The issue of dysplasia within the setting of chronic colitis is rapidly evolving, and more aggressive endoscopic management and surveillance is clearly being suggested in selected cases (1-3). With the advent of more effective therapies such as tumour necrosis factor inhibitors, it has been suggested that some patients are likely to be managed with medical therapy for longer time periods (before colectomy), possibly resulting in an increased lifetime risk of dysplasia due to the retained colon. Although supportive data for this hypothesis are lacking, there are several new studies that have improved our knowledge in these areas and may lead to increased endoscopic management of certain colonic lesions in this setting.

The cumulative risk of colon cancer in patients with colitis has been an epidemiological debate for many years (4-6). In ulcerative colitis (UC), Eaden et al (7,8) demonstrated a risk of almost 20% at 25 years, giving support to the possibility of early prophylactic colectomy. Others have argued that in an era of more effective medical therapy and more intense patient monitoring, this number may be decreased because inflammation is one of the key risk factors for dysplasia, and by treating the colitis more aggressively, dysplasia risks may be decreased although duration of disease is increased.

RISK-STRATIFYING PATIENTS WITH INFLAMMATORY BOWEL DISEASE

There are many other risk factors to consider in the setting of UC as opposed simply to duration of disease and inflammation. Patients with a family history of disease have at least a twofold increased risk of cancer. Young age of onset (independent of duration of disease) has also been demonstrated to increase the risk. Finally, the extent of disease (ie, risk similar to general population if less than 35 cm of the colon from the anal verge is involved) is critical in determining the risk stratification of patients (8,9). Perhaps the biggest risk of colon cancer in patients with inflammatory bowel disease is related to codiagnosis of primary sclerosing cholangitis (PSC) (10-13). At 25 years, these patients may have a 50% risk of developing colonic cancer and, therefore, early, aggressive surveillance protocols have been recommended.

For colitis in the setting of Crohn’s disease (CD), the data are much more recent. One of the problems with all studies in colitis and colorectal cancer risk relates to the documentation of affected bowel. For both UC and CD, the extent of affected colon is considered a risk factor; however, often a clear history of pancolitis or even documentation of the extent of disease is only inferred but not endoscopically documented. This makes it difficult, at times, to risk-stratify the patients appropriately. In CD patients who have at least one-third of the colon affected, a recent study (14) demonstrated a 25% risk of developing dysplasia over a 10-year period. This study involved 259 patients and documented seven cancers and six patients with high-grade dysplasia (HGD). A meta-analysis (15) has reviewed all appropriate studies published before 2006 and determined that there is no increased risk of colon cancer in patients with isolated ileal disease; however, individuals with significant colonic disease and ‘all comers’ with CD had an increased risk (RR 2.5 and 4.5, respectively).

RECOMMENDATIONS AND BIOPSY PROTOCOLS

With the risk factors noted above, both the Crohn’s and Colitis Foundation of America and the British Society of Gastroenterology (BSG) have suggested guidelines for screening (7,16). Both suggest beginning surveillance at eight years of disease in affected patients, with more intensive and earlier surveillance in individuals with concomitant PSC. The BSG has recommended a ‘staged’ surveillance pattern depending on how long the patient has been affected by disease. The frequency of surveillance in their recommendations is every third year during the second decade of disease, every second year during the third decade of disease and every year during the fourth decade of disease. Additionally, the BSG has suggested that initiation of surveillance in patients with isolated left-sided disease is not necessary until the individual has been affected for at least 15 to 20 years.

Although several chemotherapeutic agents (17) (eg, folic acid [18-20]), ursoecholic acid [21,22], nonsteroidal antiinflammatory drugs and 5-aminosaliclyc acid compounds [23-25]) have demonstrated benefit in decreasing risk from dysplasia, most investigators rely heavily on endoscopic biopsy protocols for their reassurance. Typically, four-quadrant biopsies, labelled geographically every 10 cm throughout the colon (minimum of 32 biopsies), is recommended. Because the rectum may be the area at highest risk, more aggressive biopsies of this area are often suggested.

Despite the fact that dysplasia protocols seem to be supported verbally by most endoscopists, the actual practice of the rigorous recommendations is uncommonly followed (26-28). The reasons for this are unclear but increased endoscopic duration may play a critical role. In a similar manner to polyp detection rate and colonoscope withdrawal in the general screening population, it...
has been demonstrated that detection rates of flat dysplasias increase with longer procedure times.

**WHAT TO DO WITH DYSPLASIA?**

There are many terms that have become popular regarding this issue that often confuse the endoscopist. Most importantly, it is critical that the endoscopist describe the areas of affected inflammation and then describe the lesion. Polypoid lesions have been termed disease-associated lesion or mass (DALM) if they reside within an area of affected bowel and are believed to be caused by the inflammation (ie, dysplasia). An adenomatous-like lesion is a polyp (adenomatous) that occurs within the area of affected colon but is believed to be a sporadic lesion. The endoscopic appearance of the lesion is how one distinguishes between these two types of polyps – meaning that the expertise of the endoscopist is of the utmost importance in making this clinical diagnosis. A sporadic adenoma is a term used to describe a polyp outside the area of inflammation that was not caused by the underlying colitis and has the appearance of a typical polyp.

