Diverting Loop Ileostomy and Colonic Lavage

An Alternative to Total Abdominal Colectomy for the Treatment of Severe, Complicated Clostridium difficile *Associated Disease*

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Objective: To determine whether a minimally invasive, colon-preserving approach could serve as an alternative to total colectomy in the treatment of severe, complicated *Clostridium difficile*–associated disease (CDAD).

Background: *C. difficile* is a significant cause of morbidity and mortality worldwide. Most cases will respond to antibiotic therapy, but 3% to 10% of patients progress to a severe, complicated, or "fulminant" state of life-threatening systemic toxicity. Although the advocated surgical treatment of total abdominal colectomy with end ileostomy improves survival in severe, complicated CDAD, outcomes remain poor with associated mortality rates ranging from 35% to 80%.

Methods: All patients who were diagnosed with severe, complicated ("fulminant") CDAD and were treated at the University of Pittsburgh Medical Center or VA Pittsburgh Healthcare System between June 2009 and January 2011 were treated with this novel approach. The surgical approach involved creation of a loop ileostomy, intraoperative colonic lavage with warmed polyethylene glycol 3350/electrolyte solution via the ileostomy and postoperative antegrade instillation of vancomycin flushes via the ileostomy. The primary end point for the study was resolution of CDAD. The matching number of patients treated with colectomy for CDAD preceding the initiation of this current treatment strategy was analyzed for historical comparison.

Results: Forty-two patients were treated during this time period. There was no significant difference in age, sex, pharmacologic immunosuppression, and Acute Physiology and Chronic Health Evaluation-II scores between our current cohort and historical controls. The operation was accomplished laparoscopically in 35 patients (83%). This treatment strategy resulted in reduced mortality compared to our historical population (19% vs 50%; odds ratio, 0.24; $P = 0.006$). Preservation of the colon was achieved in 39 of 42 patients (93%).

Conclusions: Loop ileostomy and colonic lavage are an alternative to colectomy in the treatment of severe, complicated CDAD resulting in reduced morbidity and preservation of the colon.

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Clostridium difficile is the most common cause of hospital-acquired diarrhea and is a significant cause of morbidity and mortality worldwide.[1–3] Not only has the incidence of *C. difficile*-associated disease (CDAD) increased, but also hypervirulent strains have recently appeared.[4–7] *C. difficile* is a spore-forming gram-positive bacteria that produces exotoxins that are toxic to colonic mucosa and can trigger local and systemic inflammatory cascades.[8] Almost all cases will respond to oral antibiotic therapy, but 3% to 10% of patients with CDAD progress to a severe, complicated, or "fulminant" state of life-threatening systemic toxicity.[8–10]

The indications for surgical management of patients with CDAD are not clearly defined; however, most advocate surgical intervention in patients with worsening clinical examinations or peritonitis or patients in shock.[11] Total abdominal colectomy with end ileostomy has been advocated as the operation of choice and has been demonstrated to marginally improve survival compared to nonoperative management in these critically ill patients.[10,12] This operation was undertaken even before the etiology of the CDAD was known, primarily because of its superficial similarities to "toxic megacolon" as a late acute manifestation of inflammatory bowel disease.

Colectomy for severe, complicated CDAD has many disadvantages. Most notably, mortality rates in small series continue to range from 35% to 80%.[8,10,12–15] In addition, laparotomy and subtotal or total abdominal colectomy can result in significant morbidity, and survivors often require permanent ileostomy. Furthermore, there are no universally accepted definitions of severity and physicians cannot predict which patients will progress to fulminant disease.[7,10,15,16] Although standardized strategies of medical management for mild or moderate disease have long been established, the approaches to the treatment of severe and severe complicated (fulminant) CDAD have remained tentative and fragmented.[8,17–19]

We now present our experience with an alternative surgical approach to the management of severe, complicated CDAD, which may prove a safer and simpler option. On the basis of the nature of the disease as a bacterial toxin-mediated mucosal inflammatory process with delayed and indirect systemic threats to life, we hypothesized that minimally invasive ileal diversion with intraoperative colonic lavage using a high-volume polyethylene glycol or electrolyte solution will clear *C. difficile* infection, resulting in eradication of CDAD, while preserving the colon. Furthermore, we hypothesize that this will reduce morbidity and mortality compared to colectomy.

