for low-risk lesions and evaluated for use in certain malignant lesions. The polyp is disassociated from the colon wall by the snare so that the resection can be performed hot or cold, depending on the technique applied. The advantage of a method like this is the reduction in procedure time and possible complications, however in the case of larger lesions this technique is still not reliable as it can result in incomplete resections (DUMOULIN; HILDENBRAND, 2019). According to Mathews, Draganov and Yang (2021), treatments like this represent a lower cost and lead to greater patient satisfaction compared to the surgical approach.

Dumoulin and Hildenbrand (2019) and Kuellmer et al. (2019) indicate that the endoscopic full-thickness resection (EFTR) technique, for example, can safely and feasibly reach difficult-to-reach lesions and is an advance in the treatment of colorectal cancer in the early stages. Mathews, Draganov and Yang (2021) also point out that the correct detection of the lesion, considering endoscopic images and histopathology, together with a multidisciplinary action of the professionals involved in the diagnosis and analysis are essential for an efficient

practice in the management of colorectal polyps.

Preoperative evaluation requires accurate characterization of the cancer with respect to the proximity of the anal sphincters and the extent of invasion (depth and penetration of the intestinal wall) as well as spread to adjacent lymph nodes.

Surgical treatment is considered curative when it promotes complete removal of the primary tumor, organs and structures locally compromised with identified metastases. It is then considered palliative when it aims to alleviate and reduce symptoms in patients who cannot be cured by resection (unresectable distant or locally disseminated metastases and invasion of vital structures) (PLUMMER et al., 2016).

The indication of the best surgical approach (laparoscopic or laparotomy; total or segmental colectomy; resection with primary reconstruction or construction of a temporary proximal diversion colostomy or ileostomy) will depend on the location of the neoplasm, its extension, level of involvement, behavior (especially in involving genetic association), the patient's clinical conditions, the surgical indication (elective or emergency) and the surgeon's experience (CLINICAL OUTCOMES OF SURGICAL THERAPY STUDY GROUP, 2004; FLESHMAN et al., 2007).

A case study carried out in 2020, with a 54-year-old male patient, demonstrated surgery (laparoscopic route) as a therapeutic strategy for the treatment of ascending colon cancer, with satisfactory results and hospital discharge after 4 days of hospitalization. The treatment was performed with reduced surgery time, in addition to the reduction of metabolic and traumatic changes, brief return of intestinal peristalsis, lower risk of infection and shorter hospital stay (PEREIRA et al., 2020).

The proper selection of patients is extremely important to obtain short and long-term oncological results. Thus, the initial management of patients with distant metastatic disease is individualized. The most common site of metastasis is the liver. Currently, hepatic metastasectomy in colorectal cancer in selected patients is being considered, in cases where a complete resection and maintenance of functional residual liver volume is achieved. Surgical case series have shown a 5-year survival rate of between 24 and 60%. However, only 20-25% of patients meet the appropriate criteria for resection during the course of the disease (GORGUN; BENLICE; CHURCH, 2016; MOEHLER et al., 2021; ZHAI et al., 2021).

## CONCLUSION

In Brazil, even with applied studies on the importance of prevention and early diagnosis of CRC, as well as the existence of undeniable statistics on the benefit of screening tests, there are several national determinants that make it difficult to carry out an effective preventive policy in public health for the CCR. As a result, there is a delay in the diagnosis and initiation of treatment for injuries, which are usually diagnosed in advanced, complex stages, requiring prolonged hospitalizations and associated with high mortality rates.

Several studies have shown that the quality of the surgical treatment instituted represents one of the main prognostic factors, and can be evaluated through aspects such as operative mortality, sphincter preservation, local recurrence and survival. The population's lack of knowledge about the importance of CRC screening contributes to a reduced rate of adherence to diagnostic tests and an increase in its incidence.

Diagnosis is made through biopsy during colonoscopy, and staging is performed through physical examination, CT scans of the chest,



abdomen, and pelvis, and carcinoembryonic antigen dosage. The treatment of CRC varies according to the stage, and can be surgical, chemotherapy or radiotherapy, or even a combination of two types of treatment. CRC prevention is based on the concept that the time interval between the onset of the lesion and the onset of cancer is generally long, which allows the adoption of public policies for population screening.

Population actions aimed at promoting food reeducation in health and encouraging the practice of regular physical activity can have an impact on epidemiological aspects in CCR. In addition, early detection and treatment of precursor lesions or early-stage cancer leads to a reduction in the prevalence and mortality of the disease.

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