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MINIEVIEWS

Current status of surgical treatment for fulminant *clostridium difficile* colitis

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Abstract

Mortality rates attributable to fulminant *Clostridium difficile* (*C. difficile*) colitis remain high and are reported to be 38%-80%. Historically, the threshold for surgical intervention has been judged empirically because level I evidence to guide decision making is lacking. Studies of the surgical management of *C. difficile* infection have been limited by small sample size and the lack of a standard definition of fulminancy. Multiple small and medium-sized series have examined the surgical management of *C. difficile*. However, because of a lack of prospective, randomized studies, it has been difficult to identify the optimal point for surgical intervention in patients with severe fulminant *C. difficile* colitis. Our goal was to analyze the existing body of literature in an attempt to define host constellations, which would predict the development of the more aggressive form of this disease and hence justify an early or earlier surgical intervention. A Pubmed search was conducted using the keywords "fulminant", "clostridium difficile", "surgery", and "colitis". Reviews and meta-analyses proposing indications for surgical consultation or operative management in patients with *C. difficile* colitis were included. After analyzing current literature, we identified a number of parameters that are associated with unfavorable outcomes. The parameters include age greater than 65 years old, peritoneal signs on physical examination, abdominal distension, signs of end-organ failure, hypotension less than 90 mmHg systolic blood pressure, tachycardia greater than 100 bpm, vasopressor requirement, elevated WBC count of greater than at least 16 × 10^9/μL, serum lactate of greater than 2.2 mmol/L, and lastly, radiologic findings suggestive of pancolitis, ascites, megacolon, or colonic perforation. Even though fairly strong evidence exists in contemporary literature, we recommend use of these identified parameters with caution in clinical practice when it comes to the actual decision to treat certain patients more aggressively. The identified risk factors should be used to lower surgeons' threshold for operative treatment early in the course of the disease.

Key words: Fulminant Clostridium difficile; Colitis; Toxic megacolon; Total colectomy; Surgical management

Core tip: Studies of the surgical management of *Clostridium difficile* infection have been limited by small sample size and the lack of a standard definition of fulminancy. Our goal was to analyze the existing body of literature in an attempt to define host constellations which would predict the development of the more aggressive form of this disease and hence justify an early or earlier surgical intervention. We identified a number of parameters that are associated with unfavorable outcomes. The identified risk factors should be used to lower surgeons' threshold for operative treatment early in the course of the disease.

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INTRODUCTION

Clostridium difficile (*C. difficile*), a Gram-positive, spore-forming, anaerobic bacillus has surpassed methicillin-resistant *Staphylococcus aureus* as the most common healthcare-associated infection in the United States and is currently the number one cause of hospital-acquired diarrhea in the country. *Clostridium difficile* infection (CDI) is traditionally associated with risk factors including advanced age, antibiotic use (particularly fluoroquinolones), and acute care hospitalization[1]. National rates of CDI listed as either a primary or secondary diagnosis per ICD-9-CM codes on discharge reporting rose from 5.6/1000 in 2001 to 11.5/1000 in 2010[2]. The rise in incidence of CDI has been largely attributed to a hypervirulent strain of *C. difficile* designated BI/NAP1/027 which exhibits significant fluoroquinolone resistance, increased toxin production, polymorphisms in a toxin production down-regulatory gene, and the presence of a gene encoding an additional binary toxin[3]. While most cases of CDI respond well to oral antibiotic therapy, approximately 3%-10% of patients progress to a fulminant colitis involving concomitant systemic toxicity, organ dysfunction, or the need for vasoactive agents or ventilatory support[4-6]. The number of death certificates with enterocolitis due to *C. difficile* listed as a primary cause of death increased from 793 in 1999 to 7483 in 2008 according to preliminary data from US Vital records[2]. Management of patients with fulminant CDI includes surgical intervention in up to 20% cases and post-operative mortality remains high with various studies citing between 35% and 80%[4]. Traditional surgical management includes subtotal colectomy with margins of resection based on gross colonic appearance in conjunction with end ileostomy. As an alternative to colectomy, a recent study by Neal *et al*[5] has shown diverting loop ileostomy and colonic lavage to be a less morbid and viable option for surgical treatment[6]. Given the increasing incidence of CDI and the underlying imperative to reduce the morbidity and mortality suffered by patients, the aim of this article is to review and summarize information available to date regarding the best practice indications for surgical management of cases of fulminant CDI.

