Outcomes following colectomy for *Clostridium difficile* colitis

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ABSTRACT

Introduction: Clostridium difficile associated diarrhoea has become an important health problem in UK hospitals but surgical intervention is rarely required. There is little evidence regarding best practice for patients requiring surgical intervention. The aim of this multicentre study was to review our experience in patients requiring surgery for *C. difficile* colitis.

Methods: Patients who underwent surgery for *C. difficile* colitis in 5 hospitals in Southeast England over a 7-year period (1 teaching hospital and 4 district general hospitals) were identified from histopathology databases. Data were collected regarding the presentation, indication for surgery and post-operative outcomes.

Results: 15 patients (9 males; mean age = 71 years (range 35–84 years)) underwent surgery. 46% of patients ($n = 7$) contracted *C. difficile* during their hospital admission for other medical reasons and 73% of patients were initially admitted under other medical specialties. Diagnosis was only made preoperatively in 8 patients (53%). Indications for surgery were peritonitis and systemic toxicity ($n = 12$), failure of medical management ($n = 2$) and unresolving large bowel dilatation ($n = 1$). 12 patients underwent total colectomy and the rest underwent segmental resection. All patients were admitted to the intensive care unit post operatively with a mean stay of 6 days. 2 patients needed a second look laparotomy. Mortality rate was 67% ($n = 10$), with all but 1 patient dying within the 30-day mortality period. The mean length of hospital stay of survivors was 30 days (range 17–72).

Conclusions: Surgical intervention for *C. difficile* colitis remains uncommon. Total colectomy and end ileostomy is the procedure of choice. The outlook for patients requiring surgery remains poor.

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1. Introduction

Clostridium difficile is an anaerobic spore-forming gram positive bacteria. It is the most common cause of infectious diarrhoea in hospitalised and institutionalised patients.[1] It is resistant to alcohol and, importantly, can only be eliminated by good hand washing. It is common in surgical patients due to antibiotic usage. Broad spectrum penicillins and cephalosporins are common aetiological factors although the use of nearly all antibiotics has been implicated.[2,3] Exposure to the normal commensal gut flora to antibiotics allows colonisation of the gut with *C. difficile* and production of enterotoxins. Symptoms arise from these enterotoxins producing an inflammatory response in the gut mucosa. Symptoms can range from asymptomatic colonisation to mild diarrhoea to severe colitis associated with the formation of pseudomembranes (Fig. 1). The vast majority of patients respond to conservative management with either oral metronidazole or vancomycin, although in more recent years a hypervirulent strain (the NAP1/027 strain) has emerged which is resistant to fluoroquinolones and has an increased mortality rate.[4]

A small proportion of patients infected with *C. difficile* may fail to settle with medical treatment and then may go on to develop severe fulminant *C. difficile* colitis. The diagnosis of fulminant colitis may be made endoscopically or radiologically in conjunction with a positive *C. difficile* toxin.[5,6] Those patients who exhibit symptoms and signs of sepsis or peritonism or develop complications such as perforation or bleeding may require prompt surgical intervention. In some cases, an emergency laparotomy is performed for peritonitis without a preoperative diagnosis of *C. difficile* colitis and the diagnosis is only subsequently made histological.

There is little data regarding outcome of patients who have had colectomy for *C. difficile* colitis. Mortality rates have been reported

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Fig. 1. Colectomy specimen showing severe mucosal ulceration and pseudomembrane formation.

to be as high as 80%.[7] There is also no standard procedure of choice for this condition although total colectomy with end ileostomy appears to be associated with a lower mortality and morbidity rate than segmental resections.[8,9] Therefore the aim of this multicentre study was to review our experience in patients requiring surgery for *C. difficile* colitis.

2. Methods

Data were collected from 5 hospitals in Southeast England (1 teaching hospital and 4 district general hospitals) over a 7-year period from 2000 to 2007. Patients who underwent surgery for *C. difficile* colitis were identified from histopathology databases. Data were collected regarding patient demographics, clinical presentation, laboratory indices and microbiological diagnosis. Indication for surgery, type of surgery performed and post-operative outcomes were examined.

3. Results

3.1. Patient demographics

Fifteen patients (9 males; mean age = 71 years (range 35–84 years)) were identified from our five hospitals during the study period (total catchment population of approximately 2.8 million). 10 patients were admitted under the care of other medical teams and transferred to the care of the general surgeons. 5 patients were admitted directly under the care of the general surgeons with abdominal pain and distension. Of these 15 patients, 6 patients presented with signs and symptoms consistent with *C. difficile* infection while 8 patients contracted *C. difficile* during their hospital admission for other reasons. 6 patients had their diagnosis confirmed by positive stool toxin while 2 patients were diagnosed by endoscopic findings of pseudomembranous colitis. The remaining 7 patients' diagnoses were made histologically after colectomy. 14 out of the 15 patients were on broad spectrum antibiotics prior to diagnosis with the remaining 1 patient on an antifungal prior to diagnosis (see Table 1). Metronidazole was first line treatment in 12 patients (80%) with vancomycin being used as treatment in the remaining 3 patients.

