BMJ
open

Thirty-day mortality after elective and emergency total colectomy in Danish patients with inflammatory bowel disease:
A population-based nationwide cohort study

SCHOLARONE™
Manuscripts

Thirty-day mortality after elective and emergency total colectomy in Danish patients with inflammatory bowel disease: A population-based nationwide cohort study

A. Tøttrup[1], R. Erichsen[2], C. Sværke[2], S. Laurberg[1], H.T. Sørensen[2].

[1]Department of Surgery P, Aarhus University Hospital

[2]Department of Clinical Epidemiology, Aarhus University Hospital

Corresponding author: Dr. Anders Tøttrup, Department of Surgery P, Aarhus University Hospital, Tage Hansensgade, 8000 Aarhus C, Denmark. Mail: andtoe@rm.dk. Phone: +45 89497703. Fax: +45 89497549

Abstract

Background

There is little population-based data available on postoperative mortality and potential prognostic factors in patients with inflammatory bowel disease (IBD), who undergo elective or emergency total colectomy. The purpose of our investigation was to assess 30-day mortality among Danish IBD patients and to examine the prognostic impact of hospital total colectomy volume, age, gender, and comorbidity.

Methods

We compared 30-day survival over the 1996-2010 period among 2,889 IBD patients with total colectomy identified in the Danish National Registry of Patients. This registry covers all hospitals in Denmark. Postoperative survival patterns for patients with ulcerative colitis and Crohn's disease were compared, using proportional hazard regression. The regression model accounted for the timing of surgery, hospital total colectomy volume, age, gender, and comorbidity.

Results

Among 2,889 IBD patients with total colectomy, 50% underwent surgery during an emergency hospitalization. Thirty-day mortality was 5.3% among emergency cases, compared to 1% among elective cases. The highest mortality (8.1%) was observed among Crohn's patients undergoing emergency surgery. The mortality of patients with ulcerative colitis undergoing emergency surgery was 5.2%. After elective surgery, the 30-day mortality was 0.9% among patients with ulcerative colitis and 1.5% among Crohn's disease patients. Low hospital total colectomy volume, comorbidity, and high age were associated with increased 30-day mortality in ulcerative colitis patients undergoing emergency surgery.

Conclusion

Emergency total colectomy among patients with ulcerative colitis and particularly

Crohn's disease is associated with substantial 30-day mortality.

Significance of this study

Article focus

☐   Elective and emergency total colectomy is commonly performed in

inflammatory bowel disease

☐   Emergency operations are associated with higher mortality than elective

procedures.

Key messages

☐   IBD patients undergoing emergency total colectomy have a 30-day mortality

of 5.3% as opposed to 1% after elective total colectomy.

☐   Low hospital volume, high age and comorbidity are associated with increased

mortality in patients with ulcerative colitis undergoing emergency surgery.

☐   It is suggested to centralize treatment, and to aim for elective procedures in

high risk patients.

Strengths and limitations of this study

☐   The study covers complete national data on total colectomies performed for

inflammatory disease.

☐   The unique ID number of all patients makes recording of all events highly

reliable.

☐   The main limitation is lack of access to specific clinical parameters

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Inflammatory bowel diseases (IBD) cause serious morbidity and disability in people of all ages. Medical treatment remains the cornerstone for managing these diseases. Over the past two decades, use of immunosuppressants such as azathioprine (1;2) has increased significantly as a treatment modality. More recently, potent biological treatments have proved effective in treating both ulcerative colitis and Crohn's disease (3-7). Historical data have shown that up to 83% of patients with Crohn's disease underwent at least one bowel resection during a 10-year period (8), and up to 25% of patients with ulcerative colitis needed surgical treatment (9). While some recent studies show that modern medical treatment may decrease the need for surgery in IBD patients (10-12), others suggest that this is not the case (2;13).

In patients with severe ulcerative colitis, colectomy rates have remained stable over the past decades (14), although the introduction of biological rescue therapy is likely to decrease use of this surgical intervention in coming years (15;16). Mortality rates of up to 30% have been reported historically in patients undergoing emergency total colectomy for ulcerative colitis (17;18). Delay in patient referral for surgery has been proposed as the reason for high postoperative mortality (19). Although recent data from a highly specialized centre showed in-hospital mortality of less than 1% after emergency colectomy (20), population-based studies from the UK (21) and the US (22) have reported postoperative mortality as high as 5.4% – 5.7% after emergency colectomy. This contrasts with rates as low as 0.7% – 0.8 % after elective colectomy. Advanced age, comorbidity, delay of more than 6 days between hospital admission and colectomy, and low hospital volume have been associated with increased postoperative mortality after colectomy in IBD patients (22;23).

In many countries, including Denmark, increasing specialization has occurred, with more rare and complicated conditions treated at specialized centres. Still, severe IBD continues to be treated at general district hospitals, where the number of patients is low and outcome appears to be poor (24).

The present study aimed to investigate 30-day mortality after elective and emergency total colectomy in Danish IBD patients, with special emphasis on the prognostic impact of hospital total colectomy volume, age, sex, and comorbidity.

Material and methods

We conducted this follow-up study in the setting of the entire Danish population of 5.4 million people during the January 1, 1996 – December 31, 2010 period. The Danish National Health Service provides tax-funded medical care for all Danish residents.

Data sources

The Danish National Registry of Patients (DNRP) contains data on all non-psychiatric hospitalizations in Denmark since 1977 and on hospital outpatient clinics contacts since 1995 (25). The DNRP records civil registration number, hospital code, department code, date and type of admission (emergency/elective), dates and codes of procedures, admission and discharge dates, selected medical therapies, and up to 20 discharge diagnoses, coded by physicians according to the International Classification of Diseases (ICD), eighth revision until the end of 1993 and 10th revision thereafter. It is mandatory that all surgical procedures are coded according to the Nordic Medico-Statistical Committee (NOMESCO) classification (26).

We linked individual-level data from the DNRP using the civil registration number, a unique 10-digit identifier assigned at birth to all Danish residents by the Civil Registration System (CRS) (27). The CRS also tracks vital status and the residence of all Danish citizens and is updated daily.

Patients with IBD and total colectomy

Patients were enrolled in the study if they had a hospital registry diagnosis of IBD, with accompanying procedure codes for total colectomy. (See codes in Appendix Table 1). Hospitalizations were described as elective or emergency and patients were categorized as having Crohn's disease, ulcerative colitis, or as a mixed group if their records

contained ICD codes for both Crohn's disease and ulcerative colitis. We also obtained

information on reoperation occurring within 30 days of the primary surgery, TNF-α-

inhibitor and cyclosporine treatment in the year prior to surgery, and Clostridium

difficile infections. (See codes in Appendix Table 1). We categories IBD patients according

to age at date of total colectomy (0-39, 40-59, and 60+ years), year of colectomy (1996-

2000, 2001-2005, and 2006-2010), and hospital total colectomy volume defined as

annual number of total colectomies performed on IBD patients by the surgical

department and categorised according to Kaplan et al (low: <3, medium: 3-12, high 12+)

(22)

We also extracted information from the DNRP on comorbidity, *i.e.*, diseases coexisting

with IBD. We summarized comorbidity status using the Charlson Comorbidity Index

(CCI) (28). The CCI's scoring system assigns between one and six points to a range of

diseases. Each patient's sum of points represents a measure of his or her comorbidity

burden. We placed our study patients into three groups according to their sum of points:

0 points ("no comorbidity"), 1 to 2 points ("low comorbidity"); and 3 or more points ("high

comorbidity") (28). We defined comorbid diseases according to the ICD-10 codes provided

by Quan *et al.* (29), matching ICD-8 codes to ICD-10 codes as closely as possible. (See

codes in Appendix Table 2).

Mortality data

We followed IBD patients who were acutely or electively hospitalized for a procedure of

total colectomy in the period 1996-2010, from the date of colectomy until death, 30 days

post-surgery, or December 31, 2010, whichever came first.

Statistical analysis

Our main outcome of interest was 30-day mortality, estimated as the number of deaths

after total elective or emergency colectomy divided by the total number of IBD patients

undergoing elective/emergency colectomy. We stratified our study sample by IBD type

and by the following covariates: gender, age at colectomy, year of colectomy, hospital

total colectomy volume (22), duration of hospitalization prior to surgery (< 8 days, ≥ 8

days), presence or absence of TNF-α-inhibitor or cyclosporine therapy in the year before

the total colectomy, reoperation, CCI score, and colectomy subtype. We calculated

differences in mortality and corresponding 95% confidence intervals (95% CI) between

patients undergoing emergency vs. elective surgery overall. We also calculated mortality

rates for ulcerative colitis patients by age and hospital total colectomy volume. In

addition, we used Cox proportional-hazards regression to estimate mortality rate ratios

(MRR) for each covariate, using the reference values shown in Table 4. MRRs were

adjusted for age (0-39, ≥ 40 years), gender, and CCI score (0 and ≥1 points) to evaluate

the independent prognostic effect of the covariates included in the model. (We lacked

statistical power to mutually adjust for all covariates). In a subsequent analysis, we

estimated the proportion of patients who underwent reoperation, as a secondary

outcome.

Results

Descriptive data

In total, 2,889 IBD patients with total colectomy were identified from the DNRP for the January 1, 1996 - December 31, 2010 period. Of these, 1,439 (49.8%) underwent surgery during an emergency hospitalization (49% female). Characteristics of IBD patients by type of surgery (elective and emergency) are shown in Tables 1 and 2. The majority of patients had a total colectomy due to ulcerative colitis (64.7% for elective cases; 73.4% for emergency cases). Of the 1,450 elective cases (51.9% female), 718 (49.5%) were younger than 40 years, 438 (30.2%) were between ages 40 and 59, and the remaining 294 (20.3%) were ≥ 60 years old (Table 1). Of the 1,439 emergency cases 693 (48.2%) were younger than 40 years, 390 (27.1 %) were between ages 40 and 59, and the remaining 356 (24.7%) were ≥ 60 years old (Table 2). The majority of elective (69.9%) and emergency (65.1%) surgeries took place in high-volume hospitals with >12 total colectomies/year (Tables 1 and 2). None of the patients included in the present study were coded for infection with Clostridium difficile.

Among all IBD patients, 1,075 (74.1%) of elective cases and 1,097 (76.2%) of emergency cases had a CCI score of 0, and 375 (25.9%) of elective cases and 342 (23.8%) of emergency cases had a score of 1 or higher. Comorbidity scores were distributed almost equally between the three IBD groups (Tables 1 and 2). Total colectomy with ileostomy was performed more often in emergency cases than in elective cases (81.2% vs. 54.6%). Proctocolectomy with ileostomy was carried out in 102 emergency cases (7.1%) and 261 elective cases (18%). Frequencies of procedures by type and disease groups are shown in Tables 1 and 2.

