

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Thirty-day mortality after elective and emergency total colectomy in Danish patients with inflammatory bowel disease: A population-based nationwide cohort study
AUTHORS	A. Tøttrup, R. Erichsen, C. Sværke, S. Laurberg and H.T. Sørensen

VERSION 1 - REVIEW

REVIEWER	Professor RJ Nicholls Visiting Professor of Colorectal Surgery Department of Biosurgery and surgical Technology Imperial College London W2 I have no competing interests.
REVIEW RETURNED	25/01/2012

THE STUDY	<p>The authors report the result of a nation wide study of early (30 day) mortality after 'colectomy' for IBD among 2889 patients treated from 1992-2010, an eighteen year period. The results show a higher mortality for emergency colectomy, Crohn's disease (CD), unit volume (inverse), comorbidity and age.</p> <p>The main value of the study is that the data include the whole population of patients having colectomy for IBD, in a country well known and respected for its excellence of data recording on a national scale. It comes from a highly respected unit.</p> <p>The key conclusions stated immediately after the abstract are mostly known, however; see references 21,22,23 which demonstrate emergency treatment, volume, age, comorbidity as factors related to mortality. The recommendation to centralise services applies more to other countries and health systems, since two thirds of patients in the present study were treated in high volume units.</p> <p>Comment</p> <p>It will be easier for the reviewer to comment under headings which will answer some of the yes/no answers above.</p> <p>Numbers of patients</p> <p>The authors deal with the category of patients who were double listed as having ulcerative colitis (UC) and CD, by putting them into a separate group. To make it easier for the reader, these data might be removed from the Tables and the actual data given in an Appendix, since being a mixed group they are of no value when compared with 'true' UC and 'true' CD. It is a pity that this mixed category was so large, with a greater number of elective procedures in the UC + CD group (311) than in the CD group alone (201), and</p>
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many more in the respective emergency groups(UC + CD 247 v CD 136).

Unfortunately this leaves a rather small number of 'true' CD patients to compare with the 'true' UC patients.

There are large numbers of patients with UC but many fewer with CD. I note a mortality for colectomy with ileostomy for emergency surgery for CD of 9/97 patients. This is higher than the equivalent UC group (43/875;4.9%) but is the difference statistically significant?

The authors express concern about the numbers for statistical analysis. However the Abstract does not contain comment on statistical significance where differences exist, and it would also be helpful if total numbers as well as percentages were given.

The authors should comment on this in greater detail in the Discussion. It is a pity that some of the more interesting potential correlations were not possible owing to too few numbers in the CD group.

What was the position of interval from admission to surgery? It appears that mortality was greater in patients undergoing surgery in under eight days. Table 4 looks as though this was statistically significant for UC. What does it mean? Perhaps I have not understood.

Why there were so many patients in the elective group who were in hospital for more than eight days before they had their operation?

I also am surprised that so few patients had had medical treatment within one year of surgery, in both elective and emergency groups.

Total colectomy

The Abstract uses the term 'total colectomy' which is further used in the Method section, but later on it is apparent that this term includes all types of colorectal operations for UC and CD during the period. Thus restorative proctocolectomy, conventional proctocolectomy with ileostomy, total colectomy with ileorectal anastomosis and other procedures are all included. Did the study include all the surgical procedures involving removal of the colon (including all the pouch operations) performed in Denmark for IBD during the 18 year period?

There may well be differences in risk between them and there may also be differences between the type of operation and the pathology (UC or CD). (Although the numbers are small, it is the case that the mortality of emergency colectomy with ileorectal anastomosis is higher in the UC (15.8%; 6/38) than in the CD (6.3%;1/16) patients. I realise that these are too small for statistical analysis, but it shows that there may be hidden differences which the numbers of patients were insufficient to detect statistically).

The question of possible influence of procedure should be included in the Discussion.

The period of study

1992-2010 is a long period. During this, critical care has improved and specialisation has increased very considerably. I appreciate that in Denmark services have for many years been configured in such a way that only a few hospitals in the country take on the more difficult and potentially complicated patients. Indeed this study has demonstrated this to a considerable extent.

In the Introduction one of the rationales for determining early mortality in IBD patients is the high mortality in district hospitals.

	<p>They quote reference 24 which was published in 2001 as an abstract (with no apparent subsequent publication) and therefore would have dealt with patients treated over 10 years previously. This reference appears again in the Discussion and the study of Roberts (England, not the UK) is invoked to confirm the high mortality in emergency cases, which is almost the same as in the present study.</p> <p>Was the mortality in the present study evenly distributed throughout the whole period or was there a concentration in the early years?</p> <p>Other The methodology is similar to that used in reference 23 which also included a national population. Although the primary end point (30 day and 3 year mortality) was different and the patients groups included medically treated patients in reference 23, perhaps some comment should be included on this being the only other study using a national database, certainly when the methodology used in the present study is discussed.</p>
GENERAL COMMENTS	Having been asked to select minor or major revision, I would say somewhere between the two.

