COLORECTAL CANCER SCREENING

Guidelines for screening and surveillance of asymptomatic colorectal cancer in patients with inflammatory bowel disease

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Patients with ulcerative colitis (UC) are at increased risk of colorectal carcinoma.[1][2] Many clinicians practice colonoscopic surveillance in these patients in the hope of detecting dysplasia or an early cancer at a surgically curable stage. However, a recent audit of gastroenterologists showed such surveillance to be disorganised and inconsistent.[3] Much debate surrounds the efficacy and cost effectiveness of surveillance programmes in UC[4–6] because they were introduced without benefit of randomised controlled trials.

The following guidelines should bring uniformity to the process and be of help to both surgeons and physicians. The colorectal cancer risk in patients with colonic Crohn's disease is similar to that in UC[7][8] and thus the guidelines for UC should be equally applicable to such patients with Crohn's disease.

EXECUTIVE SUMMARY

1 Surveillance colonoscopies should be performed when the disease is in remission. **(Recommendation Grade: C).**

2 All patients should have a screening colonoscopy after 8–10 years that will also clarify disease extent. **(Recommendation Grade: C).**

3 Regular surveillance should begin after 8–10 years (from onset of symptoms) for pancolitis and after 15–20 years for left sided disease. (Recommendation Grade: C).

4 As the risk of cancer increases exponentially with time, there should be a decrease in the screening interval with increasing disease duration. For patients with pancolitis, in the second decade of disease a colonoscopy should be conducted every three years, every two years in the third decade, and yearly by the fourth decade of disease. **(Recommendation Grade: C).**

5 Two to four random biopsy specimens every 10 cm from the entire colon should be taken with additional samples of suspicious areas. **(Recommendation Grade: C).**

6 Patients with primary sclerosing cholangitis (including those with an orthotopic liver transplant) represent a subgroup at higher risk of cancer and they should have annual colonoscopy. **(Recommendation Grade: C).**

EPIDEMIOLOGY OF COLORECTAL CANCER RISK

Although it is clear long term UC carries a colorectal cancer risk, its magnitude has been difficult to estimate. Cancer is rarely encountered when disease duration is less than 8–10 years, but thereafter the risk rises at approximately 0.5% to 1.0% per year.[9] Most cancers arise in pancolitis and there is general agreement that there is little or no increased risk associated with proctitis while left sided colitis carries an intermediate cancer risk.[10][11] Patients with onset of colitis early in life are thought to have an increased risk compared with older patients.[1][10][11] A comprehensive meta-analysis of all published studies reporting a colonic cancer risk in UC has recently been presented[12] and shows the risk for *any* patient with colitis to be 2% at 10 years, 8% at 20 years, and 18% after 30 years of disease.

INTERVENTION

Surveillance is best performed during remission to eliminate the difficulty of differentiating reactive change from dysplasia on histological biopsy.[13] *All* patients with UC should be advised to have a screening colonoscopy 8–10 years after onset of symptoms (not date of diagnosis) to check disease extent. Periodic colonoscopy should begin 8 to 10 years after disease onset for extensive colitis and 15 to 20 years for left sided disease.[14] As the risk of cancer increases exponentially with time, a schedule with a gradual decrease in the screening interval should be adopted.[15] In the second decade a colonoscopy should be conducted every three years, every two years in the third decade of disease, and yearly by the fourth decade.[15]

Surveillance should start in childhood if necessary. For example, a child who presents with total colitis aged 5 should start to undergo cancer surveillance aged 15. There is no evidence in the literature recommending an upper age limit at which surveillance should be terminated. Each case has to be considered on its own merits and comorbidity taken into account. It may be reasonable to discontinue regular colonoscopy once a patient reaches 70 years or when comorbidity makes colonoscopy (or possible subsequent colectomy) distressing, of unacceptably high risk, or impossible. However, this decision should be taken after consultation with the patient.

It may be argued that colonoscopy is not necessary in a patient with left sided disease. However, disease can extend and if these patients only have a flexible sigmoidoscopy any extension of disease may be missed. Therefore, although there is no evidence, it is recommended that such patients should have a colonoscopy every five years with a flexible sigmoidoscopy in the interim years.

During colonoscopy a full examination should be performed with careful inspection of the entire mucosa and random biopsy specimens should be taken at regular intervals. The more samples taken, the better will be the sensitivity for detecting dysplasia. However, the more samples taken, the higher will be the pathology costs, the longer will be the time (and the associated costs) of the procedure, and the greater will be the morbidity of the colonoscopy. While it has not been studied, it seems a reasonable trade off between sensitivity and cost/morbidity to sample the colon with two to four biopsy specimens taken from each 10 cm of the colon.[16] Some studies report that more than 50% of neoplasia associated with UC develops in the distal colon.[17–19] These authors advocate additional sampling of the rectosigmoid area with the goal of

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Abbreviations: UC, ulcerative colitis; DALM, dysplasia associated lesions or masses; HGD, high grade dysplasia; LGD, low grade dysplasia

improving the diagnostic yield from random biopsy specimens.[17] Particular attention should be paid to raised lesions (dysplasia associated lesions or masses (DALMs)) as such areas may harbour dysplasia or carcinoma.[20 21] Extra specimens should also be taken from irregular plaques, unusual ulcers, or strictures.[20–22]

Primary sclerosing cholangitis

Several studies have indicated those patients with concomitant primary sclerosing cholangitis (PSC) are at a higher risk of colorectal neoplasia.[23–25] The absolute cumulative risk of cancer or dysplasia in this subset of patients has been estimated to be 9% after 10 years, 31% after 20 years, and 50% after 25 years of colitis.[26] Patients with PSC often have quiescent colitis and so it is difficult estimating the exact onset of UC in this group. For the above reasons it is recommended such patients should have annual surveillance colonoscopy.