Mortality

Within 30 days following colectomy, 14 of the 1,450 patients who underwent elective

surgery died (1.0%), while 76 of the 1,439 emergency patients (5.3%) died (mortality

difference = 4.3%; 95% CI: 3.1%, - 5.6%). Among ulcerative colitis patients, mortality was

0.9% (8/938) in the elective group and 5.2% in the emergency group. Patients with

Crohn's disease undergoing emergency surgery had the highest 30-day mortality (11/136

= 8.1%).

Mortality was low in ulcerative colitis patients aged under 40 (0.2%, Table 3), both for

elective and emergency surgery. For patients aged 60 years or older, mortality increased

to 3.3% for those undergoing colectomy on an elective basis and to 18.4% for those

undergoing this procedure on an emergency basis (mortality difference = 15.1%; 95% CI:

9.8%, 20.3%). Mortality was lowest in high-volume hospitals (0.5% for elective and 3.6%

for emergency cases [mortality difference = 3.1%; 95% CI: 1.6%, 4.6%], Table 3). Patients

with high CCI scores also had high mortality. Table 3 shows mortality according to

duration of hospitalization prior to colectomy, colectomy type, and time period. Numbers

of outcomes in patients with Crohn's disease or mixed Crohn's disease/ulcerative colitis

were too small to permit more detailed analysis of mortality.

In a subsequent analysis we found that reoperation within 30 days occurred in 115

(7.9%) elective cases and in 140 (9.7%) emergency cases and was associated with

particularly high mortality.

Prognostic factors in patients with ulcerative colitis.

Crude and adjusted MRRs for patients with ulcerative colitis are shown in Table 4.

Higher age at operation (≥ 40 years) was associated with major increases in MRRs in both

emergency and elective cases. A CCI score ≥ 1 was associated with an increased MRR

after emergency colectomy, but had no influence on MRR in patients undergoing elective colectomy. MRRs were lower for cases undergoing surgery at high-volume hospitals compared with low-volume hospitals. In the regression model for emergency colectomies, gender, duration of hospitalization before colectomy, and time period were not clearly associated with mortality. In the regression model for elective colectomies, hospitalization for 8 days or more prior to surgery was associated with an increased MRR. Numbers were too low to permit calculation of MRRs for patients with Crohn's disease or with both ulcerative colitis and Crohn's disease.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Discussion

Our study showed that 30-day postoperative mortality after total colectomy was 5.3% for

IBD patients undergoing surgery on an emergency basis and 1 % for those with elective

procedures. We also found that comorbidity, surgery in a hospital performing few annual

colectomies, and age over 40 were associated with increased mortality after emergency

total colectomy in patients with ulcerative colitis. Age over 40 and hospitalization for 8

days or more prior to colectomy were associated with increased mortality in ulcerative

colitis patients undergoing elective total colectomy.

Our data extend previous research with recent population based data. Mortality after

emergency total colectomy for ulcerative colitis was as high as 27% (19;30-32) in the

past. More recent data from tertiary referral centres indicates in-hospital mortality of less

than 0.6% (20;33;34). However, a short report on a small number of patients treated at a

district general hospital in the UK raised concerns that mortality remains considerably

higher than estimates based on tertiary centres (24). This was confirmed in a record

linkage study conducted in England for the 1998-2000 period by Roberts *et al.* In that

study, 30-day mortality was 0.8% following elective colectomy and 5.7% following

emergency colectomy in ulcerative colitis patients (21). A later study by Kaplan *et al.,*

based on the American Nationwide Inpatient Sample database, reported similar figures of

0.7% and 5.4% for in-hospital mortality following elective and emergency colectomy,

respectively, in ulcerative colitis patients (22). This large-scale American study, covering

approximately 20% of Veterans' Administration admissions, identified low hospital

volume for colectomies, age over 40, comorbidity, and hospitalization for more than 7

days prior to colectomy as independent prognostic factors. Our study supports these

previous population-based investigations, showing that 30-day postoperative mortality

after total colectomy is probably not as low as suggested by reports from tertiary referral

centres. In addition, both the American study and our study underscore that a high

volume of these surgeries – and consequently a high degree of experience – may be

important in reducing postoperative mortality after both emergency and elective total

colectomy in IBD patients (35).

Our finding of 8.1% 30-day mortality after emergency surgery in Crohn's disease patients

contrasts with the Roberts *et al.* (21) study, which found a 30-day mortality of only 2.9%.

The main reason for this difference may be that we included only patients with total

colectomy, while Roberts *et al.* included patients undergoing all types of colectomy,

including right hemicolectomy.

The high mortality observed in our study calls for a critical revision of indications for

elective and emergency colectomy in patients with Crohn's colitis. A key recommendation

is to treat patients with severe ulcerative colitis in highly specialized centres. Similar

recommendations could be made for patients with Crohn's disease, although the number

of patients included in the present study was too low to provide statistical support.

Our study also confirmed that older age, emergency procedures, and a high degree of

comorbidity are associated with increased mortality after intestinal surgery

(22;23;36;37). In addition, it is known from population-based studies that hospitalization

for ulcerative colitis has a two-peak age incidence in a number of countries including

Denmark (38). We found that a high proportion of patients with ulcerative colitis

underwent total colectomy after age 60. An elective procedure performed earlier in life

would most likely reduce mortality in these patients. Interestingly, comorbidity had no

influence on MRRs among patients undergoing elective surgery. This suggests that

interventions to address comorbidities such as elevated blood pressure, arrhythmias, and diabetes may have taken place preoperatively, ensuring a safer postoperative course.

When medical treatment cannot achieve remission, delaying surgery can increase morbidity and mortality (19;39). Thus Kaplan *et al* (22) reported more than a doubling of the MRR among patients who were hospitalized (and presumably treated medically) for more than 7 days prior to surgery. Our study confirmed these findings for the subgroup undergoing elective surgery.

The main strength of the present study is its nationwide population-based design in the setting of a free tax-supported healthcare system with complete information on follow-up. Moreover, we used a validated approach to identify IBD patients undergoing surgery (40). These features ensure generalizability of our results and minimize selection bias. In addition, we were able to adjust for a number of important covariates, including comorbidity, for which we had high-quality data (41).

Our study also had several limitations. Although we used a validated approach to identify colectomized IBD patients, approximately 16% had codes corresponding to both Crohn's disease and ulcerative colitis. This likely reflected some degree of coding error. We therefore grouped IBD patients with mixed codes separately to minimize misclassification of the Crohn's and ulcerative colitis groups. We also did not have access to important clinical parameters, such as reasons for deciding to proceed with surgery or to discontinue medical treatment. Thus we were unable to investigate the role of these important issues in relation to postoperative mortality.

In conclusion, we observed high 30-day mortality among IBD patients undergoing emergency total colectomy. Among patients with ulcerative colitis, 30-day mortality was 5.2% after total emergency colectomy, and among patients with Crohn's disease, it was 8.1%. Low hospital volume of colectomy, comorbidity, and age over 40 were important prognostic factors.

Table 1: Characteristics of patients with an inflammatory bowel disease (IBD) diagnosis undergoing elective total colectomy in the period 1996-2010 in Denmark.

		Ulcerative colitis	Crohn's disease	Ulcerative colitis and Crohn's disease*
Total number (n=1450)		938 (64.7 %)	201 (13.9 %)	311 (21.4 %)
Males		485 (51.7%)	76 (37.8 %)	137 (44.1 %)
Females		453 (48.3 %)	125 (62.2 %)	174 (55.9 %)
Age at operation:				
	0-39 years	436 (46.5 %)	121 (60.2 %)	161 (51.8 %)
	40-59 years	292 (31.1 %)	55 (27.4 %)	91 (29.3 %)
	≥ 60 years	210 (22.4 %)	25 (12.4 %)	59 (19.0 %)
Number of annual colectomies for IBD performed in the surgical department				
	≤3/year	131 (14.0 %)	22 (11.0 %)	45 (14.5 %)
	3-12/year	166 (17.7 %)	28 (13.9 %)	44 (14.1 %)
	>12/year	641 (68.3 %)	151 (75.1 %)	222 (71.4%)
Duration of hospitalization before colectomy				
Admitted < 8 days before colectomy		557 (59.4 %)	136 (67.7 %)	178 (57.2 %)
Admitted ≥ 8 days before colectomy		381 (40.6 %)	65 (32.3 %)	133 (42.8 %)
Medical treatment within one year before colectomy				
TNF--α and Cyclosporine		64 (6.8 %)	10 (5.0 %)	37 (11.9 %)
Reoperation within 30 days postoperatively		73 (7.8 %)	21 (10.4 %)	21 (6.8 %)
Charlson Comorbidity Index Score				
	0	705 (75.2 %)	146 (72.6 %)	224 (72.0 %)
	1-2	194 (20.7 %)	45 (22.4 %)	69 (22.2 %)
	≥3	39 (4.2 %)	10 (5.0 %)	18 (5.8 %)
Colectomy type				
Colectomy with ileorectal anastomosis	KJFH00 - 01	54 (5.8 %)	42 (20.9 %)	39 (12.5 %)
Colectomy with ileostomy	KJFH10 - 11	523 (55.8 %)	99 (49.3 %)	170 (54.7 %)
Proctocolectomy with ileostomy	KJFH20 - 21	147 (15.7 %)	49 (24.4 %)	65 (20.9 %)
Restorative proctocolectomy ± ileostomy	KJFH30 - 33	197 (21.0 %)	5 (2.5 %)	28 (9.0 %)
Proctocolectomy with Koch reservoir	KJFH40	1 (0.1 %)	0 (0 %)	0 (0 %)
Other form of colectomy	KJFH96	16 (1.7 %)	6 (3.0 %)	9 (2.9 %)
Time period				
	1996-2000	307 (32.7 %)	67 (33.3 %)	114 (36.7 %)
	2001-2005	343 (36.6 %)	78 (38.8 %)	95 (30.6 %)
	2006-2010	288 (30.7 %)	56 (27.9 %)	102 (32.8 %)

* Patients for who codes for both ulcerative colitis and Crohn's disease were used at any preceding or subsequent admission or hospital contact.

Table 2: Characteristics of patients with an inflammatory bowel disease (IBD) diagnosis undergoing emergency total colectomy in the period 1996-2010 in Denmark.

