Mortality in ulcerative colitis—what should we tell our patients? Three year mortality following admission for the treatment of ulcerative colitis: a 6 year retrospective case review

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Objectives To determine the 3 year mortality of patients admitted to hospital for the treatment of ulcerative colitis (UC).

Design Retrospective case note review of all patients admitted to hospital for treatment of active UC over a 6 year period from 1 January 2000.

Setting Teaching hospital with a tertiary referral practice for the management of inflammatory bowel disease.

Patients 106 patients (134 admissions) met the inclusion criteria.

Interventions Elective and emergency colectomy was undertaken in 16 and 26 patients, respectively.

Main outcome measures Mortality at 3 years.

Results There were six deaths after 3 years. Case fatality at 30 days, 1, 2 and 3 years was 1.0% (95% CI 0.2 to 5.1), 1.9% (95% CI 0.2 to 6.6), 2.9% (95% CI 5.9 to 8.0) and 5.7% (95% CI 2.1 to 11.9), respectively. There were no deaths in either surgical group. One patient (89 years, female) died while awaiting emergency colectomy. Patients who died were significantly older at the time of admission (79 years (95% CI 71 to 88 years) vs 41.2 years (95% CI 38 to 45 years)) and were more likely to have comorbid illness ($p<0.001$). Severity of disease, prior immunosuppressive use, first presentation and smoking status were not associated with increased mortality.

Conclusions Three year mortality following admission for treatment of UC was 5.7% (95% CI 2.1 to 11.9), significantly lower than that reported previously. Mortality was significantly associated with increasing age and the presence of comorbid disease. Disease specific factors such as severity, extent and first presentation were associated with emergency colectomy but not mortality.

Introduction

Ulcerative colitis (UC) is a chronic inflammatory disease of the colon characterised

by a relapsing remitting course and the passage of urgent, loose and bloody stools during active disease. The incidence in western Europe is 10 per 100 000 patients per year.¹ Intensive medical therapy and timely surgical intervention has dramatically reduced mortality from severe disease² and most contemporary studies show no increase in mortality for patients with UC compared with the general population.^{3–10} The risk of death is unevenly distributed within the UC population. Studies have shown an increased mortality in the first years following diagnosis, especially when the disease is extensive, severe or the patient older.^{3–5} The converse is also true. Patients with distal disease may have better than average survival.^{3,5} Severe disease is invariably treated in hospital; it follows that mortality might be higher among these patients. Roberts *et al* have reported a 3 year mortality of 12.2% following admission to hospital for the treatment of UC.¹¹ Furthermore, those who underwent emergency colectomy or who were admitted but did not undergo surgery had a significantly higher mortality than those who underwent elective colectomy (13.2% and 13.6% vs 3.7%, respectively). The implication was twofold: firstly, emergency admission for treatment represents a significant risk for death; and secondly, the threshold for elective colectomy is too high. We investigated 3 year mortality following admission to our centre for the treatment of active UC.

Methods

Our centre is a teaching hospital that provides secondary care services to a population of 300 000 people in South Bristol, UK. We care for 1500 local patients with inflammatory bowel disease (IBD) and

provide a tertiary referral service to the surrounding region (predominantly out-patient based). All patients admitted to our hospital for treatment of active UC between 1 January 2000 and 31 December 2005 were identified by discharge code (International classification of disease, 10th revision, codes K51.0–K51.9). Case notes, electronic hospital records and laboratory systems were reviewed. An admission was considered to be a first presentation if the diagnosis of UC had been made within the preceding month. A patient's first admission during the study period is referred to as the index admission. Patients were included if the diagnosis of UC had been confirmed by standard methods and there was evidence of active disease during the admission. Data were extracted, including age, date of diagnosis, extent of disease, medical therapy at the time of admission, stool frequency, haemodynamic data and laboratory parameters, including haemoglobin, C reactive protein (CRP) and albumin. The presence of significant comorbidity was derived from the admission documentation, including cardiovascular disease (ischaemic or valvular heart disease, stroke, venous thromboembolic disease (VTE)), respiratory (asthma or chronic obstructive pulmonary disease), diabetes, renal impairment, inflammatory arthritis, concurrent malignancy or significant neurological or psychiatric illness. Disease severity was determined retrospectively according to the following criteria: (1) severe colitis, equal to six or more stools daily with one or more of the following: temperature $>37.5^{\circ}\text{C}$, pulse $>90/\text{min}$, haemoglobin $<10.5\text{ g/dl}$ or CRP >12 ; (2) mild colitis, equal to four stools daily without significant fever, tachycardia, anaemia or raised CRP; (3) moderate colitis was intermediate between mild and severe.^{12 13} Plasma viscosity was rarely measured. Disease was considered distal if it only affected the rectum and sigmoid colon, left sided when it extended as far as the splenic flexure and extensive when disease extended proximal to the splenic flexure. Mortality data, including cause of death, was retrieved from hospital records or the patient's general practitioner. Where patients were lost to follow-up, mortality was discovered using the NHS Summary Care Record.

