Mortality from Crohn's disease in Leicestershire, 1972–1989: an epidemiological community based study

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Abstract

Mortality among 610 people with Crohn's disease identified in a population based study from 1972–89 was assessed. In Europeans the overall mortality was not increased, the standardised mortality ratio (SMR) was 71·8 (95% confidence interval (CI) 49 to 101). The SMR in South Asians was 0, (95% CI 0 to 1590). The SMR varied with the site of disease ($\chi^2_4 = 10\cdot5$, $p < 0\cdot05$) and was highest in those with duodenal and jejunal involvement (SMR=210, 95% CI 44 to 621). Survival curve comparisons showed that colonic disease carried a worse prognosis than terminal ileal disease ($\chi^2 = 9$, $p < 0\cdot01$) or mixed site disease ($\chi^2 = 4\cdot7$, $p < 0\cdot05$). Mortality was particularly high during the first six years. It was increased in patients who had undergone more than one resection (SMR=137, 95% CI 28 to 401) or an ileoanal anastomosis (SMR=357, 95% CI 9 to 1070), although no difference was significant. Mortality did not change significantly during the study. Such information needs to be made available, not just to patients, their families, and their doctors, but perhaps more importantly, to actuaries, insurers, and those advising employers.

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Crohn's disease causes chronic gastrointestinal symptoms which may require prolonged medication and surgical intervention. There is concern from earlier studies[1–6] that the disorder shortens life. Patients are anxious that the diagnosis may jeopardise their chance of acquiring life insurance, mortgages, and employment.[7 8] Studies from various referral centres have suggested that these fears are justified,[2–5] although community based reports offer some reassurance.[9 10] The aim of this study was to investigate the mortality from Crohn's disease among 610 patients on a community based register in Leicestershire.[11]

Methods

Altogether 610 patients diagnosed as having Crohn's disease while resident in Leicestershire between 1 January 1972 and 31 December 1989 were included in this study. A total of 582 were Europeans and 28 South Asians. The site of disease and demographic details have been described elsewhere.[11] Each patient's state of health on 1 January 1990 was investigated during the spring of 1991. This allowed a period of one year for information on deaths to emerge. Patients were contacted at their last known address. Those who had moved were traced through various means including the local Electoral Register, Leicestershire Family Health Services Authority, the local Registrar of Births and Deaths, and the NHS Central Register at Southport in Lancashire. The date on which patients had died but not the cause was recorded.

In Europeans the expected mortality for each patient was found by summating the risk each year according to current age from standardised mortality statistics from the East Midlands[12] obtained from the Office of Population Censuses and Surveys. This was done from the year of diagnosis until 1 January 1990 or until death. Patients were considered at risk of death until death or 1 January, 1990. For Asians, the expected mortality was calculated in a similar manner, using immigrant mortality data.[13] Age specific mortality was used throughout the study taking into account increasing age, but in Asians unlike Europeans this could not be adjusted for changing mortality rates from year to year as these data were unavailable.

The sum of each subject's cumulative hazard of death was compared with observed deaths to find the standardised mortality ratio.[1] Expected mortality was found for each age band, disease site, and decade of diagnosis. Standardised mortality ratios (SMR) were compared with one another by χ^2 tests. Confidence intervals (CIs) were found using a Poisson distribution.[14] A survival curve and life table were constructed using the Kaplan-Meier technique and CI calculated.[14 15] Survival curves were compared using a log rank test.[15] The survival for each disease site and decade of diagnosis was also calculated by Cox's model, using stepwise regression with stratification by age at diagnosis with BMDP software.[16]

Results

The state of health of 605 of the 610 patients was determined; the remaining five were lost to follow up, but their deaths had not been reported to the NHS Central Register. In Europeans there were 32 deaths during the study period, although 44·6 were expected. Those who died were aged between 15 and 84 years. The SMR was 71·8 (95% CI 49 to 101, $\chi^2_1 = 3\cdot6$, NS) in Europeans. No deaths occurred in South Asians (95% CI 0 to 1590, $\chi^2_1 = 0\cdot2$ NS), though only 0·2 would be expected. In view of the small numbers and lack of deaths South Asians were not studied further. The only group for which the estimated SMR was raised was that of patients aged under 20 years at diagnosis in which only one death occurred (SMR=191, 95% CI 5 to 1060, $\chi^2_1 = 0\cdot44$ NS) (Table I). Overall, there was little

