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Colorectal cancer risk in Crohn's disease

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Abstract

There is recognized increased risk for colorectal cancer in patients with inflammatory bowel disease, particularly in long-standing and extensive ulcerative colitis. There also appears to be an increased rate of intestinal cancer in Crohn's disease, including both colon and small bowel sites. In Crohn's disease, evidence suggests that detection of colorectal cancer may be delayed with a worse prognosis. Some risk factors for cancer in Crohn's disease include the extent of inflammatory change within the colon and the presence of bypassed or excluded segments, including rectal "stump" cancer. In addition, the risk for other types of intestinal neoplasms may be increased in Crohn's disease, including lymphoma and carcinoid tumors. Earlier detection of colorectal cancer based on colonoscopy screening and surveillance may be achieved but, to date, this has not translated into a positive survival benefit. Moreover, newer staining methods and evolving micro-endoscopic techniques show promise, but have not significantly altered management. Future research should focus on development of molecular or other bio-markers that might predict future dysplasia or cancer development in Crohn's disease.

Key words: Colon cancer; Crohn's disease; Surveillance; Small bowel cancer

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INTRODUCTION

Previous studies documented that patients with inflammatory bowel disease, particularly those with extensive and long-standing ulcerative colitis, have an increased risk of later colorectal cancer development. This data, however, was largely based on investigations conducted in tertiary care settings, especially from the United States and the United Kingdom. Later studies, particularly from similar geographic locations in the United States, demonstrated that the magnitude of this increased risk may not be so significant in a private or community practice setting[1,2]. In contrast, others have suggested that the risk of colorectal cancer in patients with colitis is not universally increased[3]. In part, this may be influenced by the underlying colorectal cancer risk related to individual inherited, geographic or other environmental factors, rather than inflammatory bowel disease *per se*.

CROHN'S DISEASE AND CANCER RISK

In Crohn's disease, specifically, precise cancer risk data are very limited. If colorectal cancer does develop, however, the prognosis is recognized to be poor with reduced survival[4]. Several studies, again from tertiary care centers, have suggested that patients with Crohn's disease have an increased risk of colorectal cancer[5,6] and an excess overall mortality attributed to digestive tract tumors, including small bowel carcinoma[7]. The latter occur at a younger age, usually in males compared to those with small bowel carcinoma unrelated to Crohn's disease[8].

Weedon *et al*[5] reported colorectal cancer in 8 of 449 patients with Crohn's disease, or about 1.2% (i.e., an estimated 20 times greater risk than a control population). Similarly, Gyde *et al*[6] described an approximately 4-fold increased risk in patients with Crohn's disease. More recent cohort and population-based studies from Canada, where reporting of malignant disease is legally mandated[7,9], are also consistent with an increased intestinal cancer risk in Crohn's disease. In Europe, north-south differences in intestinal and extra-intestinal cancers have also been recently noted[10]. Interestingly, in Asia, with Crohn's disease now dramatically increasing, there is a high rate of colorectal cancer, particularly in the lower rectum and anal area[11]). A recent and extensive meta-analysis has also recently confirmed the increased colorectal and small bowel cancer risk in Crohn's disease[12]. Moreover, other malignancies have been reported in Crohn's disease, including myeloid and lymphoid malignancies[13], possibly related, in part, to wider use of immunosuppressants or biological agents (e.g., infliximab)[14,15]. Finally, carcinoid tumors may be increased

in Crohn's disease[16], and this has recently been estimated as a 15-fold risk[17].

RISK FACTORS

In a cohort-based study of Crohn's disease followed over more than 2 decades, 1% had intestinal cancers detected[13]. The clinical features of the intestinal cancers included: a long history of Crohn's disease, often (but not exclusively) over 20 years predating cancer development; a relatively young age of intestinal cancer diagnosis in Crohn's disease; and, the appearance of other histopathological types, including mucinous adenocarcinoma. Most cancers occur in the distal colorectum, often in the presence of extensive inflammatory disease. Cancers were also detected in bypassed or excluded segments of intestine, including rectal "stump" cancer, a potentially important and independent risk factor for later cancer development following colonic resection. The prognosis has also been disconcerting as disease is often detected late and mortality has been significant[8]. Even though epithelial dysplasia (thought to be a neoplastic intestinal marker for later or concomitant invasive cancer) has been defined in both small and large intestine supporting the concept of a dysplasia-carcinoma sequence in Crohn's disease, most cases of intestinal cancer, even in large tertiary care centers, are discovered incidentally at the time of surgical resection for treatment of the Crohn's disease.

FUTURE RESEARCH

To date, specific recommendations for screening and surveillance colonoscopy, even in chronic and extensive Crohn's colitis, have been supported by only very limited data in older patients[18]. Indeed, it can be anticipated that the focal nature of dysplasia (as occurs even in extensive ulcerative colitis) may make detection of dysplasia even more difficult in Crohn's disease, a disorder generally characterized by patchy or segmental inflammatory change. As a result, establishing a productive screening program for epithelial dysplasia or focal cancers in Crohn's disease can be expected to prove difficult, even with dye staining or the intriguing potential of newly evolving technologies, such as confocal microendoscopy. Even in extensive colitis, a recent report found that colonoscopy surveillance may not improve survival, but only detect cancers at an earlier stage[19]. Other tools that might predict later cancer development in Crohn's disease, employing molecular or genetically-based markers[20], are still desperately needed and should be aggressively pursued.

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