METHODS

All patients were treated at the University of Pittsburgh Medical Center between June 2009 and January 2011, and all patients met the diagnostic criteria of severe, complicated, or "fulminant" CDAD as previously described at our institution.[8] No patients with CDAD who presented during the study period at either institution were excluded. Our indications for operation are outlined in Table 1. This operative therapy was approved by the Quality Improvement Review Committee of University of Pittsburgh Medical Center, and the Total Quality Council. Operation specific informed consent was obtained in all cases. The operation and/or postoperative care was supervised by a single practitioner (Dr Zuckerbraun) in all cases. The surgical approach involved an attempted laparoscopic creation of a loop ileostomy after visually assessing the colon to ensure viability. Intraoperatively, 8 L of warmed polyethylene glycol 3350/electrolyte solution (GoLytely; Braintree Laboratories) was infused into the colon

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TABLE 1. Indications for Operative Management in Patients With Severe, Complicated CDAD

A diagnosis of CDAD as determined by history of ongoing or recent diarrhea and one of the following:
1. Positive toxin assay
2. Endoscopic findings
3. CT scan findings consistent with *C. difficile* colitis (pancolitis +/− ascites)

Plus any one of the following criteria:
1. Peritonitis
2. Worsening abdominal distention/pain
3. Sepsis
4. New onset ventilatory failure
5. New or increasing vasopressor requirement
6. Mental status changes
7. Unexplained clinical deterioration
8. Nonimproving or worsening while blood cell count more than 20 or less than 3 despite appropriate antibiotic therapy for 96 hours
9. Nonimproving and worsening bandemia (>10%) despite appropriate antibiotic therapy for 96 hours

via the ileostomy and collected via a rectal drainage tube. Postoperatively, the patients received antegrade vancomycin flushes (500 mg in 500 mL of Lactated Ringers; q8 hours for a duration of 10 days) via a Malecot catheter (24 French) left in the efferent limb of the ileostomy (Fig. 1). In addition, patients were continued on intravenous (IV) metronidazole (500 mg q8 hours) for 10 days. Clinical status was monitored on the basis of hemodynamics, vasopressor requirements, and serial abdominal examinations according to standard intensive care unit protocols.

The primary end point for the study was resolution of CDAD, as documented by resolution of clinical symptoms and normalization of the peripheral leukocyte count. Clinical parameters, risk factors, mortality, and Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scores of these patients were determined. A matching number of patients (42) treated with colectomy for CDAD in the immediate period before initiation of this new treatment strategy were analyzed for historical comparison.

All data were summarized as mean ± standard deviation, median (interquartile range), or percentage (%). Student *t* test was used to compare continuous variables, whereas chi-square test was used for categorical variables.

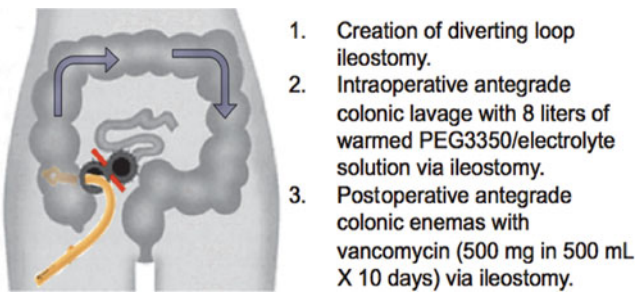

FIGURE 1. Operative treatment strategy for loop ileostomy and colonic lavage for severe, complicated *C. difficile*-associated disease. When possible laparoscopic exploration of the colon and abdominal cavity is performed and a diverting loop ileostomy is created. The colon is then lavaged in an antegrade fashion through the ileostomy with a high volume (8 L) of polyethylene glycol 3350 or balanced electrolyte solution and the effluent is collected via a rectal drainage tube. A catheter is placed in the efferent limb of the ileostomy to deliver vancomycin flushes in an antegrade fashion in the postoperative period.