PUBMED SEARCH

A Pubmed search was conducted using the keywords "fulminant", "clostridium difficile", "surgery", and "colitis". Inclusion criteria for our study were restricted to all original articles, reviews and meta-analyses proposing specific indications or guidelines for surgical consultation and operative management in patients with CDI. Of the sixty-three resulting articles dating from 1989 to 2012, four were found to summarize or propose criteria for operative management of fulminant CDI that were relevant to our review.

PATHOGENESIS

CDI can manifest clinically along a wide spectrum spanning from mild diarrhea to fulminant and potentially fatal toxic colitis. It is widely accepted that the primary risk factor for the development of *C. difficile* Associated Disease (CDAD) is recent exposure to broad spectrum antibiotics, particularly ampicillin, amoxicillin, second and third generation cephalosporins, clindamycin, and fluoroquinolones[6-8]. The association of particular antibiotics with predisposition for the development of CDAD is influenced by the drug's dosage, frequency of use, route of administration, and most importantly the individual impact on the typical colonic normal flora[9,10]. It is understood that the disruption of normal colonic flora by antibiotic use inhibits the protective barrier to outside colonization generally provided by these organisms which allows *C. difficile* spores ingested from a contaminated environmental source to germinate and colonize the colon. While the rate of chronic intestinal carriage of *C. difficile* is reported to be low at 0%-3% among asymptomatic adults in the community, the hospital and long-term care facility environments that commonly surround infected individuals as well as the hands and instruments of health-care workers caring for them remain the major source of infection for susceptible individuals *via* environmentally-resistant spore transmission[8]. In contrast to the asymptomatic community carriage rate, the rate of colonization with *C. difficile* was reported to be as high as 20%-40% in hospitalized patients[6].

Colonization with *C. difficile* occurs by the fecal-oral route *via* ingestion of the organism's aforementioned acid-resistant spores. In individuals whose normal colonic flora are depleted by antibiotic use, *C. difficile* is able to vegetate, overgrow, and release its toxins A and B into the colonic lumen from which they are taken up by enterocytes and subsequently become responsible for colonic damage and local inflammation (colitis) *via* cellular cytotoxicity and activation of inflammatory cascades including nuclear factor κB (NF-κB), mitogen-activated protein (MAP) kinases, and COX-2 which lead to release of the proinflammatory cytokines interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α), and interleukin-8 (IL-8).

According to the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America Treatment Guidelines updated in 2010, confirmed CDI can be graded according to the following scale: Mild or moderate showing diarrhea, severe with WBC > $15 \times 10^9/\mu L$ or creatinine 1.5 × greater than baseline, and Severe Complicated characterized by ileus, "megacolon", hypotension requiring vasoactive agents, or shock with organ-failure and/or need for ventilatory assistance[6,11]. In those patients developing severe fulminant colitis, the effects of these cytokines are evident at a systemic level as manifested by complications of shock and hypotension. Clearly however, not all patients undergoing antimicrobial therapy develop CDI and from there only a small percentage of patients suffering from CDAD progress to the development of fulminant colitis. It is important then to understand the variables that can be relied upon to predict which patients are at higher risk

Table 1 Major risk factors for the development of *Clostridium difficile* infection and associated disease

Risk factor	Risk	Proposed mechanism	Notes
Age (> 70 yr[10])	CDI and Severe CDAD	Diminished efficacy of immune response with aging[7]	
Medical comorbidities[7]: multiple or those involving major organ systems	CDI and Severe CDAD	Diminished efficacy of immune response	Studies are conflicting with regards to which comorbid illnesses are specifically associated
Broad spectrum antibiotics	CDI	Alteration of normal colonic floral barrier to *C. difficile* colonization	The evidence supporting the association with multiple/prolonged antibiotic use is controversial as this often occurs in patients with recurrent or refractory disease who are already at risk of unfavorable outcomes
Use of 3-4 antibiotics concurrently or prolonged (> 4 wk) use[12]	Severe CDAD		
Suppression of gastric acid production, particularly by proton pump inhibitors[6,7]	CDI	Increased survival of the acid-labile vegetative form of *C. difficile* while passing through the stomach[6,7]	
Immunosuppression[6,13]	CDI and severe CDAD	Disruption of host ability to mount an effective response to both infection and toxemia	