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TABLE I Age at diagnosis in 572 European patients with Crohn's disease in Leicestershire and their standardised mortality ratios

Age at diagnosis (years)*	Total no of cases (n=572)	No of deaths (n=32)	Expected deaths	SMR	95% confidence interval
0-19	96	1	0·52	191	5 to 1060
20-29	163	0	1·1	0	0 to 330
30-39	93	1	1·5	67	2 to 371
40-49	61	2	3·1	65	8 to 236
50-59	60	7	7·5	93	38 to 193
60-69	46	9	12·7	71	33 to 134
70-79	47	11	15·6	71	35 to 127
80+	6	1	2·6	38	1 to 213

*No SMR was significantly raised. To compare the age bands with one another, the expected deaths were adjusted to sum to 32 (the actual number of deaths), there was no difference ($\chi^2_7=2\cdot8$, NS).

TABLE II Site of Crohn's disease in 568 patients in Leicestershire and standardised mortality ratio

Site of disease*	Total no of cases (n=568)	Patient years	No of deaths (n=32)	Expected deaths	SMR	95% confidence interval
Terminal ileum	241	2128	8	15·1	53	23 to 105
Colon	159	1064	16	15·5	103	59 to 168
Mixed sites	108	943	4	4·8	82	22 to 211
Non-terminal ileal small bowel	33	295	3	1·4	210	44 to 621
Proctitis/perianal	27	171	1	7·8	13	0 to 72

*In order to compare disease at different sites with each other the number of expected deaths was adjusted to sum to 32 (the actual number of deaths) the difference was significant ($\chi^2_4=10\cdot5$, p<0·05). Four cases of Crohn's disease of the stomach and oesophagus were not included in this analysis.

evidence that the SMR varied with the age at diagnosis ($\chi^2=2\cdot8$, NS).

The SMR varied with the site of Crohn's disease ($\chi^2_4=10\cdot6$, NS) (Table II). A comparison using the log rank test showed a difference in survival times in patients with disease at various sites. A significantly smaller proportion of patients with colonic disease survived compared with those with Crohn's disease of the terminal ileum or mixed sites ($\chi^2_1=9$, p<0·01 and $\chi^2_1=4\cdot7$, p<0·05 respectively). The highest mortality was among those who had had colonic disease for less than six years (Fig 1), although the CIs of the difference between survival proportions are wide. These findings also reflect the higher proportion of elderly patients with colonic disease.

The survival curve for the study shows that the highest mortality is during the first four years after diagnosis. Subsequently survival plateaus (Fig 2). A log rank test analysis showed survival
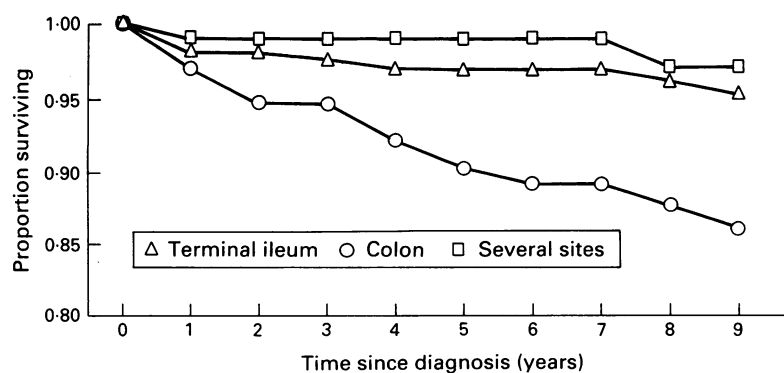
was significantly better in the 1970s than the 1980s ($\chi^2_1=8$, p<0·05). To assess whether mortality was changing during the study, the SMRs for patients diagnosed from 1972-80 and from 1981-9 were compared at 1 January 1981 (SMR=44·7) and 1 January 1990 (SMR=94·5) respectively and were not significantly different ($\chi^2_1=2\cdot15$ NS), which suggests the difference in survival curves for the two decades is due to a different age distribution of patients and does not reflect poorer clinical care in the 1980s. Such survival curves take no account of the age structure of the patients.