3.2. Clinical and laboratory findings

Diarrhoea was reported in 9 out of 15 patients. The remainder had abdominal pain and distension. The most common laboratory

Table 1
Patient demographics and outcomes.

Patient No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Age (years)	82	67	75	84	72	78	88	78	35	76	56	77	66	60	77
Sex	M	M	F	F	M	M	F	F	F	M	M	F	M	M	M
Preoperative diagnosis	Yes	Yes	No	No	Yes	Yes	No	No	No	Yes	No	No	Yes	Yes	Yes
Duration of symptoms (days)	1	7	21	2	7	12	2	2	5	1	3	1	7	2	21
WBC (×10^9/l)	13.9	20.0	24.8	9.3	15.0	7.5	41.1	51.2	16.1	19.1	52.9	22.1	3.6	28.4	17.2
Preoperative antibiotics	Cipro, clarithro	Fluclox, benxylpen	Cef, vanc	Cef, met	Cipro	Flucon	Cef, met	Cipro	Cef, clarithro	Fluclox	Cef, met	Cef, met	Cipro	Cef, met	Met, vanc
Type of surgery	Total colectomy	Total colectomy	Total colectomy	Hartmann's	Total colectomy	Total colectomy	Total colectomy	Total colectomy	Right hemi	Total colectomy	Total colectomy	Hartmann's	Total colectomy	Total colectomy	Total colectomy
Immuno-suppression	No	No	Renal failure	No	No	No	No	No	No	No	No	No	Steroids	Steroids aza	No
30-Day mortality	No	No	No	No	No (but died later)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Length of stay (days)	43	17	21	18	67	32	3	92	14	9	4	10	18	72	35

Key: cipro = ciprofloxacin, clarithro = clarithromycin, fluclox = flucloxacillin, benxylpen = benzylpenicillin, cef = cefuroxime, vanc = vancomycin, met = metronidazole, flucon = fluconazole, aza = azathioprine.

Table 2
Summary of previous reported series of colectomy for C. difficile.

Authors	Number of patients	Mean age	Male:female ratio	Contracted during hospital stay	Previous antibiotic treatment	Preoperative diagnosis	Total colectomy	30-Day mortality
Byrn et al.[25]	73	68	33:40	56% (n = 43)	92% (n = 67)	80% (n = 58)	86% (n = 63)	34% (n = 25)
Hall and Berger[26]	36	67	Not stated	Not stated	100% (n = 36)	100% (n = 36)	94% (n = 34)	36% (n = 13)
Koss et al.[7]	14	64	5:9	71% (n = 10)	100% (n = 14)	42% (n = 6)	64% (n = 9)	36% (n = 5)
Longo et al.[27]	67	69	66:1	53% (n = 36)	97% (n = 65)	82% (n = 55)	79% (n = 53)	48% (n = 32)
Synnott et al.[15]	5	69	3:2	100% (n = 5)	100% (n = 5)	100% (n = 5)	100% (n = 5)	80% (n = 4)
Lipsett et al.[8]	13	59	7:6	54% (n = 7)	100% (n = 13)	69% (n = 9)	54% (n = 7)	38% (n = 5)
Grundfest-Broniatowski et al.[20]	12	59	6:6	100% (n = 12)	92% (n = 11)	75% (n = 8)	58% (n = 7)	42% (n = 5)

abnormality in our series was a raised urea and creatinine in 14 patients. A leucocytosis with a raised white cell count (WBC) between 13.9 and 52.9×10^9/l (median WBC = 19.1×10^9/l) was seen in 12 patients. 2 patients did not have a raised WBC due to immunosuppression from steroid treatment or pre-existing renal disease. 1 patient had a normal WBC despite not being immunosuppressed.12 patients had evidence of organ failure in at least one system with 3 patients needing haemofiltration and 6 patients needing inotropic support preoperatively. 9 out of 15 patients were receiving critical care input on either HDU or ITU preoperatively. Post operatively all patients were admitted to ITU.

Preoperative investigations included endoscopy (n = 2), plain radiographs (n = 12) and CT scans (n = 4). Pseudomembranes were seen on both patients undergoing flexible sigmoidoscopy. Large bowel dilatation was seen in 10 patients on the plain abdominal X-rays. One patient had no radiological findings of colitis and 1 patient had evidence of small bowel dilatation only. Of the CT scans 3 patients had features of colitis and 1 patient had thickened oedematous small bowel loops. There was no radiological evidence of perforation in any of the plain X-rays or CT scans.