Statistical analysis

Analysis is by index admission unless otherwise stated. Admissions more than 3 years after the index admission were not counted as new patients. The influence of age, disease activity, disease extent, first presentation, prior immunosuppressive use and comorbidity on mortality and emergency colectomy were determined by Fisher's exact test and Pearson's χ^2 test, respectively, using SPSS (SPSS Inc, Chicago, Illinois, USA). Means are compared using the Mann–Whitney U test. Two tailed p values of <0.05 were considered significant; 95% CI for proportions were calculated using the exact binomial method (Stata V.9; StataCorp LP, Texas, USA). The study was approved by the hospital audit committee.

Results

Patients

A total of 277 admissions (196 patients) were identified. Records were reviewed for 188 patients (265 admissions). A total of 106 patients met the entry criteria and had a total of 164 admissions. Of these, 134 admissions met entry criteria and 30 did not (previous colectomy 21, day case admission for drug infusion five, no admission two, no active IBD one, infectious diarrhoea one). Notes for eight patients (12 admissions, one patient died within the follow-up period) could not be located and were not included. The demographic and disease characteristics of the patients are shown in table 1. Eighty-two patients (101 admissions) did not meet the inclusion criteria (table 2).

There were equal numbers of men and women. Mean age at admission was 43.5 years and median length of stay was 10 days. Mean age and median length of stay of each group on their index admission is shown in table 1. There was no significant age difference between the groups. There were 59 admissions for severe colitis, 37 for moderate and seven for mild (insufficient data 15). Sixteen patients underwent elective colectomy and 26 patients underwent emergency colectomy. Seventeen patients were admitted more than once during the study period.

Mortality

There were six deaths after 3 years (four men and two women). Case fatality at 30 days, 1, 2 and 3 years was 1.0% (95% CI 0.2 to 5.1), 1.9% (95% CI 0.2 to 6.6),

Table 1 Baseline characteristics

Elective colectomy				
Patients (n)	11			
Age (years) (mean (SD))	38.6 (11.3)			
Men (n (%))	4 (36)			
Duration of stay (days) (median (interquartile range))	11 (9–12.8)			
Emergency colectomy				
Patients (n)	20			
Age (years) (mean (SD))	44.6 (17.1)			
Men (n (%))	13 (65)			
Duration of stay (days) (median (interquartile range))	25 (17.3–31.8)			
No colectomy				
Patients (n)	75			
Age (years) (mean (SD))	44.0 (20.8)			
Men (n (%))	36 (48)			
Duration of stay (days) (median (interquartile range))	8.0 (6.0–14.0)			
All patients				
Patients (n)	106			
Age (years) (mean (SD))	43.5 (19.3)			
Men (n (%))	53 (50)			
Duration of stay (days) (median (interquartile range))	10 (7–17)			
Smoking status (index admission)				
Current	13			
Ex-smoker	28			
Non-smoker	49			
Never smoked	3			
Unknown	13			
Immunomodulator use (excluding incident cases n=96)				
Azathioprine (n (%))	19 (19.8)			
Methotrexate (n (%))	1 (1)			
Extent of disease				
	Index admission	All admissions	Emergency colectomy	Mortality
Distal	27	32	2*, 1†	3*
Left-sided	17	18		1*
Extensive	53	73	17*, 4†	1*
Unknown extent	9	11	1*, 1†	1*
Total	106	134	26	6
Severity				
	Index admission	All admissions	Emergency colectomy	Mortality
Mild	7	7	0	2*
Moderate	29	37	4*, 1†	2*
Severe	51	59	15*, 3†	2*
Unknown	8	15	1*, 2†	0
Elective colectomy	11	16		
Total	106	134	26	6

Comparison of means: elective vs medical $p=0.87$; medical vs emergency $p=0.476$; elective vs emergency $p=0.69$.

*First admission.

†Subsequent admission.