		Ulcerative colitis	Crohn's disease	Ulcerative colitis and Crohn's disease*
Total number (n=1,439)		1056 (73.4 %)	136 (9.5 %)	247 (17.2%)
Males		559 (52.9 %)	62 (45.6 %)	113 (45.7 %)
Females		497 (47.1 %)	74 (54.4 %)	134 (54.3 %)
Age at operation:				
	0-39 years	503 (47.6 %)	56 (41.2 %)	134 (54.3 %)
	40-59 years	286 (27.1 %)	39 (28.7 %)	65 (26.3 %)
	≥ 60 years	267 (25.3 %)	41 (30.1 %)	48 (19.4 %)
Number of annual colectomies for IBD performed in the surgical department				
	≤3/year	168 (15.9 %)	31 (22.8 %)	43 (17.4 %)
	3-12/year	186 (17.6 %)	24 (17.6 %)	50 (20.2 %)
	>12/year	702 (66.5 %)	81 (59.6 %)	154 (62.4%)
Duration of hospitalization before colectomy				
	Admitted < 8 days before colectomy	296 (28.0 %)	45 (33.1 %)	85 (34.4 %)
	Admitted ≥ 8 days before colectomy	760 (72.0 %)	91 (66.9 %)	162 (65.6 %)
Medical treatment within one year before colectomy				
	TNF--α and cyclosporine	67 (6.3 %)	12 (8.8 %)	23 (9.3 %)
Reoperation within 30 days postoperatively		102 (9.7 %)	11 (8.2 %)	27 (10.9 %)
Charlson Comorbidity Index score				
	0	810 (76.7 %)	96 (70.6 %)	191 (77.3 %)
	1-2	194 (18.4 %)	30 (22.1 %)	49 (19.8 %)
	≥3	52 (4.9 %)	10 (7.3 %)	7(2.8 %)
Colectomy type				
Colectomy with ileorectal anastomosis	KJFH00 - 01	38 (3.6 %)	16 (11.8 %)	19 (7.7 %)
Colectomy with ileostomy	KJFH10 - 11	875 (82.9 %)	97 (71.3 %)	196 (74.4 %)
Proctocolectomy with ileostomy	KJFH20 - 21	73 (6.9 %)	8 (5.9 %)	21 (8.5 %)
Restorative proctocolectomy ± ileostomy	KJFH30 - 33	31 (2.9 %)	2 (1.5 %)	4 (1.6 %)
Proctocolectomy with Koch reservoir	KJFH40	1 (0.1 %)	0 (0 %)	0 (0 %)
Other form of colectomy	KJFH96	38 (3.6 %)	13 (9.6 %)	7 (2.8 %)
Time period				
	1996-2000	371 (35.1 %)	54 (39.7 %)	90 (36.4 %)
	2001-2005	385 (36.5 %)	36 (7.1 %)	84 (34.0 %)
	2006-2010	300 (28.4 %)	46 (11.0 %)	73 (30.0 %)

* Patients for who codes for both ulcerative colitis and Crohn's disease were used at any preceding or subsequent admission or hospital contact.

Table 3. Thirty-day mortality (in percent) in patients with an inflammatory bowel disease (IBD) diagnosis undergoing total colectomy in the period 1996-2010 in Denmark, by emergency vs. elective surgery.

		Ulcerative colitis		Crohn's disease		Ulcerative colitis and Crohn's disease*	
		Emergency	Elective	Emergency	Elective	Emergency	Elective
All		5.2 (55/1056)	0.9 (8/938)	8.1 (11/136)	1.5 (3/201)	4.0 (10/247)	1.0 (3/311)
Males		5.8 (31/559)	0.8 (4/485)	6.5 (4/62)	2.6 (2/76)	2.7 (3/113)	0.7 (1/137)
Females		5.2 (24/497)	0.9 (4/453)	9.5 (7/74)	0.8 (1/125)	5.2 (7/134)	1.1 (2/174)
Age at operation:							
	0-39 years	0.2 (1/503)	0.2 (1/436)	0 (0/56)	0 (0/121)	0 (0/134)	0 (0/161)
	40-59 years	1.7 (5/286)	0.0 (0/292)	5.1 (2/39)	0 (0/55)	3.1 (2/65)	1.1 (1/91)
	≥ 60 years	18.4 (49/267)	3.3 (7/210)	22.0 (9/41)	12 (3/25)	16.7 (8/48)	3.4 (2/59)
Number of annual colectomies for IBD performed by the surgical department							
	≤3/year	11.3 (19/168)	1.5 (2/131)	22.6 (7/31)	4.5 (1/22)	4.7 (2/43)	0 (0/45)
	3-12/year	5.9 (11/186)	1.8 (3/166)	8.3 (2/24)	0 (0/28)	4.0 (2/50)	0 (0/44)
	>12/year	3.6 (25/702)	0.5 (3/641)	2.5 (2/81)	1.3 (2/151)	3.9 (6/154)	1.4 (3/222)
Duration of hospitalization before colectomy							
	Admitted < 8 days before colectomy	7.1 (21/296)	0.2 (1/557)	20.0 (9/45)	1.5 (2/136)	4.7 (4/85)	0.0 (0/178)
	Admitted ≥ 8 days before colectomy	4.5 (34/760)	1.8 (7/381)	2.2 (2/91)	1.5 (1/65)	3.7 (6/162)	2.3 (3/133)
Medical treatment within one year before colectomy							
	TNF--α or cyclosporine	0 (0/67)	0 (0/64)	0 (0/12)	0 (0/10)	0 (0/23)	0 (0/37)
Reoperation within 30 days postoperatively		8.8 (9/102)	4.1 (3/73)	18.1 (2/11)	4.8 (1/21)	7.4 (2/27)	0 (0/21)
Charlson Comorbidity Index score:							
	0	2.2 (18/810)	0.6 (4/705)	3.1 (3/96)	0.0 (0/146)	2.1 (4/191)	0.9 (2/224)
	1-2	12.9 (25/194)	1.6 (3/194)	20.0 (6/30)	4.4 (2/45)	6.1 (3/49)	1.4 (1/69)
	≥3	23.1 (12/52)	2.6 (1/39)	20.0 (2/10)	10 (1/10)	42.9 (3/7)	0 (0/18)
Colectomy type							
Colectomy with ileorectal anastomosis	KJFH00 - 01	15.8 (6/38)	0 (0/54)	6.3 (1/16)	0 (0/42)	0 (0/19)	0 (0/39)
Colectomy with ileostomy	KJFH10 - 11	4.9 (43/875)	1.5 (8/523)	9.3 (9/97)	3.0 (3/99)	4.6 (9/196)	1.2 (2/170)
Proctocolectomy with ileostomy	KJFH20 - 21	5.5 (4/73)	0 (0/147)	0 (0/8)	0 (0/49)	0 (0/21)	0 (0/65)
Restorative proctocolectomy ± ileostomy	KJFH30 - 33	6.5 (2/31)	0 (0/197)	0 (0/2)	0 (0/5)	0 (0/4)	3.6 (1/28)
Proctocolectomy with Koch reservoir	KJFH40	0 (0/1)	0 (0/1)	0 (0/0)	0 (0/5)	0 (0/0)	0 (0/0)
Other form of colectomy	KJFH96	0 (0/38)	0 (0/16)	7.7 (1/13)	0 (0/6)	14.3 (1/7)	0 (0/9)
Time period							
	1996-2000	5.9 (22/371)	0.3 (1/307)	7.4 (4/54)	1.5 (1/67)	1.1 (1/90)	0.9 (1/114)
	2001-2005	5.2 (20/385)	0.3 (1/343)	2.8 (1/36)	2.6 (2/78)	6.0 (5/84)	1.1 (1/95)
	2005-2010	4.3 (13/300)	2.1 (6/288)	13.0 (6/46)	0 (0/56)	5.5 (4/73)	1.0 (1/102)

* Patients for who codes for both ulcerative colitis and Crohn's disease were used at any preceding or subsequent admission or hospital contact.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Table 4. Mortality rate ratios in patients with ulcerative colitis undergoing total colectomy in the period 1996-2010 in Denmark.

	Emergency		Elective	
	Crude	**Adj***	**Crude**	**Adj***
Females	Ref.	Ref.	Ref.	Ref.
Males	**1.15**	**1.16**	**0.94**	**0.79**
	(0.68-1.97)	(0.68-1.98)	(0.23-3.74)	(0.20-3.19)
Age at operation:				
0-39 years	Ref	Ref	Ref	Ref
≥ 40 years				
	26.18	**17.78**	**24.65**	**24.51**
	(11.2-61.1)	(7.3-43.1)	(3.0-200)	(2.81-213.8)
Number of annual colectomies for IBD performed by the surgical department				
≤ 3/year	Ref.	Ref.	Ref.	Ref.
3-12/year	**0.51**	**0.58**	**1.18**	**1.51**
	(0.24-1.06)	(0.28-1.23)	(0.20-7.08)	(0.25-9.18)
>12/year	**0.30**	**0.46**	**0.30**	**0.63**
	(0.17-0.55)	(0.25-0.84)	(0.05-1.82)	(0.10-3.89)
Duration of hospitalization before colectomy				
Admitted < 8 days before colectomy	Ref.	Ref.	Ref.	Ref.
Admitted ≥ 8 days before colectomy	**0.62**	**0.67**	**10.30**	**10.26**
	(0.36-1.06)	(0.39-1.16)	(1.27-83.6)	(1.25-84.2)
Charlson Comorbidity Index score:				
0	Ref.	Ref.	Ref.	Ref.
≥1	**7.20**	**2.56**	**3.05**	**1.06**
	(4.10-12.65)	(1.42-4.61)	(0.76-12.2)	(0.25-4.46)
Time period				
1996-2000	Ref.	Ref.	Ref.	Ref.
2001-2005	**0.87**	**0.90**	**0.90**	**0.90**
	(0.48-1.60)	(0.49-1.64)	(0.06-14.31)	(0.06-14.54)
2005-2010	**0.72**	**0.60**	**6.47**	**5.18**
	(0.36-1.43)	(0.30-1.20)	(0.78-53.7)	(0.62-43.6)

*Adj: Adjusted for age, gender and comorbidity.

Reference List

(1) Andersson P, Olaison G, Bodemar G *et al*. Surgery for Crohn colitis over a twenty-eight-year period: fewer stomas and the replacement of total colectomy by segmental resection. *Scand J Gastroenterol* 2002;**37**(1):68-73.

(2) Cosnes J, Nion-Larmurier I, Beaugerie L *et al*. Impact of the increasing use of immunosuppressants in Crohn's disease on the need for intestinal surgery. *Gut* 2005;**54**(2):237-41.

(3) Actis GC, Pellicano R, Pinna-Pintor M *et al*. Rescue with infliximab and surgical outcomes for refractory ulcerative colitis. *J Am Coll Surg* 2007;**205**(4):e3-e4.

(4) Hanauer SB, Feagan BG, Lichtenstein GR *et al*. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. *Lancet* 2002;**359**(9317):1541-9.

(5) Jakobovits SL, Jewell DP, Travis SP. Infliximab for the treatment of ulcerative colitis: outcomes in Oxford from 2000 to 2006. *Aliment Pharmacol Ther* 2007;**25**(9):1055-60.

