

Intestinal and Nonintestinal Cancer Risks for Patients with Crohn's Disease



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KEYWORDS

- Inflammatory bowel diseases • Colorectal neoplasms • Skin neoplasms/secondary
- Lymphoma • Monoclonal antibodies/adverse effects
- 6-mercaptopurine/adverse effects

KEY POINTS

- Population-based studies show that patients with Crohn's disease (CD) are at increased risk of cancers of the colorectum, small bowel, skin, lymph nodes, and uterine cervix.
- Intestinal cancers seem to be more common among patients with long-standing and poorly controlled CD; cancers outside the intestines seem to be increased by immunosuppressive therapies.
- Cancers of the colorectum, skin, and uterine cervix are preventable; patients should be counseled on cancer risks and receive tailored cancer surveillance.

INTRODUCTION

Crohn's disease (CD) is a form of chronic inflammatory bowel disease (IBD) with an incidence in North America of 20 cases per 100,000 person-years¹ and a prevalence of approximately 200 to 300 cases per 100,000 adults.² In CD, inflammation occurs transmurally, extending from the mucosa to the muscularis layer and serosa. The most commonly affected intestinal segments are the terminal ileum and colon. At the time of diagnosis, 40% of patients exhibit disease with an ileocolic distribution, 30% suffer from an isolated ileal disease, and 30% have disease affecting only the colon. Approximately 5% to 10% of patients exhibit associated lesions of the upper

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gastrointestinal tract, and 20% to 30% show perianal disease. Onset of disease typically occurs in the second or third decade of life; thus, patients can be exposed to decades of chronic inflammation in the intestines and other sites of CD-related extraintestinal disease.

Chronic immune-mediated inflammatory diseases such as CD are strongly associated with cancer.³ Accordingly, patients with CD have increased rates of intestinal and nonintestinal cancers.⁴ The risk of cancer in CD patients can be related to cellular damage sustained during chronic inflammatory disease itself, or owing to life style factors like smoking, or owing to medications, which may blunt innate immune system cancer surveillance. Measuring the magnitude of cancer risks for patients with CD has evolved in recent years. Historically, the scientific literature on this topic has been dominated by case-control studies conducted in referral centers. More recently, large observational studies in administrative databases and population-level cohorts are thought to provide more realistic estimates of neoplastic complication rates with greater levels of precision. We, therefore, aimed to review the magnitude of risk for the development of intestinal and nonintestinal cancer in CD patients, discuss modifiable and nonmodifiable covariates, and inform these estimates largely from data published within the last 10 years. The focus of this review is to evaluate the epidemiologic characteristics, pathogenesis, and surveillance to prevent most commonly reported cancers in patients with CD.

COLORECTAL CANCER IN CROHN'S DISEASE

Epidemiology

Colorectal cancer (CRC) is ranked as the third most common cancer in the world.⁵ Each year, approximately 900,000 new cases of CRC are identified and 500,000 deaths occur worldwide. From 2009 to 2013, the number of new cases of colon and rectal cancer was 41.0 per 100,000 and the number of deaths was 15.1 per 100,000 per year.⁶ Adenocarcinoma of the colorectum is a major cause of morbidity and mortality in IBD. CRC accounts for about 10% to 15% of deaths in patients with IBD,⁷ and causes 1 in 12 deaths of patients with CD.⁴ The prognosis of sporadic CRC and IBD-related CRC are thought to be similar, both having an overall 5-year survival of 50%.⁸ However, the median age at diagnosis of IBD-related CRC, at 60 years of age, seems to be lower than that of sporadic CRC, at 70 years of age.⁹

It has long been understood that patients with IBD of the colon are at increased risk for CRC; however, our understanding of the magnitude of that risk is evolving. In recent years, high-quality population-based studies have shown that patients with IBD have about a 2- to 3-fold increase in CRC risk compared with the general population. CD seems to increase the risk of colonic but not rectal cancers.¹⁰ Important and emerging trends in CRC risk among CD patients are shown in **Table 1**. There may be a decreased risk in more recent years, as shown by many recent large studies.^{9,11–14} Caution must be taken when comparing these results because not all reports stratify CD patients by disease distribution; risk seems to remain considerably higher for patients with known colonic CD.¹⁵ It is likely that recent advances are due to the impact of modern biologic therapy for CD, aggressive and appropriate surgical CD management, and the role of surveillance colonoscopy for CRC. These practices have been influenced by a greater understanding of the pathogenesis of CD-associated CRC.

Pathogenesis of Colorectal Cancer in Crohn's Disease

The pathogenesis of ulcerative colitis-induced CRC has been studied extensively. Most of the literature on colitis-induced CRC is from ulcerative colitis. Like sporadic

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