2.9% (95% CI 5.9 to 8.0) and 5.7% (95% CI 2.1 to 11.9), respectively (figure 1). Patients that died were significantly older (mean 79.3 years, 95% CI 70.6 to 88.1) than those that survived (mean 41.4 years, 95% CI 37.9 to 44.9) ($p<0.0001$) (figure 2). Median age at death was 80.5 years. The median interval between admission and death was 19.5 months. Cause of

death was not recovered for two patients (81 and 89 years, female); one of these patients had severe chronic obstructive pulmonary disease requiring home oxygen. One patient died during the index admission while awaiting emergency colectomy (89 years, female, receiving intravenous hydrocortisone and azathioprine); the patient was profoundly unwell

Table 2 Exclusion criteria

Exclusion	
Crohn's disease	15
Controlled ulcerative colitis	15
Prior colectomy	14
Day case procedure	14
No inflammatory bowel disease	7
<i>Clostridium difficile</i> colitis	4
Ischaemic colitis	2
No admission	2
One each of: appendicitis, drug induced colitis, antibiotic related diarrhoea, diverticular colitis, teaching for home parenteral nutrition, admission for drug trial, non <i>C difficile</i> infectious diarrhoea, enteropathic arthritis, microscopic colitis	
All patients	82
Age (years) (mean (SD))	53 (20)
Mortality (n (%))	18.3 (15)

and prior anaesthetic and surgical review had predicted a substantial operative mortality. Deaths in the other patients were due to pneumonia during a subsequent admission for a flare of UC (80 years, female, 33 months after the index admission), lung cancer (70 years, male) and complications of discitis (70 years, male, 3 months after the index admission, receiving azathioprine since discharge). Except where indicated, details of immunosuppressant use at or prior to death are unknown. Forty-two colectomies were performed, among whom there were no deaths. No association was found between mortality and severity of disease,

prior immunosuppressive use, first presentation or smoking status.

Notes for eight patients could not be located, one of whom died within the follow-up period. Inclusion of this patient increased the 3 year mortality to 6.5%. All of those readmitted during the 6 year study period survived 3 years beyond their last admission. Of the readmissions, four patients were readmitted more than 3 years after their index admission. Inclusion of these patients as de novo attendees reduced the observed 3 year mortality to 5.5%.

Comorbidity

Of the six observed deaths, four had a history of cardiovascular disease, four a history of respiratory disease and one cerebrovascular disease. Of those that survived, the prevalence of cardiovascular, respiratory, renal, diabetic, neoplastic (non-gastrointestinal) and thromboembolic comorbidity was 7%, 10%, 2%, 5%, 1% and 1%, respectively. Patients that died had significantly more comorbidity than those that survived ($p < 0.001$).

Emergency colectomy

The colectomy rate for emergency index admissions was 21.1% (20/95), and for all emergency admissions, 22.0% (26/118). Eight patients underwent emergency colectomy during their first presentation with disease (8/38, 21.1%). Median time from admission to colectomy was 9.5 days (mean 10.7 days, range 2–35 days). There were 59 admissions with severe UC and 18 underwent emergency colectomy during that admission (30.5%). Five patients underwent colectomy for moderate disease. Of 26 emergency colectomies, 21 were inpatients with extensive colitis. Travis criteria¹⁴ (>8 stools/day or 3–8 stools with a CRP >45) on the third day of intravenous hydrocortisone treatment predicted colectomy in 65% of patients. Rescue therapy with ciclosporin was given in nine cases and was successful in seven. One patient had a septic complication of ciclosporin use. Emergency colectomy was significantly associated with severity of disease ($p = 0.027$), extent ($p < 0.001$), first presentation ($p = 0.035$) and fulfilment of Travis criteria ($p < 0.001$).

Discussion

Three year mortality following admission to our hospital for the treatment of UC

Figure 1 Kaplan–Meier plot. Survival after admission for the treatment of active ulcerative colitis.

was 5.7% (95% CI 2.1 to 11.9), significantly lower than that previously reported by Roberts *et al* (12.2%).¹¹ Furthermore, and in contrast with Roberts' study, there were no deaths among 42 patients undergoing colectomy, 26 of which were undertaken during emergency admissions. Three year mortality following admission without colectomy was 8% (95% CI 3.0 to 16.6). In this cohort and consistent with previous studies, 3 year mortality was significantly associated with old age and the presence of comorbid illness.³ Only one death was unequivocally the consequence of active UC. Our study population represents all admissions to secondary care for the management of active UC from a geographically defined area of South Bristol. We do not believe our status as a teaching hospital or as a tertiary referral centre (largely outpatient based) significantly affects case mix with respect to this group of patients. Our population is therefore likely to be similar to that of other UK centres.