(6) Järnerot G, Hertervig E, Friis-Liby I *et al*. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study. *Gastroenterology* 2005;**128**(7):1805-11.

(7) Rutgeerts P, Sandborn WJ, Feagan BG *et al*. Infliximab for induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2005;**353**(23):2462-76.

(8) Bernell O, Lapidus A, Hellers G. Risk factors for surgery and recurrence in 907 patients with primary ileocaecal Crohn's disease. *Br J Surg* 2000;**87**(12):1697-701.

(9) Langholz E, Munkholm P, Davidsen M *et al*. Course of ulcerative colitis: analysis of changes in disease activity over years. *Gastroenterology* 1994;**107**(1):3-11.

(10) Sandborn WJ, Rutgeerts P, Feagan BG *et al*. Colectomy rate comparison after treatment of ulcerative colitis with placebo or infliximab. *Gastroenterology* 2009;**137**(4):1250-60.

(11) Taxonera C, Rodrigo L, Casellas F *et al*. Infliximab maintenance therapy is associated with decreases in direct resource use in patients with luminal or fistulizing Crohn's disease. *J Clin Gastroenterol* 2009;**43**(10):950-6.

(12) Ramadas AV, Gunesh S, Thomas GA *et al*. Natural history of Crohn's disease in a population-based cohort from Cardiff (1986-2003): a study of changes in medical treatment and surgical resection rates. *Gut* 2010;**59**(9):1200-6.

(13) Lazarev M, Ullman T, Schraut WH *et al*. Small bowel resection rates in Crohn's disease and the indication for surgery over time: experience from a large tertiary care center. *Inflamm Bowel Dis* 2010;**16**(5):830-5.

(14) Turner D, Walsh CM, Steinhart AH *et al*. Response to corticosteroids in severe ulcerative colitis: a systematic review of the literature and a meta-regression. *Clin Gastroenterol Hepatol* 2007;**5**(1):103-10.

(15) Aratari A, Papi C, Clemente V *et al*. Colectomy rate in acute severe ulcerative colitis in the infliximab era. *Dig Liver Dis* 2008;**40**(10):821-6.

(16) Gustavsson A, Halfvarson J, Magnuson A *et al*. Long-Term Colectomy Rate After Intensive Intravenous Corticosteroid Therapy for Ulcerative Colitis Prior to the Immunosuppressive Treatment Era. *Am J Gastroenterol* 2006.

(17) Goligher JC. Surgical treatment of ulcerative colitis. *Br Med J* 1961;**1**(5220):151-4.

(18) Lennard-Jones JE, VIVIAN AB. Fulminating ulcerative colitis. Recent experience in management. *Br Med J* 1960;**2**(5192):96-102.

(19) Goligher JC, Hoffman DC, De Dombal FT. Surgical treatment of severe attacks of ulcerative colitis, with special reference to the advantages of early operation. *Br Med J* 1970;**4**(737):703-6.

(20) Alves A, Panis Y, Bouhnik Y *et al*. Subtotal colectomy for severe acute colitis: a 20-year experience of a tertiary care center with an aggressive and early surgical policy. *J Am Coll Surg* 2003;**197**(3):379-85.

(21) Roberts SE, Williams JG, Yeates D *et al*. Mortality in patients with and without colectomy admitted to hospital for ulcerative colitis and Crohn's disease: record linkage studies. *BMJ* 2007;**335**(7628):1033.

(22) Kaplan G, McCarthy EP, Ayanian JZ *et al*. Impact of Hospital Volume on Postoperative Morbidity and Mortality Following a Colectomy for Ulcerative Colitis. *Gastroenterology* 2008;**134**(3):680-7.

(23) Nicholls RJ, Clark DN, Kelso L *et al*. Nationwide linkage analysis in Scotland implicates age as the critical overall determinant of mortality in ulcerative colitis. *Aliment Pharmacol Ther* 2010;**31**(12):1310-21.

(24) Stenner JMC, White P, Gould SR. Audit of the management of severe ulcerative colitis in a DGH. *Gut* 2001;**48**(Suppl 1):A87.

(25) Andersen TF, Madsen M, Jørgensen J *et al*. The Danish National Hospital Register. A valuable source of data for modern health sciences. *Dan Med Bull* 1999;**46**(3):263-8.

(26) NOMESCO Classification of Surgical Procedures. 1-1-2010. Copenhagen.

(27) Frank L. Epidemiology. When an entire country is a cohort. *Science* 2000;**287**(5462):2398-9.

(28) Charlson ME, Pompei P, Ales KL *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**(5):373-83.

(29) Quan H, Sundararajan V, Halfon P *et al*. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;**43**(11):1130-9.

(30) EDWARDS FC, Truelove SC. The course and prognosis of ulcerative colitis. *Gut* 1963;**4**:299-315.

(31) Koudahl G, Kristensen M. Postoperative mortality and complications after colectomy for ulcerative colitis. *Scand J Gastroenterol Suppl* 1976;**37**:117-22.

(32) Frykholm G, Pahlman L, Enblad P *et al*. Early outcome after emergency and elective surgery for ulcerative colitis. *Acta Chir Scand* 1989;**155**(11-12):601-5.

(33) Carter FM, McLeod RS, Cohen Z. Subtotal colectomy for ulcerative colitis: complications related to the rectal remnant. *Dis Colon Rectum* 1991;**34**(11):1005-9.

(34) Hyman NH, Cataldo P, Osler T. Urgent subtotal colectomy for severe inflammatory bowel disease. *Dis Colon Rectum* 2005;**48**(1):70-3.

(35) Ananthakrishnan AN, McGinley EL, Binion DG. Does it matter where you are hospitalized for inflammatory bowel disease? A nationwide analysis of hospital volume. *Am J Gastroenterol* 2008;**103**(11):2789-98.

(36) Faiz O, Warusavitarne J, Bottle A *et al*. Nonelective excisional colorectal surgery in English National Health Service Trusts: a study of outcomes from Hospital Episode Statistics Data between 1996 and 2007. *J Am Coll Surg* 2010;**210**(4):390-401.

(37) Kurian A, Suryadevara S, Ramaraju D *et al*. In-hospital and 6-month mortality rates after open elective vs open emergent colectomy in patients older than 80 years. *Dis Colon Rectum* 2011;**54**(4):467-71.

(38) Sonnenberg A. Age distribution of IBD hospitalization. *Inflamm Bowel Dis* 2010;**16**(3):452-7.

(39) Brooke BN. Cortisone and ulcerative colitis; and adverse effect. *Lancet* 1956;**271**(6954):1175-7.

(40) Erichsen R, Sværke C, Tøttrup A. The coding quality of acute total colectomy in inflammatory bowel disease patients in a nationwide hospital registry. *Pharmacoepidemiology and Drug Safety* 2011;**20**(S1):S165.

(41) Thygesen SK, Christiansen CF, Christensen S *et al*. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. *BMC Med Res Methodol* 2011;**11**:83.

It is declared that each author contributed to
- conception and design, or analysis and interpretation of data
- drafting the article or revising it critically for important intellectual content
- and final approval of the version to be published.

Anders Tøttrup and Henrik Toft Sørensen af garantors for the whole manuscript.

Conflicts of interest: The authors declare no conflicts of interest.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Appendix Table 1. Codes used in this study from the Danish National Registry of

Patients.

International Classification of Diseases (ICD) codes:

Inflammatory Bowel Disease:

ICD-8: 563.01 (Crohn's disease); 563.19+569.04 (Ulcerative colitis)

ICD-10: K50 (Crohn's disease); K51 (Ulcerative colitis)

Clostridium difficile infection

ICD-10: A047

Surgical procedure codes (NOMESCO) and treatment codes:

Total colectomy:

KJFH

Reoperation:

KJW

TNF-α treatment and cyclosporine:

BOHJ18A and BOHJ20

Appendix Table 2. Definition of diseases included in the Charlson Comorbidity Index

(International Classification of Diseases (ICD) codes).

	Disease	**ICD-8 codes**	**ICD-10 codes**	**Score**
1	Myocardial infarction	410	I21;I22;I23	1
2	Congestive heart failure	427.09; 427.10; 427.11; 427.19; 428.99; 782.49	I50; I11.0; I13.0; I13.2	1
3	Peripheral vascular disease	440; 441; 442; 443; 444; 445	I70; I71; I72; I73; I74; I77	1
4	Cerebrovascular disease	430-438	I60-I69; G45; G46	1
5	Dementia	290.09-290.19; 293.09	F00-F03; F05.1; G30	1
6	Chronic pulmonary disease	490-493; 515-518	J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2; J98.3	1
7	Connective tissue disease	712; 716; 734; 446; 135.99	M05; M06; M08; M09;M30;M31; M32; M33; M34; M35; M36; D86	1
8	Ulcer disease	530.91; 530.98; 531-534	K22.1; K25-K28	1
9	Mild liver disease	571 57301 57304	B18; K70.0-K70.3; K70.9; K71; K73; K74; K76.0	1
10	Diabetes type 1	249.00; 249.06; 249.07; 249.09 250.00; 250.06; 250.07; 250.09	E10.0, E10.1; E10.9	1
	Diabetes type 2		E11.0; E11.1; E11.9	

11	Hemiplegia	344	G81; G82	2
12	Moderate to severe renal disease	403; 404; 580-583; 584; 590.09; 593.19; 753.10-753.19; 792	I12; I13; N00-N05; N07; N11; N14; N17-N19; Q61	2
13	Diabetes with end-organ damage: - type 1 - type 2	 249.01-249.05; 249.08 250.01-250.05; 250.08	 E10.2-E10.8 E11.2-E11.8	2
14	Any tumor	140-194	C00-C75	2
15	Leukemia	204-207	C91-C95	2
16	Lymphoma	200-203; 275.59	C81-C85; C88; C90; C96	2
17	Moderate/severe liver disease	57300 07000 07002 07004 07006 07008 4560	B15.0; B16.0; B16.2; B19.0; K70.4; K72; K76.6; I85	3
18	Metastatic solid tumor	195-198; 199	C76-C80 C78.7)	6
19	AIDS	079.83	B21-B24	6

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Thirty-day mortality after elective and emergency total colectomy in Danish patients with inflammatory bowel disease:
A population-based nationwide cohort study

SCHOLARONE™
Manuscripts

Thirty-day mortality after elective and emergency total colectomy in Danish patients with inflammatory bowel disease: A population-based nationwide cohort study

A. Tøttrup[1], R. Erichsen[2], C. Sværke[2], S. Laurberg[1], H.T. Sørensen[2].

[1]Department of Surgery P, Aarhus University Hospital

[2]Department of Clinical Epidemiology, Aarhus University Hospital

Corresponding author: Dr. Anders Tøttrup, Department of Surgery P, Aarhus University Hospital, Tage Hansensgade, 8000 Aarhus C, Denmark. Mail: andtoe@rm.dk. Phone: +45 89497703. Fax: +45 89497549

Abstract

Objectives

The purpose of our investigation was to assess 30-day mortality among Danish IBD patients and to examine the prognostic impact of hospital total colectomy volume, age, gender, and comorbidity.

