Surveillance in ulcerative colitis: burdens and benefit

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SUMMARY A review of all patients with ulcerative colitis in one health district between 1975-84 revealed an incidence and prevalence of 7.1 and 84/100 000 population respectively. One hundred and ninety five new patients were diagnosed and 313 patients seen and followed up in the clinic for 1168 patient years. None of these patients died from colitis or a complication. On routine colonoscopy three cases had high grade dysplasia and two asymptomatic carcinomas (Duke's stage A and B). Eighty four patients were known to have ulcerative colitis, but were lost to follow up from the hospital clinic; the total time they were not under hospital surveillance was 315 patient years. At the end of the study these patients were contacted or clinical details obtained from their general practitioners. Five of these patients subsequently presented with symptomatic carcinomas (two Duke's B, one Duke's C and two with metastases); three of these five patients have died from their tumours. Of 48 patients thought to have only mild colitis on initial investigation 21 (43%) had substantial colitis (and two carcinomas) on colonoscopy after eight years of disease. Therefore, patients with apparently distal colitis should be followed in the clinic as well as those with known extensive colitis. For a surveillance programme in a district general hospital, eight patients per 100 000 population need to be seen weekly, 12 colonoscopies/100 000 population need to be carried out annually and the cost for each carcinoma detected is approximately £6015.

The risk of colonic cancer in patients with ulcerative colitis is well established,¹⁻⁴ but estimates of its incidence vary.^{5,6} Most reports come from teaching centres, where referral patterns may bias the figures. A report from private practice in the USA suggests that the incidence of carcinoma may have been over estimated.⁷ We know of no studies from district hospitals in this country.

Epithelial dysplasia can be found in 43-87% of patients who develop carcinomas,^{4,8} so the majority of cancers can be detected early or prevented by careful surveillance. Therefore, regular surveillance of patients with ulcerative colitis is recommended. It is unknown if all patients should be reviewed in the clinic, or only those with extensive disease. Many clinics do discharge those with distal disease as the risk of progressing to extensive disease after 10 years is only 6-7% and the risk of surgery is 2-5%.^{9,10} There may be an increased risk of carcinoma, however, in left sided colitis after 20-30 years.¹¹ Most authors

recommend regular rectal biopsy and colonoscopy with multiple biopsies in all patients with ulcerative colitis. It has not been established yet how often these examinations are needed, but most suggest colonoscopy after eight to 10 years of disease and subsequently one to three yearly in those with extensive disease.^{4,12-17}

The workload involved in these recommendations is unknown and they are based on data largely from teaching hospitals. Referral patterns to teaching centres may bias the sample by selecting those with severe or extensive disease liable to develop carcinomas. The incidence of ulcerative colitis is known,¹⁸ but the need for colonoscopy cannot be calculated from the prevalence of ulcerative colitis alone. It is necessary to know the number of patients with substantial ulcerative colitis of eight to 10 years' duration, but we know of no studies that give these data for Britain.

We have reviewed all the patients with ulcerative colitis seen in one health district over a 10 year period. The aim was to discover whether surveillance was justified in a district general hospital, firstly

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by finding if there are appreciable numbers of carcinomas in unselected patients with ulcerative colitis in a district general hospital. In addition to see if regular patient follow up and surveillance affected the outcome, the fate of those patients followed in the clinic was compared with that of those patients lost to follow up. The cost and workload of regular review and colonoscopic surveillance in patients with ulcerative colitis has been calculated.

Methods

All the patients with either ulcerative colitis or indeterminate colitis seen in the health district between 1 January 1975 and 31 December 1984 were traced from a review of all rectal biopsies and large bowel resections undertaken during the 10 year period. It is standard practice for all patients with suspected inflammatory bowel disease in this health district (population 274000) to have a rectal biopsy taken as part of the routine diagnostic workup. The records were checked against physicians' disease indexes and the hospital diagnostic index. Only those patients resident within the boundaries of the health district were included. The details of investigations, management and complications were recorded together with the date of diagnosis. The duration of colitis was calculated from the date of firm diagnosis, although some patients had symptoms suggestive of previous undiagnosed disease. With one exception diagnosis was made on referral to hospital. New patients consisted only of those patients diagnosed in the district. The number of complete years that patients were symptom free was assessed. In the year after the study period attempts were made to contact all patients lost to follow up. The number of acute attacks, incidence of colonic cancer and mortality in those seen in the clinic or with a first attack was compared with those lost to follow up.