Methodological differences are expected to account for the contrasting results of our study compared with its forerunner. Roberts, through use of the Oxford Record Linkage Database and the English National Record Linkage Database, performed a study of more than 11 000 patients who, according to discharge code, had been admitted to hospital for the treatment of UC between 1968 and 1996 (Oxford) and between 1998 and 2000 (English). While enlarging the study population, the use of administrative data prevented a detailed description of the patients. We set out to investigate 3 year mortality in our own centre in a similar group of patients. As in Roberts' study, cases were identified by discharge code but we then performed a thorough case note review, including confirmation of diagnosis and extent of disease, prior drug exposure, severity of disease, inpatient course, treatment and cause of death. In addition to fully characterising our study population, full case note review discovered 82 patients who had been wrongly coded or who did not meet the inclusion criteria of active UC. Among these patients there were 15 deaths. Had we not scrutinised the notes, we would have found a 3 year mortality of 11.2% (22/196, 95% CI 7.2 to 16.5), similar to that reported by Roberts *et al*. This suggests that the patients we identified

Figure 2 Age of survivors and deceased at the time of their index admission for the treatment of active ulcerative colitis. Values are mean, 95% CI and range.

using discharge coding are representative of the larger group of patients studied by Roberts.

Both old age and comorbid illness are known to contribute to mortality in UC.³ While highly descriptive, the size of our study was insufficient to allow multiple regression analysis and the independence of these variables could not be determined. In Roberts' study, the presence of comorbidity was more common in those groups with highest mortality. Surprisingly, adjusting for age, sex and major comorbidity did not affect the significance of their results. Median age of case fatalities was not reported.

In line with our data, previous studies confirm UC related death to be rare.^{15 16} Indeed, most contemporary epidemiological studies show no increased mortality for patients with UC compared with the general population.^{4-10 17} While reassuring, it would be naive to believe that severe, or refractory UC, would not be associated with adverse events, and the same studies that report no increased risk of death also document disease related death.¹⁷ When attributable to IBD, death is most commonly a consequence of sepsis, colonic perforation, multiorgan failure, VTE or postoperative cardiovascular complications.^{3 18} A 4 year follow-up of a 528 patient multicentre inception cohort from Europe observed only two deaths as a direct consequence of UC (toxic megacolon, 67 years; exacerbation of UC, 80 years); a third patient died from

colorectal cancer. Despite the recognised adverse effects of immunosuppressant therapy, no increased risk of death has been associated with their use, either here or previously.⁶

Mortality following colectomy for UC is variably reported. In the present study, there were no deaths among 42 surgical patients over 3 years of follow-up. In a large retrospective review from St Mark's Hospital, six postoperative deaths were reported (6/422, 1.42%), one after elective colectomy, three following emergency colectomy (two from bronchopneumonia and a third from a bleeding duodenal ulcer) and two from VTE after subsequent surgical procedures in patients who had initially undergone elective surgery.¹⁹ Travis *et al*¹⁴ reported no perioperative deaths but one death from myocardial infarction 5 months after surgery. A study from Leicestershire reported mortality following colectomy to be similar to the non-surgical UC population.⁵ Thirty day mortality following ileal pouch anal anastomosis is reported to be 0–0.5%.²⁰ ²¹ In contrast with these studies, Roberts *et al* reported a 3 year mortality after elective and emergency surgery of 3.7% and 13.2%, respectively. Most deaths occurred within 2–4 months of surgery. This high surgical mortality may be a consequence of real life reporting of outcomes from all, including non-specialist, centres. Alternatively, there may be an excess of non-operative, non-UC related death, as suggested by a trend of increasing age between the groups in the order of elective, emergency and no colectomy.

We have presented the results of a 6 year retrospective case review of admission to hospital for the treatment of UC. Three year mortality following admission was 5.7%. There were no deaths in the surgical group assuaging concern over unexpectedly high mortality following emergency colectomy reported previously.¹¹ Mortality following admission was significantly associated with the presence of comorbid disease and old age but not with disease specific factors such as disease extent, severity or first presentation. These results are reassuring for patients and of interest to both physicians and surgeons to whom we recommend the continued use of established guidelines for the management of severe colitis.^{14 22}

Competing interests None.

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