Design

Cohort study.

Setting

We compared 30-day survival over the 1996-2010 period among 2,889 IBD patients with total colectomy identified in the Danish National Registry of Patients. This registry covers all hospitals in Denmark. Postoperative survival patterns for patients with ulcerative colitis and Crohn's disease were compared, using proportional hazard regression. The regression model accounted for the timing of surgery, hospital total colectomy volume, age, gender, and comorbidity.

Participants

Patients were enrolled in the study if they had a hospital registry diagnosis of IBD, with accompanying procedure codes for total colectomy. (See codes in Appendix Table 1). Hospitalizations were described as elective or emergency and patients were categorized as having Crohn's disease, ulcerative colitis, or as a mixed group.

Outcome Measures

Primary outcome measure was 30-day mortality.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Results

Among 2,889 IBD patients with total colectomy, 1439 (50%) underwent surgery during

an emergency hospitalization. Thirty-day mortality was 5.3% (76/1439) among

emergency cases, compared to 1% (14/1450) among elective cases. The highest mortality

(8.1%; 11 out of 136)) was observed among Crohn's patients undergoing emergency

surgery. The mortality of patients with ulcerative colitis undergoing emergency surgery

was 5.2% (55/1056). After elective surgery, the 30-day mortality was 0.9% (8/938)

among patients with ulcerative colitis and 1.5% (3/201) among Crohn's disease patients.

Low hospital total colectomy volume, comorbidity, and high age were associated with

increased 30-day mortality in ulcerative colitis patients undergoing emergency surgery.

Conclusion

Emergency total colectomy among patients with ulcerative colitis and particularly

Crohn's disease is associated with substantial 30-day mortality.

Significance of this study

Article focus

☐   Elective and emergency total colectomy is commonly performed in

inflammatory bowel disease

☐   Emergency operations are associated with higher mortality than elective

procedures.

Key messages

☐   IBD patients undergoing emergency total colectomy have a 30-day mortality

of 5.3% as opposed to 1% after elective total colectomy.

☐   Low hospital volume, high age and comorbidity are associated with increased mortality in patients with ulcerative colitis undergoing emergency surgery.

☐   It is suggested to centralize treatment, and to aim for elective procedures in high risk patients.

Strengths and limitations of this study

☐   The study covers complete national data on total colectomies performed for inflammatory disease.

☐   The unique ID number of all patients makes recording of all events highly reliable.

☐   The main limitation is lack of access to specific clinical parameters

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Inflammatory bowel diseases (IBD) cause serious morbidity and disability in people of all ages. Medical treatment remains the cornerstone for managing these diseases. Over the past two decades, use of immunosuppressants such as azathioprine (1;2) has increased significantly as a treatment modality. More recently, potent biological treatments have proved effective in treating both ulcerative colitis and Crohn's disease (3-7). Historical data have shown that up to 83% of patients with Crohn's disease underwent at least one bowel resection during a 10-year period (8), and up to 25% of patients with ulcerative colitis needed surgical treatment (9). While some recent studies show that modern medical treatment may decrease the need for surgery in IBD patients (10-12), others suggest that this is not the case (2;13).

In patients with severe ulcerative colitis, colectomy rates have remained stable over the past decades (14), although the introduction of biological rescue therapy is likely to decrease use of this surgical intervention in coming years (15;16). Mortality rates of up to 30% have been reported historically in patients undergoing emergency total colectomy for ulcerative colitis (17;18). Delay in patient referral for surgery has been proposed as the reason for high postoperative mortality (19). Although recent data from a highly specialized centre showed in-hospital mortality of less than 1% after emergency colectomy (20), population-based studies from the England (21) and the US (22) have reported postoperative mortality as high as 5.4% – 5.7% after emergency colectomy. This contrasts with rates as low as 0.7% – 0.8 % after elective colectomy. Advanced age, comorbidity, delay of more than 6 days between hospital admission and colectomy, and low hospital volume have been associated with increased postoperative mortality after colectomy in IBD patients (22;23).

In many countries, including Denmark, increasing specialization has occurred, with more rare and complicated conditions treated at specialized centres. Still, severe IBD continues to be treated at general district hospitals, where the number of patients is low and outcome appears to be poor (24).

The present study aimed to investigate 30-day mortality after elective and emergency total colectomy in Danish IBD patients, with special emphasis on the prognostic impact of hospital total colectomy volume, age, sex, and comorbidity.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Material and methods

We conducted this follow-up study in the setting of the entire Danish population of 5.4 million people during the January 1, 1996 – December 31, 2010 period. The Danish National Health Service provides tax-funded medical care for all Danish residents.

Data sources

The Danish National Registry of Patients (DNRP) contains data on all non-psychiatric hospitalizations in Denmark since 1977 and on hospital outpatient clinics contacts since 1995 (25). The DNRP records civil registration number, hospital code, department code, date and type of admission (emergency/elective), dates and codes of procedures, admission and discharge dates, selected medical therapies, and up to 20 discharge diagnoses, coded by physicians according to the International Classification of Diseases (ICD), eighth revision until the end of 1993 and 10th revision thereafter. It is mandatory that all surgical procedures are coded according to the Nordic Medico-Statistical Committee (NOMESCO) classification (26).

We linked individual-level data from the DNRP using the civil registration number, a unique 10-digit identifier assigned at birth to all Danish residents by the Civil Registration System (CRS) (27). The CRS also tracks vital status and the residence of all Danish citizens and is updated daily.

Patients with IBD and total colectomy

Patients were enrolled in the study if they had a hospital registry diagnosis of IBD, with accompanying procedure codes for total colectomy. (See codes in Appendix Table 1). Hospitalizations were described as elective or emergency and patients were categorized as having Crohn's disease, ulcerative colitis, or as a mixed group if their records

contained ICD codes for both Crohn's disease and ulcerative colitis. We also obtained information on reoperation occurring within 30 days of the primary surgery, TNF-α-inhibitor and cyclosporine treatment in the year prior to surgery, and Clostridium difficile infections. (See codes in Appendix Table 1). We categorised IBD patients according to age at date of total colectomy (0-39, 40-59, and 60+ years), year of colectomy (1996-2000, 2001-2005, and 2006-2010), and hospital total colectomy volume defined as annual number of total colectomies performed on IBD patients by the surgical department and categorised according to Kaplan et al (low: <3, medium: 3-12, high 12+) (22)

We also extracted information from the DNRP on comorbidity, *i.e.*, diseases coexisting with IBD. We summarized comorbidity status using the Charlson Comorbidity Index (CCI) (28). The CCI's scoring system assigns between one and six points to a range of diseases. Each patient's sum of points represents a measure of his or her comorbidity burden. We placed our study patients into three groups according to their sum of points: 0 points ("no comorbidity"), 1 to 2 points ("low comorbidity"); and 3 or more points ("high comorbidity") (28). We defined comorbid diseases according to the ICD-10 codes provided by Quan *et al.* (29), matching ICD-8 codes to ICD-10 codes as closely as possible. (See codes in Appendix Table 2).

Mortality data

We followed IBD patients who were acutely or electively hospitalized for a procedure of total colectomy in the period 1996-2010, from the date of colectomy until death, 30 days post-surgery, or December 31, 2010, whichever came first.

Statistical analysis

Our main outcome of interest was 30-day mortality, estimated as the number of deaths after total elective or emergency colectomy divided by the total number of IBD patients undergoing elective/emergency colectomy. We stratified our study sample by IBD type and by the following covariates: gender, age at colectomy, year of colectomy, hospital total colectomy volume (22), duration of hospitalization prior to surgery (< 8 days, ≥ 8 days), presence or absence of TNF-α-inhibitor or cyclosporine therapy in the year before the total colectomy, reoperation, CCI score, and colectomy subtype. We calculated differences in mortality and corresponding 95% confidence intervals (95% CI) between patients undergoing emergency vs. elective surgery overall. We also calculated mortality rates for ulcerative colitis patients by age and hospital total colectomy volume. In addition, we used Cox proportional-hazards regression to estimate mortality rate ratios (MRR) for each covariate, using the reference values shown in Table 4. MRRs were adjusted for age (0-39, ≥ 40 years), gender, and CCI score (0 and ≥1 points) to evaluate the independent prognostic effect of the covariates included in the model. (We lacked statistical power to mutually adjust for all covariates). In a subsequent analysis, we estimated the proportion of patients who underwent reoperation, as a secondary outcome.

Results

Descriptive data

In total, 2,889 IBD patients with total colectomy were identified from the DNRP for the January 1, 1996 - December 31, 2010 period. Of these, 1,439 (49.8%) underwent surgery during an emergency hospitalization (49% female). Characteristics of IBD patients by type of surgery (elective and emergency) are shown in Tables 1 and 2. The majority of patients had a total colectomy due to ulcerative colitis (64.7% for elective cases; 73.4% for emergency cases). Of the 1,450 elective cases (51.9% female), 718 (49.5%) were younger than 40 years, 438 (30.2%) were between ages 40 and 59, and the remaining 294 (20.3%) were ≥ 60 years old (Table 1). Of the 1,439 emergency cases 693 (48.2%) were younger than 40 years, 390 (27.1 %) were between ages 40 and 59, and the remaining 356 (24.7%) were ≥ 60 years old (Table 2). The majority of elective (69.9%) and emergency (65.1%) surgeries took place in high-volume hospitals with >12 total colectomies/year (Tables 1 and 2). None of the patients included in the present study were coded for infection with Clostridium difficile.

Among all IBD patients, 1,075 (74.1%) of elective cases and 1,097 (76.2%) of emergency cases had a CCI score of 0, and 375 (25.9%) of elective cases and 342 (23.8%) of emergency cases had a score of 1 or higher. Comorbidity scores were distributed almost equally between the three IBD groups (Tables 1 and 2). Total colectomy with ileostomy was performed more often in emergency cases than in elective cases (81.2% vs. 54.6%). Proctocolectomy with ileostomy was carried out in 102 emergency cases (7.1%) and 261 elective cases (18%). Frequencies of procedures by type and disease groups are shown in Tables 1 and 2.

Mortality

Within 30 days following colectomy, 14 of the 1,450 patients who underwent elective

surgery died (1.0%), while 76 of the 1,439 emergency patients (5.3%) died (mortality

difference = 4.3%; 95% CI: 3.1%, - 5.6%). Among ulcerative colitis patients, mortality was

0.9% (8/938) in the elective group and 5.2% in the emergency group. Patients with

Crohn's disease undergoing emergency surgery had the highest 30-day mortality (11/136

= 8.1%).

