

# ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Diseases

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## Cancer Screening and Prevention in Crohn's Disease Patients

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**G&H** Could you describe the link between Crohn's disease, inflammation, dysplasia, and colorectal cancer?

**BL** We have much information on the development of dysplasia in ulcerative colitis (UC) patients and some of this information can be extended to Crohn's disease. We know that dysplasia is very much related to extent of disease, in that patients with pancolitis have a higher risk of dysplasia than those with limited disease. We also know that long duration of the disease is a major risk factor, as is older age at symptom onset. Another risk factor is the presence of primary sclerosing cholangitis (PSC). Patients with PSC have at least three times the risk of developing dysplasia and cancer as UC patients without PSC. More recently, inflammation has been purported to be a risk factor. Patients with chronic inflammation have a higher risk of developing dysplasia and cancer. This information needs to be considered when deciding how often to survey patients in a cancer surveillance program.

We have very little information about the direct risk factors for dysplasia related to Crohn's disease. However, we believe that the "risk per inflamed segment of colon" is most likely the same for Crohn's colitis patients as it is for UC patients. Most often, patients with Crohn's disease have less colonic involvement than patients with UC. Therefore, their overall colorectal cancer incidence is probably much lower than that associated with UC. However, if a Crohn's disease patient has extensive disease of the colon, their risk approaches that of a UC patient. Although other risk factors have not been studied specifically in Crohn's disease, it is almost certain that factors

like long duration of disease, PSC, and chronic inflammation also confer greater risk for dysplasia and cancer in Crohn's patients.

**G&H** What are the benefits of colonoscopic biopsy cancer surveillance in Crohn's disease patients?

**BL** The main advantage of cancer surveillance is that it may decrease the mortality associated with colorectal cancer and, because of this benefit, surveillance should be offered to every eligible patient. In current practice, the risks of colonoscopy are very low. The risk of perforation from the procedure is exceedingly low and should not be a factor in the decision to undergo surveillance colonoscopy, because the likelihood of benefit is much greater.

Further, even though a colonoscopy test is expensive, the demonstrated ratio of cost to effectiveness is similar when compared to screening programs for breast, cervical, and prostate cancers. Cost effectiveness analyses in UC have shown an incremental cost-effectiveness ratio of approximately \$100,000 per life-year saved. In our society, this is a reasonable number and one that can be extended to Crohn's disease patients, based on similar cancer risk per colonic segment. However, Crohn's disease patients with very limited colonic Crohn's disease do not need to be entered into a cancer surveillance program.

**G&H** What are the disadvantages of this type of surveillance in Crohn's patients?

**BL** One concern specific to Crohn's disease is that dysplasia may not be as extensive as in UC. In cancer surveillance colonoscopy, random biopsies are taken throughout the colon. In UC patients, if dysplasia is present in one area, it is likely to be present in other areas as well. Therefore, random biopsies will likely detect any existing dysplasia in most UC patients. In patients with Crohn's disease, dysplasia tends to be much more localized. It is easier to miss a dysplastic lesion in a Crohn's disease patient.

Another concern in Crohn's disease cancer surveillance is that if dysplasia is detected, there are no definite recommendations regarding how to proceed. UC patients with dysplasia are often advised to undergo a total proctocolectomy. However, in Crohn's disease, this type of

surgery may not be necessary. Dysplasia and/or cancer in Crohn's patients are most likely limited to a certain region of the colon and a segmental colectomy may be more appropriate for them. However, this approach has not been studied in any formalized manner.

### **G&H** How often should at-risk Crohn's disease patients undergo screening?

**BL** We know that incidence of dysplasia and cancer increase with increasing duration of disease; therefore, frequent colonoscopy is not required in the early years of the disease, but the length of the interval between examinations should decrease as the disease progresses. For patients who have disease anywhere from 8–15 years, I recommend surveillance colonoscopies approximately every 3 years. For 15–25 years of disease, I recommend surveillance colonoscopy every 2 years. For disease duration beyond 25 years, I recommend surveillance colonoscopy annually. In addition, those patients with heightened risk due to cofactors such as the presence of PSC should have a colonoscopy every year.

### **G&H** How does the presence of active inflammation in Crohn's disease affect the screening process for colorectal cancer?

**BL** We do our best to perform surveillance colonoscopy with extensive biopsy in patients with inactive disease, because when biopsies are taken in areas of disease activity the pathologist is not able to read it for definite dysplasia. Most often, a pathologist will return an "indefinite" reading from biopsies of inflamed tissue. Patients with indefinite dysplasia need to be restudied when their inflammation is better controlled. My recommendation is to treat these patients with anti-inflammatory agents for a period of time and then perform another surveillance examination.

### **G&H** How accurately do patients perceive the risk of cancer related to Crohn's disease?

**BL** In the current era, patients are very well informed about their disease. They understand the importance of their cancer risk, not just from the disease itself but also from some of the medications used to treat it. I believe that their overall understanding is realistic and they often ask their doctors important questions related to cancer risk. There is no need for doctors to either minimize risks or to be overly pessimistic; there is a cancer risk that needs to be addressed and the appropriate cancer surveillance colonoscopy needs to be recommended and performed.

### **G&H** Do you have an overall strategy for targeting Crohn's disease patients at high risk?

**BL** Screening efforts should be concentrated in patients with extensive Crohn's colitis, disease involving at least one third of the colon. Any patient with extensive colitis should have a cancer surveillance colonoscopy every three years in the early stage of the disease. If I find confirmed low-grade dysplasia, high-grade dysplasia, or cancer, I will send the patient to surgery. One of the options, depending on the extent of disease, would be segmental resection. Again, a total proctocolectomy is not always necessary in patients with Crohn's disease who have dysplasia.

### **G&H** Are there any other therapies that can be coupled with screening to prevent cancer in Crohn's patients?

**BL** In terms of cancer chemoprevention, there are certain drugs that have been shown to minimize the risk of cancer in patients with ulcerative colitis. The 5-aminosalicylic acid (5-ASA) products provide a small but significant decrease in risk. Folic acid as a vitamin supplement also decreases the risk of cancer, as do calcium supplements. In patients with PSC, ursodioxycolic acid will decrease the risk of colorectal cancer.

However, none of these agents totally eliminates the risk of colorectal cancer. At-risk patients still need to be enrolled in a cancer colonoscopy surveillance program. I typically recommend 5-ASA therapy and supplemental folic acid and calcium to my patients with inflammatory bowel disease in order to minimize risk.

### **Suggested Reading**

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