The diagnosis of ulcerative colitis was accepted on the basis of a consistent clinical history, characteristic sigmoidoscopic appearances, histological changes in the rectal biopsy and radiological investigations. Patients with definite Crohn's colitis were excluded but those with colitis indeterminate between Crohn's and ulcerative colitis were included. Distal colitis indicates that the upper limit of the colitis can be seen at sigmoidoscopy, mild colitis indicates that macroscopic changes are visible on sigmoidoscopy but with a normal barium enema. When the colitis is said to be substantial we mean that the colitis extends beyond the splenic flexure, total colitis indicates caecal involvement.

From 1979 a policy of routine colonoscopy was introduced. All willing patients in whom the duration of colitis was at least eight years underwent col-

onoscopy. Two biopsies were taken from each of the following sites: caecum, hepatic flexure, midtransverse colon, splenic flexure, sigmoid colon and rectum. The extent of the disease was assessed on the macroscopic appearances of the colonic mucosa and on the histological changes in the biopsy specimens. Dysplasia was classified as low grade or high grade.¹⁹ Thereafter, all patients with extensive disease were seen six monthly with routine rectal biopsies. Repeat colonoscopy was undertaken every two years or when the rectal biopsy showed dysplastic changes.

STATISTICAL ANALYSIS

Student's *t* test for unpaired samples, χ^2 and Fisher's exact test were used where appropriate.

Results

PATIENTS

Three hundred and thirteen patients with ulcerative colitis or indeterminate colitis resident within the district were seen between January 1975 and December 1984. Three hundred and seven patients were traced by reviewing the histology reports of 978 rectal biopsies. A further six were found on reviewing physicians' diseases indexes but no additional patients were found in the hospital diagnostic index. Twenty two patients had a final diagnosis of indeterminate colitis. A further 11 patients initially diagnosed as indeterminate colitis were shown on histological review to have the features of ulcerative colitis and were reclassified. Four patients with an initial diagnosis of ulcerative colitis were reclassified as indeterminate colitis, one following colectomy and three following further endoscopy and biopsy.

The extent of the disease was established at diagnosis by barium enema in 259 patients, by barium enema and colonoscopy in 30 and by sigmoidoscopy alone in 17. The remaining seven patients all presen-

Fig. 1 Duration and extent of colitis in patients followed in the clinic at the end of the study period (1984).

Fig. 2 Duration and extent of colitis in all patients in the district at the end of the study period (1984).

ted acutely and underwent surgery without contrast examination. Only a small proportion of the patients had their disease for more than eight years (Figs 1 and 2). The majority of patients, therefore, had no further investigations after diagnosis.

INCIDENCE AND PREVALENCE

One hundred and ninety five new patients (114 men) presented during the 10 year period: annual in-

cidence 7.1/100000 population. The average age was 47 years (range 8–93 years). Three hundred and thirteen patients were seen, altogether, and the prevalence at the end of the study (1984) was 84/100000. Figure 1 shows the duration of colitis and those with substantial disease followed in the clinic at the end of the study period. The same information for all patients (both those seen in the clinic and those lost to follow up) is shown in Figure 2.

At the end of the study period 181 patients were still being followed in the clinic. Twenty five had been discharged after proctocolectomy. Thirteen had died, 36 had moved from the district and eight had been referred to hospitals outside the district. Fifty had been lost from follow up; 37 were successfully contacted after the end of the study period and agreed to attend the clinic. Thirteen are still in the care of their general practitioners, of whom five refused to attend the hospital and eight were considered too unwell to come to the hospital: two because of multiple sclerosis and six because of age.

OUTCOME – PATIENTS FOLLOWED IN CLINIC

New patients as well as those followed regularly in the clinic are included in this group. The details are given in Table 1. Ninety four patients had 112

Table 1 Outcome in new patients and those seen in clinic compared with patients not followed up

	New/regular follow up	Not followed up	Probability
Patients (n)	313*	84*	—
Women (n)	153 (49%)	39 (47%)	
Age end study (yrs)	51 (range 12–93)	54 (range 19–84)	
Patient years	1168	315	—
Symptom free years	797 (68%)	271 (86%)	p<0.001§
Substantial colitis at diagnosis no	78	5	
Duration >8 yrs at end of study	78	26	
Systemic steroids:			
Courses (n)	298	16	—
Patients (n)	136 (44%)	14 (19%)	p<0.001§
Courses/patient mean (SE)	2.2 (0.2)	1.1 (0.1)	p<0.001
Acute admissions	112 (94 patients)	2 (2 patients)	p<0.001§
Toxic megacolon	5	2	—
Surgery			
Emergency	17	2	N/S§
After acute attack	9	0	
Elective	5	0	
Patients with carcinomas			
Dysplasia	3	0}	
Duke's A	1†	0}	
Duke's B	1‡	2}	p=0.02¶
Duke's C	0	1}	
Distant spread	0	2}	