Mortality was low in ulcerative colitis patients aged under 40 (0.2%, Table 3), both for

elective and emergency surgery. For patients aged 60 years or older, mortality increased

to 3.3% for those undergoing colectomy on an elective basis and to 18.4% for those

undergoing this procedure on an emergency basis (mortality difference = 15.1%; 95% CI:

9.8%, 20.3%). Mortality was lowest in high-volume hospitals (0.5% for elective and 3.6%

for emergency cases [mortality difference = 3.1%; 95% CI: 1.6%, 4.6%], Table 3). Patients

with high CCI scores also had high mortality. Table 3 shows mortality according to

duration of hospitalization prior to colectomy, colectomy type, and time period. Numbers

of outcomes in patients with Crohn's disease or mixed Crohn's disease/ulcerative colitis

were too small to permit more detailed analysis of mortality.

In a subsequent analysis we found that reoperation within 30 days occurred in 115

(7.9%) elective cases and in 140 (9.7%) emergency cases and was associated with

particularly high mortality.

Prognostic factors in patients with ulcerative colitis.

Crude and adjusted MRRs for patients with ulcerative colitis are shown in Table 4.

Higher age at operation (≥ 40 years) was associated with major increases in MRRs in both

emergency and elective cases. A CCI score ≥ 1 was associated with an increased MRR

after emergency colectomy, but had no influence on MRR in patients undergoing elective

colectomy. MRRs were lower for cases undergoing surgery at high-volume hospitals

compared with low-volume hospitals. In the regression model for emergency colectomies,

gender, duration of hospitalization before colectomy, and time period were not clearly

associated with mortality. In the regression model for elective colectomies, hospitalization

for 8 days or more prior to surgery was associated with an increased MRR. Numbers

were too low to permit calculation of MRRs for patients with Crohn's disease or with both

ulcerative colitis and Crohn's disease.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Discussion

Our study showed that 30-day postoperative mortality after total colectomy was 5.3% for

IBD patients undergoing surgery on an emergency basis and 1 % for those with elective

procedures. We also found that comorbidity, surgery in a hospital performing few annual

colectomies, and age over 40 were associated with increased mortality after emergency

total colectomy in patients with ulcerative colitis. Age over 40 and hospitalization for 8

days or more prior to colectomy were associated with increased mortality in ulcerative

colitis patients undergoing elective total colectomy.

Our data extend previous research with recent population based data. Mortality after

emergency total colectomy for ulcerative colitis was as high as 27% (19;30-32) in the

past. More recent data from tertiary referral centres indicates in-hospital mortality of less

than 0.6% (20;33;34). However, a short report on a small number of patients treated at a

district general hospital in the UK raised concerns that mortality remains considerably

higher than estimates based on tertiary centres (24). This was confirmed in a record

linkage study conducted in England for the 1998-2000 period by Roberts *et al.* In that

study, 30-day mortality was 0.8% following elective colectomy and 5.7% following

emergency colectomy in ulcerative colitis patients (21). A later study by Kaplan *et al.,*

based on the American Nationwide Inpatient Sample database, reported similar figures of

0.7% and 5.4% for in-hospital mortality following elective and emergency colectomy,

respectively, in ulcerative colitis patients (22). This large-scale American study, covering

approximately 20% of Veterans' Administration admissions, identified low hospital

volume for colectomies, age over 40, comorbidity, and hospitalization for more than 7

days prior to colectomy as independent prognostic factors. Our study supports these

previous population-based investigations, showing that 30-day postoperative mortality

after total colectomy is probably not as low as suggested by reports from tertiary referral

centres. In addition, both the American study and our study underscore that a high

volume of these surgeries – and consequently a high degree of experience – may be

important in reducing postoperative mortality after both emergency and elective total

colectomy in IBD patients (35).

Our finding of 8.1% 30-day mortality after emergency surgery in Crohn's disease patients

contrasts with the Roberts *et al.* (21) study, which found a 30-day mortality of only 2.9%.

The main reason for this difference may be that we included only patients with total

colectomy, while Roberts *et al.* included patients undergoing all types of colectomy,

including right hemicolectomy. Regrettably, the number of patients in the Crohn group

was low precluding detailed statistical analysis of this cohort of patients. The group of

patients with both a diagnosis of ulcerative colitis and Crohn's disease was relatively

large, and we assume that it includes patients, whose diagnosis has indeed been re-

classified. In may also include patients, who at a single occasion has received an

incorrect diagnosis, because we expanded our search for diagnosis to a period beginning

in 1997 and continuing until conclusion of the study. In this respect, our study was

different to the previously population-based studies (21-23).

The high mortality observed in our study calls for a critical revision of indications for

elective and emergency colectomy in patients with Crohn's colitis. A key recommendation

is to treat patients with severe ulcerative colitis in highly specialized centres. Similar

recommendations could be made for patients with Crohn's disease, although the number

of patients included in the present study was too low to provide statistical support.

Our study also confirmed that older age, emergency procedures, and a high degree of

comorbidity are associated with increased mortality after intestinal surgery

(22;23;36;37). In addition, it is known from population-based studies that hospitalization for ulcerative colitis has a two-peak age incidence in a number of countries including Denmark (38). We found that a high proportion of patients with ulcerative colitis underwent total colectomy after age 60. An elective procedure performed earlier in life would most likely reduce mortality in these patients. Interestingly, comorbidity had no influence on MRRs among patients undergoing elective surgery. This suggests that interventions to address comorbidities such as elevated blood pressure, arrhythmias, and diabetes may have taken place preoperatively, ensuring a safer postoperative course. It is not possible from the present result to speculate about the influence of surgical procedure on mortality. First of all, the number of patients in the different subgroups is fairly low precluding statistical subgroup analysis, and secondly, the preoperative condition of the patients has probably had influence on the choice of surgical procedure.

When medical treatment cannot achieve remission, delaying surgery can increase morbidity and mortality (19;39). Thus Kaplan *et al* (22) reported more than a doubling of the MRR among patients who were hospitalized (and presumably treated medically) for more than 7 days prior to surgery. Our study confirmed these findings for the subgroup undergoing elective surgery.

The main strength of the present study is its nationwide population-based design in the setting of a free tax-supported healthcare system with complete information on follow-up. Moreover, we used a validated approach to identify IBD patients undergoing surgery (40). These features ensure generalizability of our results and minimize selection bias. In addition, we were able to adjust for a number of important covariates, including comorbidity, for which we had high-quality data (41).

Our study also had several limitations. Although we used a validated approach to identify colectomized IBD patients, approximately 16% had codes corresponding to both Crohn's disease and ulcerative colitis. As mentioned, this is most likely due to some degree of coding error. We therefore grouped IBD patients with mixed codes separately to minimize misclassification of the Crohn's and ulcerative colitis groups. We also did not have access to important clinical parameters, such as reasons for deciding to proceed with surgery or to discontinue medical treatment. Thus we were unable to investigate the role of these important issues in relation to postoperative mortality. Finally, registration of recue therapy with cyclosporine or infliximab was probably incomplete, because such registration has only recently become compulsory in our country.

In conclusion, we observed high 30-day mortality among IBD patients undergoing emergency total colectomy. Among patients with ulcerative colitis, 30-day mortality was 5.2% after total emergency colectomy, and among patients with Crohn's disease, it was 8.1%. Low hospital volume of colectomy, comorbidity, and age over 40 were important prognostic factors.

Table 1: Characteristics of patients with an inflammatory bowel disease (IBD) diagnosis undergoing elective total colectomy in the period 1996-2010 in Denmark.

		Ulcerative colitis	Crohn's disease	Ulcerative colitis and Crohn's disease*
Total number (n=1450)		938 (64.7 %)	201 (13.9 %)	311 (21.4 %)
Males		485 (51.7%)	76 (37.8 %)	137 (44.1 %)
Females		453 (48.3 %)	125 (62.2 %)	174 (55.9 %)
Age at operation:				
	0-39 years	436 (46.5 %)	121 (60.2 %)	161 (51.8 %)
	40-59 years	292 (31.1 %)	55 (27.4 %)	91 (29.3 %)
	≥ 60 years	210 (22.4 %)	25 (12.4 %)	59 (19.0 %)
Number of annual colectomies for IBD performed in the surgical department				
	≤3/year	131 (14.0 %)	22 (11.0 %)	45 (14.5 %)
	3-12/year	166 (17.7 %)	28 (13.9 %)	44 (14.1 %)
	>12/year	641 (68.3 %)	151 (75.1 %)	222 (71.4%)
Duration of hospitalization before colectomy				
	Admitted < 8 days before colectomy	557 (59.4 %)	136 (67.7 %)	178 (57.2 %)
	Admitted ≥ 8 days before colectomy	381 (40.6 %)	65 (32.3 %)	133 (42.8 %)
Medical treatment within one year before colectomy				
	TNF--α and Cyclosporine	64 (6.8 %)	10 (5.0 %)	37 (11.9 %)
Reoperation within 30 days postoperatively		73 (7.8 %)	21 (10.4 %)	21 (6.8 %)
Charlson Comorbidity Index Score				
	0	705 (75.2 %)	146 (72.6 %)	224 (72.0 %)
	1-2	194 (20.7 %)	45 (22.4 %)	69 (22.2 %)
	≥3	39 (4.2 %)	10 (5.0 %)	18 (5.8 %)
Colectomy type				
Colectomy with ileorectal anastomosis	KJFH00 - 01	54 (5.8 %)	42 (20.9 %)	39 (12.5 %)
Colectomy with ileostomy	KJFH10 - 11	523 (55.8 %)	99 (49.3 %)	170 (54.7 %)
Proctocolectomy with ileostomy	KJFH20 - 21	147 (15.7 %)	49 (24.4 %)	65 (20.9 %)
Restorative proctocolectomy ± ileostomy	KJFH30 - 33	197 (21.0 %)	5 (2.5 %)	28 (9.0 %)
Proctocolectomy with Koch reservoir	KJFH40	1 (0.1 %)	0 (0 %)	0 (0 %)
Other form of colectomy	KJFH96	16 (1.7 %)	6 (3.0 %)	9 (2.9 %)
Time period				
	1996-2000	307 (32.7 %)	67 (33.3 %)	114 (36.7 %)
	2001-2005	343 (36.6 %)	78 (38.8 %)	95 (30.6 %)
	2006-2010	288 (30.7 %)	56 (27.9 %)	102 (32.8 %)

* Patients for who codes for both ulcerative colitis and Crohn's disease were used at any preceding or subsequent admission or hospital contact.