RESULTS

Forty-nine patients were identified with severe, complicated CDAD during this 20-month period. The goal of care in 6 of these patients was comfort measures only; thus, surgical therapy was not considered in this group. Of the remaining 43 patients, 42 patients (mean age 65.3 ± 13 years; 45% women) were taken to the operating room for planned diverting ileostomy and colonic lavage, whereas only 1 patient underwent a planned total colectomy. The cohort was critically ill at presentation: 38 (90%) required intensive care, 27 (64%) required mechanical ventilation, and 31 (74%) needed vasopressor support. Thirty-two patients had white blood cell counts more than 15,000 (mean ± SD = 25.4 ± 12.1) and 35 had band counts more than 10% (mean ± SD = 21.4 ± 12.2) (Table 2). Nineteen patients (45%) were receiving immunosuppressive drugs. The mean albumin level was 2.0 ± 0.8 (g/dL). Both immunosuppression and hypoalbuminemia have been shown to be predictive of poor outcome in CDAD.[20,21] The mean APACHE-II score at the time of surgical evaluation for the patient population was 29.7 ± 5.5. The mean predicted mortality based on APACHE-II[22] was 67.5 ± 20.3%.

Diversion was accomplished laparoscopically in 35 patients (83%) whereas 7 patients were converted to laparotomy. Postoperatively, all patients underwent vancomycin colonic flushes (500 mg; q8 hours × 10 days) via the ileostomy and received IV metronidazole (500 mg IV; q8 hours × 10 days) (Fig. 1).

All patients who underwent diversion and lavage had resolution of leukocytosis and clinical signs of CDAD. The mean time to normalization of the white blood cell count in patients initially presenting with leukocytosis was 5.9 ± 3.2 days. The mean time to return of bowel function as determined by ileostomy output and tolerance of oral or enteral diet was 2.6 ± 1.3 and 3.1 ± 1.6 days, respectively.

In 1 patient (2%), the decision was made to perform a laparotomy and total abdominal colectomy immediately after laparoscopic loop ileostomy and colonic lavage. This decision was based on the presence of abdominal compartment syndrome, which was not immediately improved by colonic washout. Two additional patients in this cohort (5%) underwent colectomy in the postoperative period after loop ileostomy or colonic lavage. Of these, 1 patient had a recurrent vasopressor requirement 10 days after the initial operative procedure

TABLE 2. Demographics and Outcomes in Patients with Severe, Complicated CDAD Treated with Ileostomy or Colonic Lavage Versus Colectomy

	Ileostomy/Lavage	Colectomy	*P*
Age, y	65.3 ± 13	62.1 ± 14	0.28
Sex	45% women	45% women	1.0
APACHE-II (mean ± SD)	29.7 ± 5.5	28.5 ± 7.1	0.39
While blood cell count (mean ± SD)	25.4 ± 12.1	27.1 ± 13.2	0.54
Band count (mean ± SD)	21.4 ± 12.2	21.3 ± 12.9	0.97
Albumin (mean ± SD)	2.0 ± 0.8	2.2 ± 0.8	0.26
Intensive care unit	38/42 (90%)	38/42 (90%)	0.64
Intubated	27/42 (64%)	26/42 (62%)	0.82
Vasopressors	31/42 (74%)	32/42 (76%)	0.81
Immunosuppression	19/42 (45%)	17/42 (40%)	0.66
Postoperative death	8/42 (19%)	21/42 (50%)	0.006*

*Odds ratio = 0.24 (0.09–0.63).