C. difficile: *Clostridium difficile*; CDI: *Clostridium difficile* infection; CDAD: *Clostridium difficile* associated disease.

for developing these consequences of antibiotic use and resultant complications from *C. difficile* infection. These risk factors were summarized in several recent review articles and include the following presented in Table 1.

Other potential risk factors for which conflicting reports exist include steroids, anti-peristaltic medications, and gastrointestinal interventions including the various types of endoscopy (colonoscopy, sigmoidoscopy, esophagogastroduodenoscopy) and enteral feedings including nasogastric tube feedings[6,7]. Common proposed mechanisms for these factors include exposure to *C. difficile* spores *via* the hands and equipment of healthcare providers, alteration of colonic flora by gastrointestinal manipulation and motility changes, and alteration of gastrointestinal mucosa[6,7]. It can be understood then that the ultimate development of CDAD results from a confluence of factors including disruption of normal colonic flora barriers (typically by antibiotic use), combined with exposure to a high-risk contaminated hospital environment and then individually influenced by immune modifying factors including age, major medical comorbidities, and individual immune status.

RESULTS AND DISCUSSION

While the various medical treatment regimens for CDAD are reviewed elsewhere, the focus of this review will be to summarize indications for surgical consultation and management in patients with established severe, complicated CDAD. Current therapeutic guidelines for when to operate in patients with severe, complicated CDAD are poorly established and currently supported by primarily retrospective data. Overall, surgical treatment of patients with severe, complicated CDAD (traditionally with subtotal colectomy and end ileostomy) has been shown to improve morbidity and mortality compared to conservative management of patients (mortality of surgical treatment reported at 34%-80% *vs* mortality in non-surgical care of 50%-70%) with earlier diagnosis and treatment being shown to be beneficial in reducing mortality[4,6,14]. Several recent articles have compiled laboratory, radiologic, and clinical findings associated with the need for surgical consultation and operative management in patients with established severe CDI and their results are summarized in Table 2. These laboratory, radiologic, and clinical parameters represent the highest common factors from our source articles which were themselves drawn from a variety of disparate individual studies. The stated parameters were shown in our source material to demonstrate an association with unfavorable outcomes defined as need for emergent operative intervention and/or *C. difficile*-associated mortality. Table 3 represents these authors' efforts to clearly and centrally summarize the prototypical signs of fulminant *C. difficile* colitis and indications for surgical management common amongst our sources. The diversity present amongst the current body of review and retrospective data regarding the signs of fulminant *C. difficile* colitis as well as indications for surgical management underscores the importance of our efforts to compile a guideline of the highest common factors present amongst patients suffering from this disease in order to guide appropriate treatment.

According to a meta-analysis of outcomes following emergency surgery for *C. difficile* colitis by Bhangu *et al*[17] which encompasses the source material for our included reviews, the most statistically significant ($P < 0.001$) preoperative physiological indicators predictive of post-operative mortality are shock requiring the use of vasopressors, odds ratio (OR) = 3.80, preoperative intubation, OR = 6.31 , acute renal failure, OR = 5.68, and multi-system organ failure, OR = 5.56[16]. Of the signs of fulminant CDAD and indications for surgical management identified in Table 3, age > 75 years, OR = 2.29 and any elevation of white blood cell count above normal limits, OR = 8.01 were found to have a weaker association with post-operative mortality ($P < 0.01$)[16]. Our remaining sum-

Table 2 Previous studies analyzing surgical management of fulminant Clostridium difficile colitis

