Colon Cancer

Inflammation-Associated Cancer

Sherief Shawki, MD[a], Jean Ashburn, MD[a], Steven A. Signs, PhD[b], Emina Huang, MD[a,c,*]

KEYWORDS

- Colitis-associated cancer • Colitis cancer surveillance
- Colitis-associated cancer management • 3D human models

KEY POINTS

- Colitis-associated cancer is a complex disease process for which the pathogenesis is unclear.
- Advanced colonoscopic techniques are the standard of care for surveillance of those patients with colitis. Unique pathology mandates close surveillance and multidisciplinary discussion.
- When proctocolectomy is deemed necessary, specialized considerations for restorative procedures and surveillance are required.
- Novel model systems for providing personalized medicine and for understanding pathogenesis include colonic organoids.

INTRODUCTION

Although colitis-associated cancer constitutes less than 2% of all colon cancers,[1] the challenges associated with this type of this cancer have implications that relate to many other cancers, including disease progression, lack of clarity regarding pathogenesis, and a broader context for all inflammation-associated cancers.

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[a] Department of Colorectal Surgery, Cleveland Clinic, A30, 9500 Euclid Avenue, Cleveland, OH 44195, USA; [b] Department of Stem Cell Biology and Regenerative Medicine, Cleveland Clinic, Cleveland Clinic Lerner Research Institute, NE3, 9500 Euclid Avenue, Cleveland, OH 44195, USA; [c] Department of Stem Cell Biology and Regenerative Medicine, Cleveland Clinic, NE3, 9500 Euclid Avenue, Cleveland, OH 44195, USA
* Corresponding author. Cleveland Clinic, 9500 Euclid Avenue, A307, Cleveland, OH 44195.
E-mail address: huange2@ccf.org

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Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is associated with an increased risk for developing colorectal cancer (CRC). Historically, some investigators advocated prophylactic colectomy for patients with longstanding UC to reduce CRC-related mortality.[2] Although the exact magnitude remains unknown, patients with IBD are known to have an increased risk of developing colorectal neoplasia. This discrepancy in incidence is due to the wide variability in reported results as a result of variations in sources of information, such as data from low-volume versus high-volume centers, population-based data versus case reporting, and other small series.[3] In a large metaanalysis of 116 studies, the risk of cancer in patients with mucosal UC after disease duration of 10, 20, and 30 years was estimated to be 2%, 8%, and 18%, respectively. The reported prevalence of CRC in this analysis was 3.7%.[1] Another report of a 30-year surveillance program calculated the risk of neoplasia (both dysplasia and carcinoma) to be 7.7% at 20 years. This risk increased to 15.8% at 30 years of disease duration.[3] In another analysis of a 30-year colonoscopic surveillance program in patients with UC, the cumulative incidence of CRC was 2.5%, 7.6%, and 10.8% at 20, 30, and 40 years of disease, respectively.[4] Comparable findings have been demonstrated in CD and the reported incidence was 8% at 22 years.[5] Similarly, the cumulative risk of CRC in CD was reported as 0.3%, 1.6%, and 2.4% at 5, 15, and 25 years after diagnosis, respectively.[6]

CRC is one of the most devastating complications of IBD. It is associated with significant morbidity, and a mortality rate of up to 15%.[7,8] To reduce the risk of CRC in these patients, endoscopic surveillance guidelines have been developed to allow for the detection and potential removal of precancerous lesions. Such strategies aim to decrease the incidence of CRC in patients with IBD and improve mortality rates.[7,9]

With the availability of colonoscopy to evaluate the extent of the disease related to IBD and obtaining tissue biopsies, and realizing the risk factors associated with developing CRC in patients with IBD, efforts have been made to limit and/or prevent CRC-related mortality, while maximizing organ preservation. The increased risk for IBD-associated CRC prompted the practice of surveillance colonoscopy in these patients.[10] Despite the lack of prospective, controlled trials to evaluate the risk, benefit, and cost effectiveness of this surveillance approach, sufficient evidence is available to support the broad adoption of these strategies. Subsequent reports showed less risk of CRC, which could be attributed to either more timely surgical intervention, or perhaps greater use of chemopreventive agents such as aminosalicylates, or possibly more implementation of surveillance colonoscopy.[3,7,10]

EPIDEMIOLOGY

Risk Factors for Developing Carcinoma in Patients with Inflammatory Bowel Disease

There are some factors that had been associated with increased risk of developing CRC in patients with IBD, including age at the onset of disease, duration of the disease, the anatomic extent of disease, histologic changes versus macroscopic changes, backwash ileitis, primary sclerosing cholangitis, and family history.

Age at onset of disease

Early age at the onset of IBD disease has not been shown consistently to represent an independent risk factor for CRC. However, it reflects a longer duration of disease with associated colitis-related burden of increased risk of malignancy. The cumulative risk of CRC in patients with extensive UC has been estimated to be 40% in patients who had the disease before 15 years of age and 25% in patients who developed the disease between 15 and 39 years of age.[11,12]