TABLE 3. Postoperative Morbidities in Patients After Loop Ileostomy or Colonic Lavage Versus Colectomy Historical Controls

Morbidity	Ileostomy/Colonic lavage No. (%)	Colectomy No. (%)
Deep venous thrombosis/pulmonary embolism	1 (2.4%)	3 (7.1%)
Surgical site infection	3 (7.1%)	9 (21%)
Urinary tract infection	3 (7.1%)	4 (9.5%)
Pneumonia	4 (9.5%)	5 (12%)
Inadvertent enterotomy	1 (2.4%)	1 (2.4%)
Reoperation related to ileostomy	2 (4.8%)	4 (9.5%)
"Ileostomy tube" migration	1 (2.4%)	NA

and underwent a second operation with subtotal colectomy. The second patient developed abdominal compartment syndrome within 12 hours of the ileostomy and lavage and underwent a laparotomy with subtotal colectomy.

Eight patients (19%) died in the postoperative period (within 30 days). An additional 6 patients (14%) have died outside of the postoperative period, all determined to be due to preexisting illnesses other than CDAD (mean survival of 8.3 $\pm$ 3.1 months). Postoperative morbidity was relatively limited in this cohort (Table 3). Importantly, only 1 patient in our series had symptoms of recurrent CDAD approximately 2 months after this operative procedure after receiving antibiotics for a urinary tract infection. Symptoms manifested as increased abdominal pain and mucous drainage per rectum. This patient was treated with a 14-day course of vancomycin via ileostomy and symptoms resolved. To date, of surviving patients observed at least 6 months, 15 of 19 (79%) have had their ileostomy reversed.

The mean APACHE-II score of the immediate, previous 42 patients before June 2009 who were treated with colectomy at this institution was 28.5 $\pm$ 7.1, which illustrates that these cohorts had a similar severity of illness. The 30-day mortality of these previous 42 patients managed with colectomy was 50% (21 of 42) ($P = 0.006$ compared to ileostomy colonic lavage). Table 2 highlights additional demographic or clinical comparative data. Only 4 of 21 surviving patients (19%) of these patients had their ileostomies reversed.

DISCUSSION

In this case series, we found that colonic lavage using a polyethylene glycol or electrolyte solution followed by antegrade intracolonic vancomycin flushes delivered through a diverting ileostomy was an acceptable alternative to colectomy for the management of severe, complicated CDAD. Although patients treated with ileostomy or colonic lavage had severity of illness compared with historical controls treated with colectomy at our institution, the mortality was significantly lower. Only a total of 3 patients treated with this novel strategy went on to be treated with colectomy. Furthermore, a large percentage of patients have had restoration of bowel continuity after the initial loop ileostomy and colonic lavage.

There is a strong biological rationale for the success of this approach. CDAD is a toxin-mediated disease that primarily induces a local response on the colonic mucosa and surrounding tissues, most often without compromising the viability of the colonic wall. The pathogenesis of the systemic inflammatory response is unknown but also seems to derive from toxins generated within the colon and the subsequent inflammatory response. For this reason, colectomy has been generally accepted as a last resort for life-threatening disease unresponsive to oral vancomycin and oral or IV metronidazole. Others and we have employed this approach with some limited success in the past[8]; however, the mortality is high and the colon is permanently lost. Both of these factors often serve to deter timely surgical consultation until after multiple organ failure is irreversible. A diverting loop ileostomy with colonic lavage through a minimally invasive approach should achieve the same goals with minimal stress: the fecal stream is interrupted and the luminal flora deprived of nutrition; mechanical lavage should remove much of the bacteria and toxin, and direct instillation of vancomycin into the intestinal lumen should reduce the etiologic organism and reverse the pathologic process. Continuation of systemic metronidazole should be synergistic. The mortality is reduced in this series and the colon preserved in almost all survivors even in the few cases in which open laparotomy was required.