Article	Indications for surgical consultation and operative management	Notes
Carchman *et al*[6] Review	Indications for Surgical Consultation in Patients with Known or Suspected CDAD	Strength/quality of evidence, B-Ⅲ
	Ileus/significant abdominal distension	
	Admission to intensive care unit	
	Hypotension (+/- vasopressors)	
	Mental status changes	
	WBC counts ⩾ 35 × 10^9 /μL	
	Serum lactate ⩾ 2.2 mmol/L	
	Any evidence of end-organ failure	
	Age ⩾ 80 yr with severe CDAD criteria	
	Immunosuppression with severe CDAD criteria	Strength/quality of evidence, B-Ⅱ
	Indications for Operative Management in Patients with CDAD	
	Diagnosis of *C. difficile* colitis as determined by one of the following:	
	Positive toxin assay result	
	Endoscopic findings (pseudomembranes)	
	CT scan findings (pancolitis +/- ascites)	
	Plus any one of the following criteria:	
	Peritonitis	
	Perforation	
	Worsening abdominal distension/pain	
	Sepsis	
	Intubation	
	Vasopressor requirement	
	Mental status changes	
	Unexplained clinical deterioration	
	Renal failure	
	Lactate level > 5 mmol/L	
	WBC count ⩾ 50 × 10^9/μL	
	Abdominal compartment syndrome	
	Failure to improve with standard therapy within 5 d as determined by resolving symptoms and physical examination, resolving WBC per band count	
Osman *et al*[14] Original article	Summary of the clinical, laboratory, and radiologic features of fulminant *C. difficile* colitis	Severe, complicated CDAD synonymous with fulminant CDAD is considered to be indication for operative management by these authors.
	Clinical:	
	History of diarrhea following antibiotic use	
	Systemic toxicity	
	Pyrexia ⩾ 38 ℃	
	Tachycardia > 100 beats/min	
	Hypotension: BP < 90 mmHg	
	Abdominal signs of Peritonitis	
	Generalized abdominal pain	
	Tenderness	
	Abdominal distension	
	Rebound tenderness	
	Organ failure and requirement for vasopressor therapy	
	Laboratory and Radiologic:	
	Increasing leukocytosis > 16 × 10^9 /L	
	Lactate > 2.2 mmol/L	
	Hypoalbuminemia < 30 g/L	
	Radiologic evidence of toxic megacolon (abdominal X-ray or CT)	
	Free air under the diaphragm	
Butala *et al*[15] Review	Prognosticators for development of fulminant colitis	Strength/quality of evidence, B
	Age > 65 yr	
	Lactate between 2.2-4.9 mmol/L	
	WBC count > 16000/μL-surgery within 30 d	
	History of Inflammatory bowel disease	
	Treatment with intravenous immunoglobulin	
	Colitis associated with signs of organ dysfunction	
Girotra *et al*[16] Original article	Summary of red flags for development of fulminant *Clostridium difficile* colitis	
	Age > 70 yr	
	Presenting symptoms: Triad of abdominal pain, diarrhea, and distension	
	Signs: Tachycardia (heart rate > 100 beats/min), tachypnea (respiratory rate > 20 respirations/min),or hypotension (systolic BP < 90 mmHg)	
	Recent *C. difficile* infection	
	Use of antiperistaltic medications (narcotics or anticholinergics)	
	White blood cell count > 18000/mm^3	
	Radiology studies suggestive of megacolon or perforation	

C. difficile: *Clostridium difficile*; CDI: *Clostridium difficile* infection; CDAD: *Clostridium difficile* associated disease; WBC: White blood cell.

Table 3 Summary of indications for surgical management

Indicator	Carchman *et al*[6]	Bignardi *et al*[9]	Osman *et al*[14]	Butala *et al*[15]
Elevated WBC (count $\times 10^9$)	> 35		> 16	> 16
Serum lactate (mmol/L)	> 2.2 consult > 5 operate		> 2.2	2.2-4.9
Peritoneal signs on physical examination including generalized abdominal pain	Present	Present	Present	
Abdominal distension	Present	Present	Present	
End organ (renal, respiratory) failure/dysfunction	Present		Present	Present
Hypotension (mmHg)	Present	< 90 systolic	< 90 systolic	
Tachycardia (bpm)		> 100	> 100	
Vasopressor requirement	Yes		Yes	
Radiological findings of pancolitis, ascites, megacolon, or perforation	Present		Present	
Age (yr)	> 80	> 70		> 65

WBC: White blood cell.

mary indicators were either not included or unable to be incorporated into this meta-analysis and odds ratios and relative risks were therefore unavailable given the nature of the retrospective review data. It should be reiterated that within the literature, indications for operative management in cases of fulminant CDAD are unsupported by level I evidence and thus the current recommendations including our own summary are supported only by clinical experience.