*Eighty two patients were followed up at sometime and so appear in both groups. Two patients had surgery on presentation with carcinomas of the colon and so were never followed in the clinic; †Patient with 2 Duke's A tumours; ‡Patient with 1 Duke's A and 1 Duke's B tumour; §χ²; ||Student's *t* test; ¶Fisher's exact test.

admissions for acute colitis. There were four admissions with acute colitis/100000 population/year. The details are given in a separate paper.²⁰ No patient followed in the clinic died from ulcerative colitis or its complications.

Routine colonoscopy was done in 52 patients: two because of dysplasia in rectal biopsies and 50 after eight to 10 years of disease.

Three patients had high grade dysplasia in colonoscopic biopsies, but no carcinomas were found following surgery (Table 2). One was symptom free, and two had persistent ill health. Two asymptomatic patients were found to have carcinomas on routine colonoscopy, and on examination of the resected specimen one had two Duke's A carcinomas and one a Duke's A and a Duke's B. They are both alive and well two and three years after surgery.

PATIENTS NOT FOLLOWED IN THE CLINIC

We have included in this group all patients who had a diagnosis of indeterminate colitis or ulcerative colitis but who were not regularly seen at a hospital. Eighty two had been seen in the district before being lost to follow up, one had been diagnosed in another district, and seen in this district only before the beginning of the study period. Another patient had had diarrhoea with bleeding for over 10 years diagnosed as ulcerative colitis by her general practitioner but she refused investigation treatment or hospital referral until she developed a carcinoma. Fifty patients were contacted after the end of the study period and details of their progress discovered then; and a further 34 were lost to follow up for at least one year but were referred back to the clinic before the end of the study period.

A total of 84 patients were not followed for 315

patient years. They were symptom free for 271 (86%) and required 16 courses of systemic steroids both significantly different from those followed up. With one exception the steroids were prescribed when they presented again to the clinic because of symptoms. Two patients presented late with toxic megacolon, but there were no other admissions with acute attacks. Five patients presented with carcinoma, however (Table 1). Two with Duke's B tumours still survive. Three have died. Two with metastases at laparotomy died of the carcinoma soon after palliative surgery to relieve obstruction. One had a Duke's C tumour at laparotomy but died of metastases after three years.

Thirty seven patients who had been lost to follow up agreed to attend the clinic at the end of the study period. Three required steroids for acute attacks, but they had not seen a doctor before they were contacted. One was found to have a symptomless rectal stricture. Colonoscopy was carried out on eight who had had colitis for more than eight years. Of six who were thought to have mild disease at presentation, three had extensive disease on colonoscopy. Two patients were found to have carcinomas of the colon, and details are given in Table 2. As they were diagnosed after the study period they are not included in the statistical comparison between the groups followed and not followed in the clinic.

INCIDENCE OF CARCINOMA OF THE COLON

The overall incidence of carcinoma of the colon in all patients was 2/100 patients with colitis over the 10 year period. Five of the seven cancers occurred in patients who had had colitis for between 10–20 years while one occurred in a patient after eight years' colitis and the other in a patient after 20 years' colitis

Table 2 Patients with high grade dysplasia and cancer of the colon

	Patients followed up					Patients not followed up					After study	
Age	51	38	69	35	56	59	47	62	74	58	36	54
Sex	M	F	M	F	M	M	M	F	M	F	F	M
Years' colitis	13	10	12	8	15	18	13	20	12	210	12	14
Extent at diagnosis	D	T	T	D	D	Tr	D	T	D	?	T	D
Final extent	T	T	T	H	T	T	T	T	T	T	T	T
Symptoms	P	P	N	N	N	Ob	Ob	B	Ob	B	Ob	Ob
Histology												
Dysplasia	+	+	+	+	+	+	+	—	±	+	+	+
Carcinoma grade	0	0	0	AA	AB	C	DM	B	DM	B	C	C
Outcome												
Died (months post op)	—	—	—	—	—	36	3	—	1	—	—	—
Alive (years post op)	5	7	3	2	2	—	—	7	—	1	1	1

Extent colitis: D=Disease visible sigmoidoscopically; normal single contrast barium enema, Tr=transverse colon, H=hepatic, T=total; Symptoms: P=persistent ill health, N=no symptoms, Ob=intestinal obstruction, B=bleeding; Dysplasia: —=none, ±=low grade, +=high grade; Carcinoma grade: Duke's grade A, B and C. Number of letters indicate numbers of tumours; DM=distant metastases.