Despite the fact that the patients in this cohort presented with severe, complicated disease, the overall mortality of 19% was also lower than most reported series of patients treated with colectomy and lower than that of the historical controls from within our own institution.[14,15,23] Diverting ileostomy and lavage was planned on all but 1 patient during this period of time and did not represent a selected cohort. This 1 patient was offered total abdominal colectomy as an initial procedure because the operating surgeon was unaware of the new treatment strategy. In further analyzing the care of CDAD in our own institution, over the previous corresponding 20-month time period before the initiation of this current treatment strategy, 7 patients (in whom the goals of care were not limited) who were determined to have severe, complicated CDAD were denied surgical therapy on the basis of perceived operative risk and all of these patients died secondary to CDAD. However, since June 2009 when this novel therapy was instituted, all patients identified with an operative indication for severe, complicated CDAD, in which there was intent to treat, were taken to surgery. Importantly, from our entire cohort with a mean follow-up time of 11.3 $\pm$ 5.6 months, only 1 patient had a recurrence of CDAD whereas the recurrence rate quoted after medical therapy alone in multiple studies approaches 25% in many series.[24,25]

Interestingly, of the 3 patients in this series who went on to colectomy, the determined indication in 2 patients was abdominal compartment syndrome. One of these was determined at the time of the initial operation and one 12 hours postoperation from ileostomy or colonic lavage. Patients with severe, complicated CDAD may develop abdominal compartment syndrome secondary to the extent of the inflammation, colonic distention, and third spacing of fluid. Since these initial cases, we have encountered an additional patient with abdominal compartment syndrome and performed a decompressive laparotomy in conjunction with the loop ileostomy and colonic lavage, while not removing the colon. This was followed by a subsequent laparotomy to close the patient's abdominal wall. For patients with abdominal compartment syndrome, we now advocate this open approach with loop ileostomy and colonic lavage without closing the fascia. This is followed by a subsequent laparotomy and fascial closure. The third patient who had a colectomy was status post lung transplant 2 weeks before the development of CDAD and then had a new vasopressor requirement 10 days after the initial loop ileostomy or colonic lavage. There was no other obvious source of sepsis at the time and computed tomographic scan showed continued colonic wall thickening, and the decision was made to perform a colectomy. On final pathologic review, the colon showed near complete resolution of colitis with minimal inflammation. Furthermore, his status did not improve until diagnosis and treatment of an underlying viral illness was instituted.

In the majority of patients (83%), loop ileostomy and colonic lavage were performed laparoscopically. The indications to convert to laparotomy in the remainder of the patients were adhesive disease or ventral hernia from prior surgeries (n = 3), concurrent abdominal compartment syndrome (2), or large varicosities secondary to portal

hypertension (n = 2). Of the 2 patients with abdominal compartment syndrome, as previously mentioned, 1 patient underwent immediate colectomy and the other was treated with decompressive laparotomy, loop ileostomy, and colonic lavage. We believe that the only absolute contraindication to a minimally invasive approach is concurrent abdominal compartment syndrome. There are likely benefits to utilizing a minimally invasive approach in the critically ill CDAD population.

This study presents a series of an alternative surgical procedure, while avoiding the morbidity and mortality of colectomy in the management of CDAD. Despite the success of this approach, there were 8 postoperative deaths in the patient cohort. The mean duration of survival in these patients was 13 ± 4 days. The cause of death in all 8 patients was not directly attributed to CDAD; however, the critical illness of severe, complicated CDAD was likely associated with the death in most cases. Interestingly, a postmortem autopsy was performed on 2 patients both revealing minimal colitis. The respective causes of death as determined by postmortem examination were acute heart failure (postoperative day 5) in a patient who was hospitalized with severe aortic stenosis, significant coronary artery disease, and fulminant hepatic failure (postoperative day 14) in a patient with Child's C cirrhosis awaiting liver transplant.

A major challenge in the care of patients with more advanced CDAD is the lack of a validated severity-scoring system. Proposed severity-scoring systems have excellent negative predictive values and poor positive predictive values.[26–28] Thus, these scoring systems are limited and poorly predict which patients will progress to severe, complicated disease and antibiotic treatment failure. Severe disease has been classified by expert opinion of the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America as patients with a white blood cell count greater than 15,000 or an increase in serum creatinine 50% greater than baseline.[11] These organizations classify severe, complicated disease as CDAD patients with hypotension, shock, ileus, or "toxic megacolon." We believe that this classification schema understages the severity of illness in many patients and fails to adequately identify patients who are likely to become critically ill. We advocate a severity-scoring system that would be more inclusive in staging patients as having severe, complicated CDAD, thus lowering the threshold to be considered as having the most serious form of this disease. A proposed scoring system that heavily weights cardiopulmonary failure (intubation or vasopressors) or mental status changes and utilizes a number of other clinical parameters is proposed (Table 4). Advantages would be earlier surgical consultation and perhaps earlier intervention. This scoring system remains to be validated.