In terms of treatment options, the Bhangu meta-analysis also found no significant difference in overall mortality following total colectomy and end ileostomy compared to segmental colonic resection, defunctioning stoma, or non-therapeutic laparotomy[16]. While the newer treatment technique of stool transplant is currently being studied to establish its role in management of *C. difficile* infection, studies to date have focused on those patients suffering from recurrent *C. difficile* infection and have not addressed the issue of a role for patients with fulminant CDAD. Further studies in this area are needed. Stool transplant theoretically seeks to re-establish an appropriate balance of colonic microflora in those patients with the classically disturbed bacterial populations found in CDI[18].

CONCLUSION

Mortality rates attributable to fulminant *C. difficile* colitis remain high and are reported to be 38%-80%. Historically, the threshold for surgical intervention has been judged empirically because level I evidence to guide decision making is lacking. Studies of the surgical management of *C. difficile* infection have been limited by small sample size and the lack of a standard definition of fulminancy. Multiple small and medium-sized series have examined the surgical management of CDC. However, because of a lack of prospective randomized studies, it has been difficult to identify the optimal point for surgical intervention in patients with severe fulminant CDC. Therefore, the data gathered from retrospective analyses are valuable in making this decision. It was our goal to analyze the existing body of literature in an attempt to define host constellations which would predict the development of the more aggressive form of this disease and hence justify an early or earlier surgical intervention. Multiple authors have suggested that total colectomy earlier in the course of the disease was associated with improved survival. However the exact timing of the surgical intervention remains one of the main challenges. It is crucial to identify preoperative patients' characteristics that can serve as indications for operative treatment. After analyzing current literature, we identified a number of highest common parameters that are associated with unfavorable outcomes defined as need for emergent operative intervention and/or *C. difficile*-associated mortality. The parameters include age greater than 65 years old, peritoneal signs on physical examination, abdominal distension, signs of end-organ failure, hypotension less than 90 mmHg systolic blood pressure, tachycardia greater than 100 bpm, vasopressor requirement, elevated WBC count of greater than at least $16 \times 10^9/\mu L$, serum lactate of greater than 2.2 mmol/L, and lastly, radiologic findings suggestive of pancolitis, ascites, megacolon, or colonic perforation. Pre-operative intubation, acute renal failure, multi-system organ failure, and shock requiring vasopressors have been shown to be the most statistically significant indicators of post-operative mortality for fulminant CDAD.

Even though fairly strong evidence exists in contemporary literature, we recommend caution with use of these parameters in clinical practice when it comes to the actual decision to treat certain patients more aggressively. The identified risk factors should be used to lower surgeons' threshold for operative treatment early in the course of the disease. Further studies designed in the prospective fashion might be necessary to identify the actual point when irreversible multi-system organ failure occurs during the disease progression in order to reduce potentially preventable fatalities.

REFERENCES

1 **Cecil JA**. Clostridium difficile: Changing Epidemiology, Treatment and Infection Prevention Measures. *Curr Infect Dis Rep* 2012; **14**: 612-619 [PMID: 23054932 DOI: 10.1007/s11908-012-0298-9]
2 HCUP Projections: Clostridium Difficile hospitalizations

