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## Review Article

# Crohn's disease: risk factor for colorectal cancer

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### ABSTRACT

**Background:** Crohn's disease is an inflammatory disease that can reach any part of the gastrointestinal tract. This disease has been associated with an increased neoplastic risk, including colorectal carcinoma.

**Objective:** The objective of this work is to describe the mechanisms present in two diseases, and that are responsible for the increased risk in Crohn's disease.

**Methods:** A bibliographic research was conducted in PubMed database. In addition to the articles obtained with an inserted query in Pubmed, other references relevant to the topic in question were included.

**Results:** Colorectal cancer risk varies according to the presence of certain factors, and an example of this is Crohn's disease. Chronic inflammation seems to be an important contribution to carcinogenesis, since it creates a microenvironment suitable for the onset and progression of the disease. There are molecular changes that are common to two conditions, thus justifying the fact of Crohn's disease being a risk factor for colorectal carcinoma. The disease control with an appropriate therapy and with surveillance are two ways to control this risk.

**Conclusions:** A proinflammatory state is the cornerstone in the association between Crohn's disease and colorectal carcinoma. The implementation of surveillance strategies allowed a decrease in morbidity and mortality associated with this cancer.

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## Doença de Crohn: fator de risco para o carcinoma colorretal

### RESUMO

**Introdução:** A doença de Crohn é uma doença inflamatória que pode atingir todo o trato gastrointestinal. Esta patologia tem sido associada a um risco neoplásico aumentado, nomeadamente de carcinoma colorretal.

**Objetivo:** O objetivo deste trabalho é descrever os mecanismos responsáveis pelo aumento do risco de carcinoma colorretal na doença de Crohn.

#### Palavras-chave:

Doença de crohn

Carcinoma colorretal

Inflamação

Fatores de risco

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**Métodos:** A pesquisa bibliográfica foi realizada na base de dados Pubmed. Para além dos artigos obtidos com a query inserida na Pubmed, foram também incluídas outras referências com relevância para o tema em questão.

**Resultados:** O risco de carcinoma colorretal aumenta na presença de determinados fatores, entres eles a doença de Crohn. A inflamação crónica presente parece ser um importante contributo para a carcinogénese, porque permite a criação de um microambiente adequado ao aparecimento e progressão da doença. Existem alterações moleculares comuns às duas patologias justificando-se o fato desta doença inflamatória ser fator de risco para o carcinoma colorretal. O controlo da doença com terapêutica adequada e estratégias de vigilâncias são duas formas de controlar o risco.

**Conclusões:** O estado pró-inflamatório é uma peça chave na associação entre doença de Crohn e carcinoma colorretal. A implementação de estratégias de vigilância permitiu a diminuição da morbi-mortalidade associada a esta neoplasia.

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## Introduction

Inflammatory bowel diseases, of which Crohn's disease (CD), familial adenomatous polyposis, and the non-polypoid hereditary form are examples, are three diseases that confer a high risk of colorectal carcinoma (CRC).<sup>1</sup>

CD is a chronic, progressive disease characterized by a pro-inflammatory state. The quality of life of these patients is affected substantially, although benefits have occurred with the appearance of various therapies.<sup>2,3</sup>

The multifactorial etiology of this disease is not fully known, but some pathophysiological mechanisms underlying it have been described.<sup>4</sup>

CD is characterized by chronic diarrhea (the symptom most often present), weight loss, blood loss and abdominal pain. All the gastrointestinal tract can be affected, and distal ileum and colon are the parts most often affected.<sup>3-6</sup>

For the progression of this disease, genetic and environmental factors and dysbiosis are contributing factors.<sup>2,3,7</sup>

About 2 million Americans and Europeans suffer from CD, and its diagnosis is established mainly in the 2nd or 3rd decade of life.<sup>7</sup>

CD may have intestinal and extra-intestinal manifestations, and the disease shows two predominant patterns. According to the Montreal classification, patients are categorized according to their age at diagnosis, and disease location and behavior. With regard to age at diagnosis, the categories are  $\leq 16$  years, between 17 and 40 years, and  $\geq 40$  years. The disease can be found in the ileum, colon, ileum-colon, or upper gastrointestinal tract, showing a non-stenotic/non-penetrating behavior, a stenotic behavior, or a penetrating behavior.<sup>8</sup>

CRC arises due to a dysplasia of intestinal mucosa and is more common in these patients versus the general population. Thus, this inflammatory disease is a risk factor for CRC occurrence.<sup>5,9,10</sup>

CRC can cause death in these patients, and the diagnosis is rarely established before 7 years of disease progression.<sup>7,11</sup> There is no consensus as to the quantification of risk since this is influenced by several factors.<sup>12</sup>

The prognosis of CD varies from patient to patient, but there are some factors which lead to a worse outcome, including the perianal disease and the presence of upper gastrointestinal tract lesions, as well as an extensively affected colon.

## Material and methods

On July 6, 2015, a literature search in PubMed database was performed with the following query ((“crohn's disease” [MeSH Terms] OR (“crohn” [All Fields] AND “disease” [All Fields]) OR “crohn's disease” [All Fields]) AND (“neoplasms” [MeSH Terms] OR “neoplasms” [All fields] OR “cancer” [All Fields])). The inclusion criteria were: studies published in the last 10 years and articles written in Portuguese, English or Spanish. The titles and abstracts were read, and 75 articles were selected.

On December 22, 2015, a new search was conducted with the aim of updating the bibliography; the same query and the same inclusion criteria used in the previous survey were employed, and 48 articles were obtained.

Additional studies relevant to the issue in question were also included, through a cross-search with the articles already included, and a book relevant to the subject matter.

A total of 50 references were obtained.

## Results

### Epidemiology

Inflammatory bowel disease, which includes CD, is more prevalent in developed countries; this leads one to think of Westernization as a risk factor for this condition. Dietary habits and lifestyle contribute in some way to its appearance. One of the diagnostic peaks occurs in patients aged between 15 and 30 years, and 30% of patients are diagnosed under the age of 20 years.<sup>13,14</sup> The second peak occurs between 60 and 80 years, with a lower incidence versus the first peak.<sup>15</sup>

In CD, the inflammation occurs transmurally. The most commonly affected locations are the terminal ileum and colon. At the time of diagnosis, 40% of patients exhibit an

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