The difference in these terms is critical because many will argue that DALM is a term that typically has denoted a field defect – often associated with many other areas of dysplasia – in which case a colectomy is mandated. The other lesions described may be sporadic and their removal may simply consist of endoscopic polypectomy.

If one finds a flat, high-grade dysplastic lesion in the colon (usually on random biopsy), the recommendation would be colectomy. If a typical-appearing polypoid lesion is seen and is a discreet polyp without other evidence of dysplasia (biopsies suggested around the polypoid site), and it is completely removed, repeat colonoscopy in three to six months to search for other evidence of dysplasia (which, if present, colectomy would be recommended) could be considered.

If the lesion is flat with low-grade dysplasia, one can either suggest colectomy (especially if multifocal) or repeat the colonoscopy in three to six months to look for other evidence of dysplasia (which, if present, colectomy would be recommended).

If biopsies are indeterminate, repeat endoscopic examinations with appropriate biopsy protocol is recommended (six months later if probably positive indeterminate and one year if probably negative indeterminate). For no dysplasia, repeat colonoscopy with biopsy protocol in one to two years is recommended.

Although these recommendations are widely used, it must be recognized that many other issues can arise that may help guide the physician. The presence of multiple pseudopolyps may limit the ability to survey the colon accurately. The presence of a new luminal stricture in a colon with longstanding colitis is a recommendation for a colectomy in almost all circumstances. Additionally, if the patient has more difficult inflammation to manage, they may be more receptive to colectomy. Finally, some patients tend to become somewhat obsessed with the possibility of developing colon cancer; consequently, their quality of life (with the colon in situ) is dramatically reduced due to their overall concern for an adverse outcome.

**MORE CONSERVATIVE MANAGEMENT?**

The original study by Blackstone et al (29) in 1981 that followed 112 patients with UC, of which 12 developed DALM lesions, eventually reported that seven of these patients had developed colon cancer. This study was convincing regarding the inherent risk of leaving these colons in situ in this particular group of patients. However, this was a high-risk group of patients in whom typical tubular adenomas less than 1 cm in size were not considered DALMs.

Subsequently, a more generous approach with dysplasia seemed to be advocated and, therefore, other investigators have not found this high rate of cancer (30). Several studies have suggested a more conservative approach in the setting of typical-appearing adenomas found in colitis (31). In 1999, Rubin et al (32) followed 48 patients with chronic colitis who had adenomas removed (none were flat, none had dysplasia elsewhere in the colon) and found that over a four-year time period none had developed colon cancer but 48% had recurrent polyps. In 2004, Odze et al (33) described 34 patients with UC who had adenomas endoscopically removed and followed for almost seven years. Twenty patients developed recurrent adenomas, one had flat adenoma and one patient with PSC developed colon cancer. More recently, Blonski et al (1) followed 30 patients without flat adenomas (nine of them HGD). Three patients underwent colectomy and six were followed conservatively for longer than six years; there were no cancers that developed.

Ideally, differentiation of higher risk lesions would be easy to perform. Chromosomal changes and microsatellite instability (34-39) are have been assessed with some promising findings; however, more research in this area is required (40). A more recent evaluation (41) that used confocal microscopy to identify adenomatous-like lesions versus DALMs is encouraging for its sensitivity to differentiate these lesions. Unfortunately, confocal microscopy is presently not widely available.

**METHODS TO ENHANCE DETECTION OF DYSPLASIA IN COLITIS**

Random biopsy protocols have been documented to take longer than standard endoscopic procedures; ideally, methods to target biopsies could enhance the diagnostic yield while limiting the duration of the procedure. Both indigo carmine and methylene blue (42), combined with magnification endoscopy (43,44), have been shown in ‘back-to-back’ tandem endoscopies (conventional versus chromoendoscopy) to improve detection of dysplasia while limiting the number of biopsies.

Narrow band imaging (NBI) (45,46) has also been evaluated in a similar manner, with lesion patterns described (47). In a subsequent study that used both conventional endoscopy and NBI, the benefit was not realized – some lesions were recognized by the conventional method that were not recognized by NBI, thereby suggesting that both methods would have to be used for the procedure.

**SUMMARY**

There is an increased risk of colon cancer in patients with colitis, which affects both UC and CD. Biopsy protocols have been suggested at regular intervals to assess for findings of dysplasia. The assessment of dysplasia can be enhanced by the use of chromoendoscopy, which allows targeting the biopsies while increasing the diagnostic yield. Standard conventional white light biopsy continues to be the technique most commonly used; however, other imaging modalities such as NBI are gaining acceptance and further study may enhance our understanding of how to use them properly to maximize their benefit.
REFERENCES


19. Velayos FS, Terdiman JP, Walsh JM. Effect of 5-aminosalicylate use