3.3. Surgery and outcomes

Indications for surgery were peritonitis and systemic toxicity (n = 12), failure of medical management (n = 2) and unresolving large bowel dilatation (n = 1). Mean time from onset of symptoms to surgery was 5 days (range 1–21). 12 patients underwent total colectomy and the rest underwent segmental resection (2 Hartmann's procedures, 1 right hemicolectomy with double barrel ileocolostomy). All patients were admitted to the intensive care unit post operatively with a mean stay of 6 days (range 1–18 days). 2 patients needed a second look laparotomy: one for an ischaemic stoma and the other for increasing metabolic acidosis with laparotomy findings of patchy ischaemic necrosis throughout the remaining colon after right hemicolectomy. Mortality rate was 67% (n = 10), with all but 1 patient dying within the 30-day mortality period. The 9 patients who died within 30 days of surgery all died from multi-organ failure. The patient who died more than 30 days after surgery was discharged for rehabilitation one month after colectomy but was readmitted 3 weeks later with confusion and a urinary tract infection. He subsequently developed adhesional small bowel obstruction and was felt not to be fit enough for further surgery and died two and a half months post colectomy. The mean length of hospital stay of survivors was 30 days (range 17–72).

4. Discussion

The incidence of C. difficile colitis appears to be rising both in Europe and in the United States and Canada.[10,11] In the United Kingdom the incidence of C. difficile infection has increased from 15,081 to 55,681 patients from 2000 to reach a peak in 2006.[12] This is likely to be a consequence of both increasing use of broad spectrum antibiotics, increasing awareness of this condition and the introduction of mandatory reporting of all C. difficile infections since 2004. The most important risk factors for C. difficile infection are exposure to the hospital environment (especially ITU admission and prolonged hospital stay) and antibiotic usage.[1,13,14] Other risk factors predisposing to this condition also include increasing age and the presence of comorbid disease.[2,15,16]

Due to the heightened awareness and media attention of C. difficile infections in the UK the Healthcare Commission implemented both the Saving Lives campaign[17] and The Health Act 2006[18] to try and reduce C. difficile infections and other healthcare associated infections. Recommendations to implement reduction in C. difficile include prudent antibiotic prescribing, isolation of patients and good infection control nursing (e.g. hand washing, gloves and aprons) and enhanced environmental cleaning and use of a chlorine containing disinfectant where there are cases of C. difficile disease to reduce environmental contamination with the spores.

Surgical intervention in terms of colectomy is rarely required in patients with C. difficile colitis. Only 1–3.8% of patients infected with C. difficile are reported to require colectomy.[8,14,19] However, one series which specifically looked at critical care patients reported a colectomy rate of 20%.[20] Unfortunately, our hospital databases were not sufficiently robust to allow us to determine the total number of patients infected with C. difficile during the study period (Table 2).

Our mortality rate following colectomy was high (67%). It is known that the outcome following colectomy for C. difficile colitis is poor. Most series have reported mortality rates of 30–40% although the mortality may reach 80%.[7,21,22,23] Some studies have tried to determine factors which could predict mortality in patients who have undergone colectomy for C. difficile colitis.[24,25,26] Lamontagne's paper[24] compares ITU patients who had undergone colectomy for CDAD matched to patients treated in ITU with other medical problems. This group found that leukocytosis >50, lactate >5, age >75 and shock requiring vasopressors predicted 30-day mortality. In Byrn et al.'s paper[25] univariate analysis determined that preoperative vasopressor requirement, intubation, and mental state changes were significant predictors of mortality and also that the group of patients who died had a higher level of arterial lactate and longer length of medical management. Our high rate of mortality may in some part be accounted for by patient age and comorbidities but may also be due to the need for emergency laparotomy without a diagnosis. In our series 7 out of the 15 patients presented with an acute abdomen require surgery without a preoperative diagnosis of C. difficile colitis. In four of these patients colitis or C. difficile associated disease was suspected due to the presenting complaint being diarrhoea and sepsis but no definitive diagnosis

(either by positive stool toxin, radiologically or endoscopically) had been made before the need for surgery. The remaining 3 patients presented with peritonism necessitating laparotomy but with no obvious diarrhoea. This is in keeping with a number of already reported series[25,27] and further complicates the decision making process for these patients. Two out of these four patients had segmental resection rather than total colectomy and end ileostomy.

Experience in the surgical management of fulminant *C. difficile* colitis is limited. Total colectomy rather than segmental resection or non-resectional surgery such as ileostomy with placement of catheters for irrigation of the colon, appears to be associated with lower mortality rates.[8,9,14,23] As fulminant *C. difficile* colitis typically causes pancolitis, segmental resection or non-resectional surgery leaves behind diseased colon. In our series, the two patients who underwent a second look laparotomy had segmental resections and both were found to have ischaemia in the remaining colon. Our numbers in this series are small. It was not possible to determine the total numbers of patients who had contracted *C. difficile* associated disease as our hospital databases were not robust enough but our findings seem to reflect the general trends seen in other series.

5. Conclusions

Surgical intervention for *C. difficile* colitis remains uncommon despite the growing incidence of disease due to *C. difficile* infection. A proportion of patients will undergo emergency surgery without a diagnosis. Having analysed our data and reviewed the literature we would suggest having a low threshold of suspicion that patients with *C. difficile* associated disease can go on to have fulminant *C. difficile* colitis. Once diagnosed, early surgical intervention (if the patient does not improve despite medical management) may decrease mortality and morbidity. Total colectomy and ileostomy should be considered to be the procedure of choice rather than segmental resection. However, the outlook for patients requiring surgery still remains poor.

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