Table 2: Characteristics of patients with an inflammatory bowel disease (IBD) diagnosis undergoing emergency total colectomy in the period 1996-2010 in Denmark.

		Ulcerative colitis	Crohn's disease	Ulcerative colitis and Crohn's disease*
Total number (n=1,439)		1056 (73.4 %)	136 (9.5 %)	247 (17.2%)
Males		559 (52.9 %)	62 (45.6 %)	113 (45.7 %)
Females		497 (47.1 %)	74 (54.4 %)	134 (54.3 %)
Age at operation:				
	0-39 years	503 (47.6 %)	56 (41.2 %)	134 (54.3 %)
	40-59 years	286 (27.1 %)	39 (28.7 %)	65 (26.3 %)
	≥ 60 years	267 (25.3 %)	41 (30.1 %)	48 (19.4 %)
Number of annual colectomies for IBD performed in the surgical department				
	≤3/year	168 (15.9 %)	31 (22.8 %)	43 (17.4 %)
	3-12/year	186 (17.6 %)	24 (17.6 %)	50 (20.2 %)
	>12/year	702 (66.5 %)	81 (59.6 %)	154 (62.4%)
Duration of hospitalization before colectomy				
	Admitted < 8 days before colectomy	296 (28.0 %)	45 (33.1 %)	85 (34.4 %)
	Admitted ≥ 8 days before colectomy	760 (72.0 %)	91 (66.9 %)	162 (65.6 %)
Medical treatment within one year before colectomy				
	TNF--α and cyclosporine	67 (6.3 %)	12 (8.8 %)	23 (9.3 %)
Reoperation within 30 days postoperatively		102 (9.7 %)	11 (8.2 %)	27 (10.9 %)
Charlson Comorbidity Index score				
	0	810 (76.7 %)	96 (70.6 %)	191 (77.3 %)
	1-2	194 (18.4 %)	30 (22.1 %)	49 (19.8 %)
	≥3	52 (4.9 %)	10 (7.3 %)	7(2.8 %)
Colectomy type				
Colectomy with ileorectal anastomosis	KJFH00 - 01	38 (3.6 %)	16 (11.8 %)	19 (7.7 %)
Colectomy with ileostomy	KJFH10 - 11	875 (82.9 %)	97 (71.3 %)	196 (74.4 %)
Proctocolectomy with ileostomy	KJFH20 - 21	73 (6.9 %)	8 (5.9 %)	21 (8.5 %)
Restorative proctocolectomy ± ileostomy	KJFH30 - 33	31 (2.9 %)	2 (1.5 %)	4 (1.6 %)
Proctocolectomy with Koch reservoir	KJFH40	1 (0.1 %)	0 (0 %)	0 (0 %)
Other form of colectomy	KJFH96	38 (3.6 %)	13 (9.6 %)	7 (2.8 %)
Time period				
	1996-2000	371 (35.1 %)	54 (39.7 %)	90 (36.4 %)
	2001-2005	385 (36.5 %)	36 (7.1 %)	84 (34.0 %)
	2006-2010	300 (28.4 %)	46 (11.0 %)	73 (30.0 %)

* Patients for who codes for both ulcerative colitis and Crohn's disease were used at any preceding or subsequent admission or hospital contact.

Table 3. Thirty-day mortality (in percent) in patients with an inflammatory bowel disease (IBD) diagnosis undergoing total colectomy in the period 1996-2010 in Denmark, by emergency vs. elective surgery.

		Ulcerative colitis		Crohn's disease		Ulcerative colitis and Crohn's disease*	
		Emergency	Elective	Emergency	Elective	Emergency	Elective
All		5.2 (55/1056)	0.9 (8/938)	8.1 (11/136)	1.5 (3/201)	4.0 (10/247)	1.0 (3/311)
Males		5.8 (31/559)	0.8 (4/485)	6.5 (4/62)	2.6 (2/76)	2.7 (3/113)	0.7 (1/137)
Females		5.2 (24/497)	0.9 (4/453)	9.5 (7/74)	0.8 (1/125)	5.2 (7/134)	1.1 (2/174)
Age at operation:							
	0-39 years	0.2 (1/503)	0.2 (1/436)	0 (0/56)	0 (0/121)	0 (0/134)	0 (0/161)
	40-59 years	1.7 (5/286)	0.0 (0/292)	5.1 (2/39)	0 (0/55)	3.1 (2/65)	1.1 (1/91)
	≥ 60 years	18.4 (49/267)	3.3 (7/210)	22.0 (9/41)	12 (3/25)	16.7 (8/48)	3.4 (2/59)
Number of annual colectomies for IBD performed by the surgical department							
	≤3/year	11.3 (19/168)	1.5 (2/131)	22.6 (7/31)	4.5 (1/22)	4.7 (2/43)	0 (0/45)
	3-12/year	5.9 (11/186)	1.8 (3/166)	8.3 (2/24)	0 (0/28)	4.0 (2/50)	0 (0/44)
	>12/year	3.6 (25/702)	0.5 (3/641)	2.5 (2/81)	1.3 (2/151)	3.9 (6/154)	1.4 (3/222)
Duration of hospitalization before colectomy							
Admitted < 8 days before colectomy		7.1 (21/296)	0.2 (1/557)	20.0 (9/45)	1.5 (2/136)	4.7 (4/85)	0.0 (0/178)
Admitted ≥ 8 days before colectomy		4.5 (34/760)	1.8 (7/381)	2.2 (2/91)	1.5 (1/65)	3.7 (6/162)	2.3 (3/133)
Medical treatment within one year before colectomy							
TNF--α or cyclosporine		0 (0/67)	0 (0/64)	0 (0/12)	0 (0/10)	0 (0/23)	0 (0/37)
Reoperation within 30 days postoperatively		8.8 (9/102)	4.1 (3/73)	18.1 (2/11)	4.8 (1/21)	7.4 (2/27)	0 (0/21)
Charlson Comorbidity Index score:							
	0	2.2 (18/810)	0.6 (4/705)	3.1 (3/96)	0.0 (0/146)	2.1 (4/191)	0.9 (2/224)
	1-2	12.9 (25/194)	1.6 (3/194)	20.0 (6/30)	4.4 (2/45)	6.1 (3/49)	1.4 (1/69)
	≥3	23.1 (12/52)	2.6 (1/39)	20.0 (2/10)	10 (1/10)	42.9 (3/7)	0 (0/18)
Colectomy type							
Colectomy with ileorectal anastomosis	KJFH00 - 01	15.8 (6/38)	0 (0/54)	6.3 (1/16)	0 (0/42)	0 (0/19)	0 (0/39)
Colectomy with ileostomy	KJFH10 - 11	4.9 (43/875)	1.5 (8/523)	9.3 (9/97)	3.0 (3/99)	4.6 (9/196)	1.2 (2/170)
Proctocolectomy with ileostomy	KJFH20 - 21	5.5 (4/73)	0 (0/147)	0 (0/8)	0 (0/49)	0 (0/21)	0 (0/65)
Restorative proctocolectomy ± ileostomy	KJFH30 - 33	6.5 (2/31)	0 (0/197)	0 (0/2)	0 (0/5)	0 (0/4)	3.6 (1/28)
Proctocolectomy with Koch reservoir	KJFH40	0 (0/1)	0 (0/1)	0 (0/0)	0 (0/5)	0 (0/0)	0 (0/0)
Other form of colectomy	KJFH96	0 (0/38)	0 (0/16)	7.7 (1/13)	0 (0/6)	14.3 (1/7)	0 (0/9)
Time period							
	1996-2000	5.9 (22/371)	0.3 (1/307)	7.4 (4/54)	1.5 (1/67)	1.1 (1/90)	0.9 (1/114)
	2001-2005	5.2 (20/385)	0.3 (1/343)	2.8 (1/36)	2.6 (2/78)	6.0 (5/84)	1.1 (1/95)
	2005-2010	4.3 (13/300)	2.1 (6/288)	13.0 (6/46)	0 (0/56)	5.5 (4/73)	1.0 (1/102)

* Patients for who codes for both ulcerative colitis and Crohn's disease were used at any preceding or subsequent admission or hospital contact.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Table 4. Mortality rate ratios in patients with ulcerative colitis undergoing total colectomy in the period 1996-2010 in Denmark.

	Emergency		Elective	
	Crude	**Adj***	**Crude**	**Adj***
Females	Ref.	Ref.	Ref.	Ref.
Males	**1.15**	**1.16**	**0.94**	**0.79**
	(0.68-1.97)	(0.68-1.98)	(0.23-3.74)	(0.20-3.19)
Age at operation:				
0-39 years	Ref	Ref	Ref	Ref
≥ 40 years				
	26.18	**17.78**	**24.65**	**24.51**
	(11.2-61.1)	(7.3-43.1)	(3.0-200)	(2.81-213.8)
Number of annual colectomies for IBD performed by the surgical department				
≤ 3/year	Ref.	Ref.	Ref.	Ref.
3-12/year	**0.51**	**0.58**	**1.18**	**1.51**
	(0.24-1.06)	(0.28-1.23)	(0.20-7.08)	(0.25-9.18)
>12/year	**0.30**	**0.46**	**0.30**	**0.63**
	(0.17-0.55)	(0.25-0.84)	(0.05-1.82)	(0.10-3.89)
Duration of hospitalization before colectomy				
Admitted < 8 days before colectomy	Ref.	Ref.	Ref.	Ref.
Admitted ≥ 8 days before colectomy	**0.62**	**0.67**	**10.30**	**10.26**
	(0.36-1.06)	(0.39-1.16)	(1.27-83.6)	(1.25-84.2)
Charlson Comorbidity Index score:				
0	Ref.	Ref.	Ref.	Ref.
≥1	**7.20**	**2.56**	**3.05**	**1.06**
	(4.10-12.65)	(1.42-4.61)	(0.76-12.2)	(0.25-4.46)
Time period				
1996-2000	Ref.	Ref.	Ref.	Ref.
2001-2005	**0.87**	**0.90**	**0.90**	**0.90**
	(0.48-1.60)	(0.49-1.64)	(0.06-14.31)	(0.06-14.54)
2005-2010	**0.72**	**0.60**	**6.47**	**5.18**
	(0.36-1.43)	(0.30-1.20)	(0.78-53.7)	(0.62-43.6)

*Adj: Adjusted for age, gender and comorbidity.

Reference List

(1) Andersson P, Olaison G, Bodemar G *et al*. Surgery for Crohn colitis over a twenty-eight-year period: fewer stomas and the replacement of total colectomy by segmental resection. *Scand J Gastroenterol* 2002;**37**(1):68-73.

(2) Cosnes J, Nion-Larmurier I, Beaugerie L *et al*. Impact of the increasing use of immunosuppressants in Crohn's disease on the need for intestinal surgery. *Gut* 2005;**54**(2):237-41.