(Table 2). At the end of the study period patients with colitis for between 10–20 years amounted to 21% of patients with colitis in the district (Fig. 2). Patients with substantial colitis of 10–20 years' duration accounted for only 9% of the total known district population with ulcerative colitis. Six of the seven colon cancers were in patients with substantial disease of more than 10 years' duration. At the end of the study period patients with substantial colitis for more than 10 years accounted for 12% of the known patients with colitis in the district.

COLONOSCOPY

In addition to colonoscopies done for initial diagnosis, a further 75 colonoscopies were undertaken in patients with either ulcerative colitis or probable ulcerative colitis. The indications for colonoscopy were as follows: duration of colitis of more than eight years in 50 (66%) patients, doubt about the diagnosis in 16 (21%) patients, unexplained clinical deterioration in seven (9%) and dysplasia in rectal biopsies in two (3%) patients. In six patients colonoscopy changed the diagnosis; to Crohn's disease in four and to laxative abuse and infection once each. These six cases have been excluded from the analysis. In the remaining 69 patients the extent of colitis found at colonoscopy compared with that at initial diagnosis was unchanged in 32 (46%), more extensive in 33 (48%) and less extensive in four (6%). Of 48 patients thought to have mild colitis on initial diagnosis 21 (43%) had colitis extending to the mid transverse colon or further. Two of these patients were found to have unsuspected carcinomas associated with high grade dysplasia. After operation, histological examination showed two Duke's A tumours in 1 patient and the other patient had one Duke's A and one Duke's B carcinoma. There were no complications from colonoscopy.

PATIENTS WITH MILD COLITIS ON DIAGNOSIS

Of the 175 patients with mild colitis on diagnosis, seven required surgery: four for acute attacks and three for persistent ill health, of whom one had high grade dysplasia. Four underwent operation for colonic carcinoma, of whom two died. These cases have been discussed in the section on patients not followed in the clinic, and Table 2.

ESTIMATED OUTPATIENT ATTENDANCE

If all patients are under hospital review 84/100000 patients will attend the outpatient department per year. To review the 70% who are symptom free six monthly requires two patients/100000 population/week to be seen. If those who are symptomatic are seen four weekly an additional five to six patients/100000 population/week would be seen. New patients

are seen at the rate of six/100000 population/year. Therefore, about eight to nine patients/100000 population/week need to be seen.

ESTIMATED REQUIREMENTS FOR COLONOSCOPY

The number of colonoscopies required can be calculated from Figure 2. For policies of regular colonoscopy on all patients at eight years and in those with extensive disease at one, two, or five year intervals the number of colonoscopies needed are: 16, 12, and 8/100000 population/year respectively. The corresponding figures for colonoscopy started at 10 years and then at one, two, and five years in those with extensive disease are: 12, 8, and 5/100000 population/year. To initiate a new colonoscopy programme where none existed before: 40 colonoscopies/100000 population would need to be done. To replace barium enema by colonoscopy in all new patients seven colonoscopies/100000 population/year are necessary.

The cost of colonoscopy was calculated as £125 on the basis of the following: Instrument cost: £17.91. (Cost of new Olympus CF10L [£8941] divided by the number of examinations obtained by our LB3W instrument [520]. The manufacturers consider the new OES instruments may last longer so more examinations would be obtained.) Repair costs: £3.75. (One year's free guarantee and maintenance agreement for three years – £1950, based on four years' services obtained for our LB3W divided by 520.) Replacement forceps: £1.20. (Approximately one forceps-£120 replaced for each 100 examinations.) Cost of day bed: £57.55. (Figures obtained from Treasurer's Department.) Drug costs: £3.24. (Cost of preparation and sedation; drugs used for the average patient Mannitol [1 l + 20 mg metoclopramide used if no polyp suspected], diazepam 20 mg and pethidine 50 mg – cost to our pharmacy.) Staff costs: Nursing £7.31 (one SRN and one SEN for one hour per patient including cleaning and disinfecting the instrument [day ward nurses are included in day ward costs]; Medical: £13.37 (one consultant for ¾ h/patient). Histology: £21. (Total annual cost of department divided by the total number of blocks done in one year given the cost of one block £3.50 – six blocks used per colonoscopy.)