Primary sclerosing cholangitis after orthotopic liver transplantation

An increased risk of colorectal cancer after orthotopic liver transplantation in patients with PSC and UC has also been reported with an incidence of approximately 1% per person per year.[27] The risk is therefore clinically important and thus annual surveillance colonoscopy is recommended in the post-transplant period.

Dysplasia as a predictor of cancer

Dysplasia is generally recognised to be premalignant but the likelihood of progression to cancer is difficult to predict. In a literature review Bernstein *et al* analysed 1225 patients who had undergone colonoscopic surveillance.[28] If a DALM was found at colonoscopy, immediate colectomy revealed cancer in 43% of patients regardless of the grade of dysplasia in the DALM. When high grade dysplasia (HGD) in *flat* mucosa was the initial discovery, immediate surgery revealed carcinoma in 42% to 67% of the colectomy specimens.[28 29] Thus, whenever a DALM or HGD is identified and confirmed by two expert gastrointestinal pathologists, this is a strong indication for colectomy.[20] However, recent studies have highlighted the possibility of performing a colonoscopic polypectomy with subsequent increased surveillance (every six months) for patients who develop a pedunculated adenoma-like DALM (either within or outside areas of colitis) and in whom no other areas of flat dysplasia are recognised.[30 31] This alternative management plan may be offered to patients but it should be remembered that the polyp (DALM) may still be the first warning sign of cancer and colectomy should be considered.

In Bernstein's paper 29% of patients with low grade dysplasia (LGD) showed progression at some time to HGD, DALM, or cancer.[28] Moreover, the St Mark's Hospital surveillance study indicates the five year predictive value for HGD or cancer in patients with LGD is a troubling 54%.[29] Therefore the presence of LGD, even in flat mucosa, should be considered just as much an indication for colectomy as finding HGD or a DALM without waiting for a confirmatory colonoscopy.[13 16 19] A second experienced pathologist should confirm any ambiguity in the histological results. If a patient is reluctant to undergo colectomy, they should be aware of their increased risk for carcinoma and will *at least* require increased surveillance. Colonoscopy should be conducted every six months until two consecutive colonoscopies are negative for any level of dysplasia thereafter.

COST AND BENEFITS

UC has has an incidence varying from 6–15 per 100 000 population/year[32 33] and the prevalence is approximately 12 times this figure. Thus in a community of 300 000 one would expect 30 new cases per year and a prevalence of 360 patients. A previous study conducted in Leicestershire[34] estimated that 40% of patients with UC will have total/subtotal colitis and 20% will have left sided disease. This correlates with 144 patients having pancolitis and 72 having left sided disease in a population of 300 000. In the study by Probert *et al* 61% of the population had disease for more than eight years and 14% had disease for more than 15 years.[34] This would mean that there would be approximately 88 patients with pancolitis of greater than eight years duration and 10 patients with left sided disease of more than 15 years duration—that is, the period when regular surveillance in these two groups should begin. The cost of a colonoscopy is estimated as £150 (as per other BSG guidelines). If an average of one colonoscopy every two years is assumed for each group, a gastroenterologist would perform 44 colonoscopies for pancolitis and five for left sided disease. The cost of surveillance would therefore be (44×£150) + (5×£150) =£7350 per year. The cost of surveillance in Crohn's colitis based on data from another study from Leicester[35] (calculated in the same way as above) would be £2250 per year.

The Leeds group have assessed the cost effectiveness of surveillance in UC by auditing 12 published surveillance programmes.[36] Using stringent criteria they concluded only 12% of enrolled patients could be counted as surveillance successes. Other studies are more positive concerning the benefits of surveillance with respect to mortality. Data from the 18 year surveillance programme in the USA by Choi *et al* demonstrated that cancer was detected at an early stage in 80% of surveyed patients, compared with only 41% non-surveyed UC patients.[37] The overall five year survival rate was 77% for the surveillance group compared with only 36% for the control group (p<0.03). A case-control study by Karlen *et al* has also found that surveillance may reduce colorectal cancer mortality.[38]

The hazard rate of surveillance colonoscopy with multiple biopsies seems to be low.[39] In the analysis by Koobatian and Choi, the overall complication rate associated with surveillance colonoscopy was 0.26%. British experience has been similar with no incidence of complication recorded during 811 surveillance colonoscopies.[40] Thus the hazard rate seems comparable to diagnostic colonoscopy.[39]

Patients should be encouraged to take their aminosalycylate medication as the recent literature suggests that regular consumption of 5-ASA compounds may reduce their colorectal cancer risk.[41–43]

Patients need to be aware that surveillance cannot guarantee a reduced cancer risk but rather offers a reasonable chance of detecting precancer or symptomless cancer.[44] This should be made clear to patients along with an estimate of their individual risk so that those who are unenthusiastic about surveillance can make an informed decision.

RECOMMENDATIONS FOR AUDIT

The attendance of patients at colonoscopy will need to be audited in approximately five years time. This will permit time for implementation of surveillance programmes across the country and will give some indication of whether patients are complying with the surveillance regimen. Ideally computerised systems should be used that automatically send defaulters a further appointment. We know defaulters are more likely to develop colorectal cancer and for their cancers to be identified at a later stage.[45] The follow up of such patients is critical to the success of any surveillance programme.

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