REVIEWER	Michael Goldacre Professor of Public Health University of Oxford
REVIEW RETURNED	13/02/2012

GENERAL COMMENTS	<p>1. A tiny point: 'categories' on page 9, line 4, should be 'categorised'.</p> <p>2. As the authors say, they studied total colectomy for IBD. For context, is it possible and easy for the authors to state (perhaps in a sentence or two in Discussion), how many people in the same population and time period underwent all types of colectomy and maybe also how many were admitted for IBD overall (with or without colectomy)? In other words, what percentage of all who underwent colectomy, and what percentage of all admitted for IBD, underwent total colectomy?</p>
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VERSION 1 – AUTHOR RESPONSE

Professor Nicholls.

Number of patients.

We see the point made about the mixed group. The mixed group is large because we went back in the Registry to 1977 to include all IBD codes registered for each patient both before and after colectomy. The mixed group may contain patients for whom their primary diagnosis was later changed because of new information. This may be seen in patients with colitis classified as ulcerative colitis, who later develop Crohn in their small bowel or ileoanal reservoir. We realize that the number of patients in this category should be few, and we assume that the majority of patients in the mixed group fall into another category. They are more likely to have received an incorrect code at one of their admissions or visits to outpatient clinic. Administrative data like the present do not allow further discrimination of this group, but we find it relevant to show the information in the tables to enable the reader to directly compare the analyses for this particular group to the other two groups. By performing the analysis as we did, we find that data from the “pure” groups becomes more reliable.

One of the consequences of this is that the pure Crohn group is fairly small. When comparing to the

study by Roberts (ref 21), their group of Crohn patients undergoing emergency total colectomy or proctocolectomy was also substantially smaller than the equivalent group of patients with ulcerative colitis. Their total group of Crohn patients was quite large, and we notice a high number of right hemicolectomies among these patients. Without knowing their data or british coding practice, we assume that the majority of these patients had ileocaecal Crohn, and that the operation performed in many of these cases were indeed ileocaecal resections rather than true right hemicolectomies.

The proportion of patients with Crohn dying after total colectomy was not statistically significant from the proportion of patients with ulcerative colitis. We have not included this in the adjusted analyses because the number of Crohn patients was too low.

We have added the requested information about number of patients in the abstract.

The interval from admission to colectomy is an administrative figure that somehow leaves a degree of uncertainty. For patients with severe ulcerative colitis this interval will probably reflect the number of days on high dose corticosteroids (perhaps minus one). For elective cases, we are unable to extract information about what the number of days of admission before surgery means. But we were equally puzzled about the long interval spent in hospital before colectomy in a fairly high proportion of patients (table 1).

Considering emergency cases, the number of days on steroids before colectomy is of utmost interest because it brings into question the recommended practice of not delaying colectomy for more than 5-7 days in case of poor response to steroids. The population-based study of Kaplan showed an increased mortality risk after admission for more than 7 days. In table 4, we have shown the adjusted data for emergency and elective cases. For the emergency cases, the adjusted risk was not significantly different for patients who were admitted for more than 8 days prior to colectomy (MRR: 0.67; confidence interval: 0.39-1.16). Thus our data fails to support those of Kaplan in this respect. But we feel that this is one of the analyses that has to be interpreted with great care. From the administrative data we are unable to read how sick each patient was, but it is not unreasonable to assume that the most severe cases were operated early and the milder cases maybe later. This would tend to level out a possible deleterious effect of delay in surgery.

We agree about the few number of patients that had a treatment code for rescue therapy (cyclosporine or Infliximab), but we feel certain that this parameter has been underreported. Until recently, this coding was not compulsory in Denmark, in contrast to coding for operative procedures.

Total colectomy

The reviewer is correct that there was a tendency towards a lower mortality in the most recent cohort as envisaged by the reviewer. The statistical analysis failed to show a significant difference. For the smaller groups, mortality rates are fluctuating in an unforeseen way.

Other

We have added a comment about comparative methodology in the two studies.

Professor Goldacre.

1. Corrected.

2. Unfortunately, we are not able from the present dataset to extract information about total number of colectomies performed for other indications than IBD. We see the reviewers point about admissions for IBD without colectomy to correlate findings to those of Roberts et al. We are sceptical as to the interpretation of such data, because an admission without colectomy may have been for other reasons than IBD, but where the IBD diagnosis has been registered together with other diagnoses. A limitation that in the first place lead us to omit those data.