The survival curve was steeper in the 1980s than the 1970s (Fig 2). The differences between survival proportions at 3, 6, and 9 years were 0·04 (95% CI 0·016 to 0·08), 0·051 (95% CI −0·01 to 0·1), and 0·09 (95% CI −0·12 to 0·3) respectively. Although this could suggest the improved survival in the 1970s was due to better management early in the disease, the similarity of the SMRs in each decade would again suggest that the age distribution of patients is the explanation.

Stepwise regression analysis with stratification by age confirmed that colonic disease was the only variable that was significantly related to survival (log likelihood=−132·894, $\chi^2<0\cdot05$). The difference in survival between patients diagnosed during the 1970s and 1980s was due to the greater number of patients with colonic disease diagnosed during the 1980s.

Mortality was greatest in patients who had had more than one resection (SMR=137, 95% CI 28 to 401) or an ileoanal anastomosis (SMR=357, 95% CI 9 to 1070), although no difference was significant. Patients who had only one resection or a panproctocolectomy had normal SMRs of 65 (95% CI 36 to 107) and 67 (95% CI 18 to 172) respectively.

Discussion

Among Europeans the prognosis for people with Crohn's disease is comparable with that of the general population irrespective of age at diagnosis. Survival is least good for those people with isolated duodenal or jejunal disease. Surgery does not effect survival in either an adverse or beneficial way, but there is a suggestion that mortality is increased in those who undergo ileoanal anastomosis. However, observational studies such as these should be interpreted with care, all that can be fairly concluded is that the group operated on do not differ significantly from the remainder and the longer a patient is followed the greater the chance of surgery. There is still evidence that the young and newly diagnosed patients remain at increased risk of death and it is among these that we must concentrate our efforts. Despite difficulties in diagnosis and subsequent communication the survival of South Asian migrants with Crohn's disease is good and may reduce our concern about their compliance with treatment.

The survival of patients diagnosed in the 1980s was poorer than that of those diagnosed during the 1970s, although it remains comparable with that of the general population. The change was due to the greater proportion of patients with
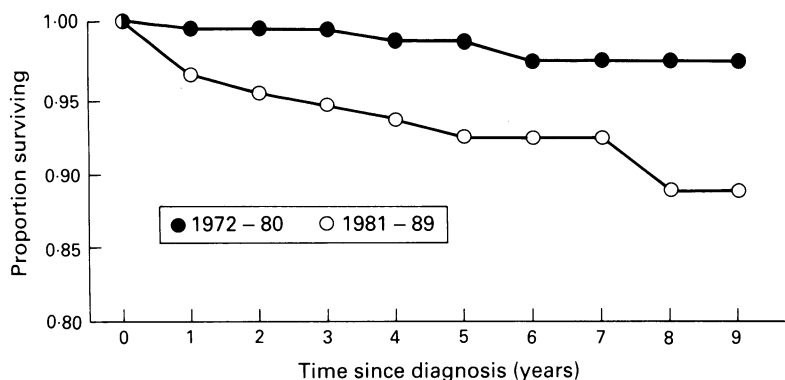

Figure 1: Survival in patients with Crohn's disease. Terminal ileal, colonic, and mixed site disease were compared.

Figure 2: Survival in patients with Crohn's disease. Cases diagnosed during the 1970s and 1980s were compared.

These results, like those from Copenhagen, should offer reassurance to patients and their families. Mortality is not increased in Europeans or South Asians. Such information needs to be made available, not just to patients and their doctors, but perhaps more importantly, to actuaries, insurers, and those advising employers.

colonic disease, which in this study had a worse prognosis. The incidence study[11] has shown that there were more older patients and relatively more patients with colonic disease during the 1980s.

There have been few community based studies of mortality in Crohn's disease.[1 9 10] In one of earliest, an SMR of 216 was reported in a study of 219 patients in the City of Cardiff.[1] In a review of 185 patients in Copenhagen County, Binder *et al*[9] reported that 'survival did not differ from an age–sex matched background population,' a finding directly comparable with that in Leicestershire. The design of the studies was similar, so although the difference is likely to be real, the reason is unclear. A different community based study in South Wales,[10] based on 79 patients, found an SMR of 127, which was not significantly different from normal. In contrast, hospital based series[3–6] have usually shown an increased mortality, which probably reflects the severity of disease in patients referred to specialist units from outside the area. Community studies give a better overall picture of disease outcome but as most are also based around units with a specialist interest in the condition they too should reflect the best rather than the average treatment.

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