Discussion

The incidence and prevalence of ulcerative colitis in this retrospective audit of patients seen in one health district are similar to those reported by Evans and Acheson for the Oxford Region between 1951–60²¹ and for Cardiff 1968–77.¹⁸ This suggests that the number of cases of colitis in Britain has remained constant over the last 20 years. Large epidemiol-

ological studies do not indicate any observable changes in the incidence of ulcerative colitis.²² It is unlikely that a significant number of cases of colitis were not identified by the study method, as only 2% were found by cross reference to physicians' diseases indexes and no further cases in the hospital diseases index. Only 2% of patients were known to have been sent to hospitals outside the district, so it is unlikely that numbers were significantly affected by outside referral. Most reports include only patients followed in hospital clinics. This study includes those in the care of their general practitioners and so may be more representative of the community as a whole. No new patient or patients followed in the clinic died of colitis. We were fortunate in that no deaths occurred at all, and it is likely that a longer study would reveal a small mortality, as in other surveys.^{23,24} The only causes of death related to ulcerative colitis were advanced cancers in patients who failed to attend the clinics. This is unexpected as previous papers have indicated that the main mortality in ulcerative colitis occurs in the first year after diagnosis.^{23,24} Our study suggests that the mortality of acute colitis and surgery has dropped, and the longterm complication of colonic cancer is the main cause of death. Surveillance, therefore, would seem to be the most likely method to further reduce the mortality of ulcerative colitis.

The increased risk of carcinoma of the colon in patients with ulcerative colitis has been well established in studies from teaching hospitals.^{5,6,16} Our results from a district hospital are similar, but with the small numbers the true incidence cannot be estimated. The real cancer risk is likely to be higher than previously predicted as most of the cancers in this study occurred in patients who were lost to follow up and so would not be detected in studies of clinic populations only. In this study those patients seen regularly had dysplasia or early carcinomas whereas those lost to follow up presented with late carcinomas. Regular follow up, therefore, is likely to result in early detection of carcinoma. Every effort must be made, however, to persuade all patients with ulcerative colitis to attend the clinic. This is possible with the majority of patients. At the end of the study most of the lapsed patients agreed to attend. Colonoscopy is essential for surveillance as dysplasia can spare the rectum,^{14,15,17,28,29} but the procedure can deter patients from attending.^{25,29} It is well tolerated with good sedation, however, and careful explanation will convince most patients.

In this study 43% of patients initially diagnosed as having mild disease were found on colonoscopy after more than eight years' disease to have extensive disease. This is a surprising finding: when the proximal limit of colitis can be seen on rigid sigmoid-

oscopy only a small proportion of patients develop extensive colitis.^{9,10} It was possible to define the extent of the disease by rigid sigmoidoscopy alone, however, in only 17 of our patients. In this study the initial diagnosis usually depended on sigmoidoscopy and single contrast barium enema. Colonoscopy at presentation would probably reveal extensive disease in some of these patients, whereas others would be found to have extended their disease over the years. Until it is known which patients with distal disease will extend their disease, this study suggests that all patients, even those with mild colitis or asymptomatic distal disease, should continue under regular review. In addition to monitoring disease activity, follow up should also include periodic reassessment of the extent of disease. If distal disease only is suspected, a flexible sigmoidoscopy could be done after a phosphate enema in outpatients. Colonoscopy to assess the extent could then be performed in those with disease extending beyond the sigmoid colon. It is possible that the estimated need for colonoscopy could be reduced in this way.

All screening programmes show a high initial yield followed by a reduction in the detection rates.³⁰ This study shows a significant incidence of late cancers in patients with ulcerative colitis not followed in the clinic. These patients would not be included in most surveys of ulcerative colitis but must be included in surveillance programmes to reduce the mortality of ulcerative colitis to a minimum.

If the Wycombe Health District is representative of the country as a whole, the work load of such a surveillance programme is large, but not prohibitive. Adequate resources, however, must be made available. This audit suggests that an inflammatory bowel clinic seeing approximately eight patients/100 000 population/week would provide a comprehensive service. Similarly, a colonoscopy programme is feasible and our results suggest that it may diagnose 2.5 carcinomas/100 000 population every 10 years. We estimate the cost as £125 for a colonoscopy, so the cost of each cancer diagnosed could be £6015. This compares favourably with cervical cancer screening programmes. The estimated cost to diagnose one case of cancer of the cervix is £300 000³¹; this has been disputed^{32,33} but fits the number of investigations needed to diagnose one case.³⁴

In conclusion, this study shows that the mortality of ulcerative colitis in district hospitals is now low in patients regularly followed, but there is a risk of late colonic carcinomas in those not reviewed in the clinic. Regular surveillance of all patients even those with apparently distal disease on diagnosis is worthwhile. The workload involved is eight outpatient attendances/100 000 population/week and 12 colonoscopies/100 000 population/year.

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