(3) Actis GC, Pellicano R, Pinna-Pintor M *et al*. Rescue with infliximab and surgical outcomes for refractory ulcerative colitis. *J Am Coll Surg* 2007;**205**(4):e3-e4.

(4) Hanauer SB, Feagan BG, Lichtenstein GR *et al*. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. *Lancet* 2002;**359**(9317):1541-9.

(5) Jakobovits SL, Jewell DP, Travis SP. Infliximab for the treatment of ulcerative colitis: outcomes in Oxford from 2000 to 2006. *Aliment Pharmacol Ther* 2007;**25**(9):1055-60.

(6) Järnerot G, Hertervig E, Friis-Liby I *et al*. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study. *Gastroenterology* 2005;**128**(7):1805-11.

(7) Rutgeerts P, Sandborn WJ, Feagan BG *et al*. Infliximab for induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2005;**353**(23):2462-76.

(8) Bernell O, Lapidus A, Hellers G. Risk factors for surgery and recurrence in 907 patients with primary ileocaecal Crohn's disease. *Br J Surg* 2000;**87**(12):1697-701.

(9) Langholz E, Munkholm P, Davidsen M *et al*. Course of ulcerative colitis: analysis of changes in disease activity over years. *Gastroenterology* 1994;**107**(1):3-11.

(10) Sandborn WJ, Rutgeerts P, Feagan BG *et al*. Colectomy rate comparison after treatment of ulcerative colitis with placebo or infliximab. *Gastroenterology* 2009;**137**(4):1250-60.

(11) Taxonera C, Rodrigo L, Casellas F *et al*. Infliximab maintenance therapy is associated with decreases in direct resource use in patients with luminal or fistulizing Crohn's disease. *J Clin Gastroenterol* 2009;**43**(10):950-6.

(12) Ramadas AV, Gunesh S, Thomas GA *et al*. Natural history of Crohn's disease in a population-based cohort from Cardiff (1986-2003): a study of changes in medical treatment and surgical resection rates. *Gut* 2010;**59**(9):1200-6.

(13) Lazarev M, Ullman T, Schraut WH *et al*. Small bowel resection rates in Crohn's disease and the indication for surgery over time: experience from a large tertiary care center. *Inflamm Bowel Dis* 2010;**16**(5):830-5.

(14) Turner D, Walsh CM, Steinhart AH *et al*. Response to corticosteroids in severe ulcerative colitis: a systematic review of the literature and a meta-regression. *Clin Gastroenterol Hepatol* 2007;**5**(1):103-10.

(15) Aratari A, Papi C, Clemente V *et al*. Colectomy rate in acute severe ulcerative colitis in the infliximab era. *Dig Liver Dis* 2008;**40**(10):821-6.

(16) Gustavsson A, Halfvarson J, Magnuson A *et al*. Long-Term Colectomy Rate After Intensive Intravenous Corticosteroid Therapy for Ulcerative Colitis Prior to the Immunosuppressive Treatment Era. *Am J Gastroenterol* 2006.

(17) Goligher JC. Surgical treatment of ulcerative colitis. *Br Med J* 1961;**1**(5220):151-4.

(18) Lennard-Jones JE, VIVIAN AB. Fulminating ulcerative colitis. Recent experience in management. *Br Med J* 1960;**2**(5192):96-102.

(19) Goligher JC, Hoffman DC, De Dombal FT. Surgical treatment of severe attacks of ulcerative colitis, with special reference to the advantages of early operation. *Br Med J* 1970;**4**(737):703-6.

(20) Alves A, Panis Y, Bouhnik Y *et al*. Subtotal colectomy for severe acute colitis: a 20-year experience of a tertiary care center with an aggressive and early surgical policy. *J Am Coll Surg* 2003;**197**(3):379-85.

(21) Roberts SE, Williams JG, Yeates D *et al*. Mortality in patients with and without colectomy admitted to hospital for ulcerative colitis and Crohn's disease: record linkage studies. *BMJ* 2007;**335**(7628):1033.

(22) Kaplan G, McCarthy EP, Ayanian JZ *et al*. Impact of Hospital Volume on Postoperative Morbidity and Mortality Following a Colectomy for Ulcerative Colitis. *Gastroenterology* 2008;**134**(3):680-7.

(23) Nicholls RJ, Clark DN, Kelso L *et al*. Nationwide linkage analysis in Scotland implicates age as the critical overall determinant of mortality in ulcerative colitis. *Aliment Pharmacol Ther* 2010;**31**(12):1310-21.

(24) Stenner JMC, White P, Gould SR. Audit of the management of severe ulcerative colitis in a DGH. *Gut* 2001;**48**(Suppl 1):A87.

(25) Andersen TF, Madsen M, Jørgensen J *et al*. The Danish National Hospital Register. A valuable source of data for modern health sciences. *Dan Med Bull* 1999;**46**(3):263-8.

(26) NOMESCO Classification of Surgical Procedures. 1-1-2010. Copenhagen.
Ref Type: Serial (Book,Monograph)

(27) Frank L. Epidemiology. When an entire country is a cohort. *Science* 2000;**287**(5462):2398-9.

(28) Charlson ME, Pompei P, Ales KL *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**(5):373-83.

(29) Quan H, Sundararajan V, Halfon P *et al*. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;**43**(11):1130-9.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

(30) EDWARDS FC, Truelove SC. The course and prognosis of ulcerative colitis. *Gut* 1963;**4**:299-315.

(31) Koudahl G, Kristensen M. Postoperative mortality and complications after colectomy for ulcerative colitis. *Scand J Gastroenterol Suppl* 1976;**37**:117-22.

(32) Frykholm G, Pahlman L, Enblad P *et al*. Early outcome after emergency and elective surgery for ulcerative colitis. *Acta Chir Scand* 1989;**155**(11-12):601-5.

(33) Carter FM, McLeod RS, Cohen Z. Subtotal colectomy for ulcerative colitis: complications related to the rectal remnant. *Dis Colon Rectum* 1991;**34**(11):1005-9.

(34) Hyman NH, Cataldo P, Osler T. Urgent subtotal colectomy for severe inflammatory bowel disease. *Dis Colon Rectum* 2005;**48**(1):70-3.

(35) Ananthakrishnan AN, McGinley EL, Binion DG. Does it matter where you are hospitalized for inflammatory bowel disease? A nationwide analysis of hospital volume. *Am J Gastroenterol* 2008;**103**(11):2789-98.

(36) Faiz O, Warusavitarne J, Bottle A *et al*. Nonelective excisional colorectal surgery in English National Health Service Trusts: a study of outcomes from Hospital Episode Statistics Data between 1996 and 2007. *J Am Coll Surg* 2010;**210**(4):390-401.

(37) Kurian A, Suryadevara S, Ramaraju D *et al*. In-hospital and 6-month mortality rates after open elective vs open emergent colectomy in patients older than 80 years. *Dis Colon Rectum* 2011;**54**(4):467-71.

(38) Sonnenberg A. Age distribution of IBD hospitalization. *Inflamm Bowel Dis* 2010;**16**(3):452-7.

(39) Brooke BN. Cortisone and ulcerative colitis; and adverse effect. *Lancet* 1956;**271**(6954):1175-7.

(40) Erichsen R, Sværke C, Tøttrup A. The coding quality of acute total colectomy in inflammatory bowel disease patients in a nationwide hospital registry. *Pharmacoepidemiology and Drug Safety* 2011;**20**(S1):S165.

(41) Thygesen SK, Christiansen CF, Christensen S *et al*. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. *BMC Med Res Methodol* 2011;**11**:83.

It is declared that each author contributed to
- conception and design, or analysis and interpretation of data
- drafting the article or revising it critically for important intellectual content
- and final approval of the version to be published.

Anders Tøttrup and Henrik Toft Sørensen af garantors for the whole manuscript.

Conflicts of interest: The authors declare no conflicts of interest.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Appendix Table 1. Codes used in this study from the Danish National Registry of

Patients.

International Classification of Diseases (ICD) codes:

Inflammatory Bowel Disease:

ICD-8: 563.01 (Crohn's disease); 563.19+569.04 (Ulcerative colitis)

ICD-10: K50 (Crohn's disease); K51 (Ulcerative colitis)

Clostridium difficile infection

ICD-10: A047

Surgical procedure codes (NOMESCO) and treatment codes:

Total colectomy:

KJFH

Reoperation:

KJW

TNF-α treatment and cyclosporine:

BOHJ18A and BOHJ20

Appendix Table 2. Definition of diseases included in the Charlson Comorbidity Index

(International Classification of Diseases (ICD) codes).

	Disease	**ICD-8 codes**	**ICD-10 codes**	**Score**
1	Myocardial infarction	410	I21;I22;I23	1
2	Congestive heart failure	427.09; 427.10; 427.11; 427.19; 428.99; 782.49	I50; I11.0; I13.0; I13.2	1
3	Peripheral vascular disease	440; 441; 442; 443; 444; 445	I70; I71; I72; I73; I74; I77	1
4	Cerebrovascular disease	430-438	I60-I69; G45; G46	1
5	Dementia	290.09-290.19; 293.09	F00-F03; F05.1; G30	1
6	Chronic pulmonary disease	490-493; 515-518	J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2; J98.3	1
7	Connective tissue disease	712; 716; 734; 446; 135.99	M05; M06; M08; M09;M30;M31; M32; M33; M34; M35; M36; D86	1
8	Ulcer disease	530.91; 530.98; 531-534	K22.1; K25-K28	1
9	Mild liver disease	571 57301 57304	B18; K70.0-K70.3; K70.9; K71; K73; K74; K76.0	1
10	Diabetes type 1	249.00; 249.06; 249.07; 249.09 250.00; 250.06; 250.07; 250.09	E10.0, E10.1; E10.9	1
	Diabetes type 2		E11.0; E11.1; E11.9	

11	Hemiplegia	344	G81; G82	2
12	Moderate to severe renal disease	403; 404; 580-583; 584; 590.09; 593.19; 753.10-753.19; 792	I12; I13; N00-N05; N07; N11; N14; N17-N19; Q61	2
13	Diabetes with end-organ damage: - type 1 - type 2	 249.01-249.05; 249.08 250.01-250.05; 250.08	 E10.2-E10.8 E11.2-E11.8	2
14	Any tumor	140-194	C00-C75	2
15	Leukemia	204-207	C91-C95	2
16	Lymphoma	200-203; 275.59	C81-C85; C88; C90; C96	2
17	Moderate/severe liver disease	57300 07000 07002 07004 07006 07008 4560	B15.0; B16.0; B16.2; B19.0; K70.4; K72; K76.6; I85	3
18	Metastatic solid tumor	195-198; 199	C76-C80 C78.7)	6
19	AIDS	079.83	B21-B24	6

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60