2011 to 2012 Report #. 2012-1. Available from: URL: http://www.hcup-us.ahrq.gov/reports/projections/CDI_Regional_projections_Final.pdf
3 **Lessa FC**, Gould CV, McDonald LC. Current status of Clostridium difficile infection epidemiology. *Clin Infect Dis* 2012; **55** Suppl 2: S65-S70 [PMID: 22752867 DOI: 10.1093/cid/cis319]
4 **Markelov A**, Livert D, Kohli H. Predictors of fatal outcome after colectomy for fulminant Clostridium difficile Colitis: a 10-year experience. *Am Surg* 2011; **77**: 977-980 [PMID: 21944509]
5 **Neal MD**, Alverdy JC, Hall DE, Simmons RL, Zuckerbraun BS. Diverting loop ileostomy and colonic lavage: an alternative to total abdominal colectomy for the treatment of severe, complicated Clostridium difficile associated disease. *Ann Surg* 2011; **254**: 423-427; discussion 423-427 [PMID: 21865943 DOI: 10.1097/SLA.0b013e31822ade48]
6 **Carchman EH**, Peitzman AB, Simmons RL, Zuckerbraun BS. The role of acute care surgery in the treatment of severe, complicated Clostridium difficile-associated disease. *J Trauma Acute Care Surg* 2012; **73**: 789-800 [PMID: 23026914 DOI: 10.1097/TA.0b013e318265d19f]
7 **Potter VA**, Aravinthan A. Identifying patients at risk of severe Clostridium difficile-associated disease. *Br J Hosp Med* (Lond) 2012; **73**: 265-270 [PMID: 22585325]
8 **Samore MH**, DeGirolami PC, Tlucko A, Lichtenberg DA, Melvin ZA, Karchmer AW. Clostridium difficile colonization and diarrhea at a tertiary care hospital. *Clin Infect Dis* 1994; **18**: 181-187 [PMID: 8161624 DOI: 10.1093/clinids/18.2.181]
9 **Bignardi GE**. Risk factors for Clostridium difficile infection. *J Hosp Infect* 1998; **40**: 1-15 [PMID: 9777516 DOI: 10.1016/S0195-6701(98)90019-6]
10 **Andrews CN**, Raboud J, Kassen BO, Enns R. Clostridium difficile-associated diarrhea: predictors of severity in patients presenting to the emergency department. *Can J Gastroenterol* 2003; **17**: 369-373 [PMID: 12813602]
11 **Cohen SH**, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald LC, Pepin J, Wilcox MH. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). *Infect Control Hosp Epidemiol* 2010; **31**: 431-455 [PMID: 20307191 DOI: 10.1086/651706]
12 **Dharmarajan T**, Sipalay M, Shyamsundar R, Norkus E, Pitchumoni C. Co-morbidity, not age predicts adverse outcome in clostridium difficile colitis. *World J Gastroenterol* 2000; **6**: 198-201 [PMID: 11819556]
13 **Byrn JC**, Maun DC, Gingold DS, Baril DT, Ozao JJ, Divino CM. Predictors of mortality after colectomy for fulminant Clostridium difficile colitis. *Arch Surg* 2008; **143**: 150-154; discussion 155 [PMID: 18283139 DOI: 10.1001/archsurg.2007.46]
14 **Osman KA**, Ahmed MH, Hamad MA, Mathur D. Emergency colectomy for fulminant Clostridium difficile colitis: Striking the right balance. *Scand J Gastroenterol* 2011; **46**: 1222-1227 [PMID: 21843039 DOI: 10.3109/00365521.2011.605469]
15 **Butala P**, Divino CM. Surgical aspects of fulminant Clostridium difficile colitis. *Am J Surg* 2010; **200**: 131-135 [PMID: 20409527 DOI: 10.1016/j.amjsurg.2009.07.040]
16 **Girotra M**, Kumar V, Khan JM, Damisse P, Abraham RR, Aggarwal V, Dutta SK. Clinical predictors of fulminant colitis in patients with Clostridium difficile infection. *Saudi J Gastroenterol* 2012; **18**: 133-139 [PMID: 22421720 DOI: 10.4103/1319-3767.93820]
17 **Bhangu A**, Nepogodiev D, Gupta A, Torrance A, Singh P. Systematic review and meta-analysis of outcomes following emergency surgery for Clostridium difficile colitis. *Br J Surg* 2012; **99**: 1501-1513 [PMID: 22972525 DOI: 10.1002/bjs.8868]
18 **Weissman JS,** Coyle W. Stool transplants: ready for prime time? *Curr Gastroenterol Rep* 2012; **14**: 313-316 [PMID: 22585070 DOI: 10.1007/s11894-012-0263-7]

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