Colorectal Neoplasia and Inflammatory Bowel Disease

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KEYWORDS

• Colorectal cancer • Inflammatory bowel disease • Neoplasia • Crohn's disease
• Ulcerative colitis

KEY POINTS

- Ulcerative colitis and Crohn's colitis are associated with a 2- to 5-fold increased risk of colorectal cancer.
- Patients with ulcerative colitis and Crohn's colitis should undergo surveillance colonoscopy to detect dysplasia, and if detected, should generally undergo prophylactic surgical resection.
- Patients that have undergone restorative proctocolectomy should have their ileal pouch and the anal transition zone surveyed via endoscopy.
- Patients with Crohn's disease are at increased risk of developing small bowel and anal cancers.

INTRODUCTION

Crohn's disease and ulcerative colitis are significant risk factors for the development of gastrointestinal neoplasias.[1] The association between ulcerative colitis and colorectal cancer has long been recognized, and surveillance protocols to detect neoplasia in the setting of ulcerative colitis are well established. Engaging in surveillance has been shown to decrease the risk of death from colorectal cancer among ulcerative colitis patients. Although the cancer risk related to Crohn's disease is not as well defined, all inflamed segments of bowel are at increased risk for the development of neoplasia. Crohn's colitis is associated with a risk of colorectal cancer similar to that of ulcerative colitis, and the risk of small bowel adenocarcinoma in patients with Crohn's enteritis is greatly elevated compared with that of the general population.

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MECHANISM OF ACTION OF INCREASED RISK

Sporadic colorectal cancers develop via the classic adenoma-dysplasia-carcinoma sequence. The development of colorectal cancer in the setting of colitis also progresses from dysplasia to carcinoma, although the process appears to be different and the progression is accelerated. It is thought that the inflammatory process leads to oxidative stress-induced DNA damage of the affected mucosa. Loss of p53 function is seen early in this sequence, unlike in sporadic cancers wherein this is usually a late finding.[2,3] Constant attempts at regeneration provide more opportunities for transcription errors and the subsequent development of neoplasia via activation of procarcinogenic genes and inhibition of tumor suppressor genes. Alteration in the colonic flora has also been proposed as a mechanism to increase the cancer risk. Altered flora may increase the degree of inflammation, or possibly produce procarcinogenic substances. *Bacteroides fragilis* and *Enterococcus feacalis* have been implicated as procarcinogens.

The use of immunosuppression to treat inflammatory bowel disease plays a role as well. Optimal control of inflammation is important, because the degree of inflammation correlates with the cancer risk.[4] However, immunosuppression may also allow neoplasia to advance at a faster rate. 5-Aminosalicylic acid drugs, on the other hand, have been shown to have a protective effect.[5] Cancers that arise in the setting of inflammatory bowel disease are more likely to be poorly differentiated,[2] although whether this portends a poorer prognosis is not clear. Studies have been contradictory, with some showing similar overall survival to sporadic cancers,[6,7] and others showing a poorer stage-for-stage survival.[8,9] As the increased risk is a field effect to all areas of inflamed bowel, inflammatory bowel disease–related cancers are also associated with a higher risk of both synchronous (12.4%) and metachronous (14.3%) cancers.[8]

ULCERATIVE COLITIS AND COLORECTAL CANCER

Ulcerative colitis is associated with a 2- to 5-fold risk for the development of colorectal cancer,[10–12] although the reported increased risk varies widely from study to study. The incidence has been estimated as approximately 1% per year, or 30% at 35 years.[13] Alternatively, Choi and colleagues[14] found the incidence of colorectal cancer to be only 10% at 40 years. Those who also have primary sclerosing cholangitis are at an even greater risk for colorectal cancer, and that increased risk is present at the onset of disease.[15]

SURVEILLANCE

Prophylactic total proctocolectomy is the recommended surgical treatment option for those at greatest risk of colorectal cancer. As the risk of developing neoplasia increases with the duration of disease, prophylactic surgery used to be recommended after 10 years of active disease to reduce cancer risk. The current trend is toward a more individualized approach, with surveillance recommended for most patients. Multiple societies have published recommended surveillance guidelines, although they are all quite similar. National Comprehensive Cancer Network (NCCN) guidelines recommend beginning surveillance after 8 to 10 years of pancolitis[16] with colonoscopies performed every 1 to 2 years, because the incidence of colorectal cancer increases after 8 years of disease.[1,17] Biopsies should be taken in 4 quadrants every 10 cm, resulting in more than 30 biopsy specimens for pathology. The chance of a false-negative surveillance colonoscopy decreases with the more biopsies that are taken.