Surgical management in the treatment of CDAD has essentially been limited to use as a salvage therapy in patients with critical illness. This was generally true in the patients treated in this case series as demonstrated by high APACHE-II scores, as many of the patients were not identified until they were already critically ill. However, we believe that all patients with severe, complicated CDAD should be considered for surgical management. One of the hypothetical advantages to our new approach is that on the basis of the reduced short- and long-term morbidity of the procedure compared to total abdominal colectomy and that practitioners will consider surgical treatment earlier in the management of this disease process and not exclusively as a therapy of last resort. Earlier surgical intervention will likely further improve outcomes; however, this remains to be shown.

There are several limitations to this analysis. Given that this is a series from a single center, conclusions regarding the broad application of this technique to the general medical population are limited. Furthermore, the long-term outcomes and risk of recurrence in treated patients remain to be assessed. Although the exact timing of surgical intervention in CDAD remains unclear, we encourage early surgical consultation in patients with severe, complicated CDAD to optimize the chances for successful eradication with minimal morbidity. Elderly, malnourished, and immunosuppressed patients are at high risk for the development of severe, complicated CDAD, and thus early operative intervention with a minimally invasive diverting ileostomy and lavage should be contemplated in these populations.

In summary, we have shown that in a critically ill and complex patient population, we can successfully avoid the need for colectomy in severe, complicated CDAD by performing a diverting ileostomy with colonic lavage. This represents a novel surgical approach to a frustrating and devastating disease and presents a potential mechanism for surgical eradication of disease with less short- and long-term morbidity.

TABLE 4. Proposed CDAD Severity Scoring System

1-3 points "mild-moderate disease," 4-6 points "severe" disease, 7 or more points 'severe complicated' disease

Criteria	Points
Immunosuppression and/or chronic medical condition	1
Abdominal pain and/or distention	1
Hypoalbuminemia (<3 g/dL)	1
Fever > 38.5°C	1
Intensive care unit admission	1
CT scan with nonspecific findings of pancolitis, ascites, and/or bowel wall thickening	2
While blood cell count >15,000 or < 1500 and/or band count >10%	2
Creatinine 1.5 fold > baseline	2
Abdominal peritoneal signs	3
Vasopressors required	5
Mechanical ventilation required attributed to CDAD	5
Disorientation, confusion, or decreased consciousness	5

*This scoring system is for patients with a diagnosis of CDAD and is not yet validated.

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DISCUSSANTS

R. Sawyer (Charlottesville, VA):

Severe *C. difficile* disease continues to be a highly morbid and lethal illness, particularly in centers with large numbers of critically ill patients, such as the University of Pittsburgh. The difficult decision when to operate in fulminant and *C. difficile* colitis falls squarely on the surgeon's shoulder Dr Zuckerbraun's novel technique allows us to offer a less morbid and probably more successful approach for the management of this illness.

According to your data, performing a loop ileostomy with antegrade instillation of vancomycin resulted in better survival than performing colectomy and also leads to preservation of the colon in about 90% of your patients. I believe that it may become the standard technique and treatment for severe *C. difficile* colitis in the future.

I have four questions: first, in your table on the diagnosis of *C. difficile* disease, you list a positive CT scan as one of the single qualities that will qualify someone for this treatment. I presume this means you have operated on patients with a characteristic CT scan but a negative toxin assay for *C. difficile* or a negative sigmoidoscopy? Also, have you taken out any colons or operated on any patients who truly did not have *C. difficile* disease?

Second, how did you derive your matched set of 42 patients? Was this based on APACHE-II score only, or was it a convenience sample, or was this a consecutive sample of 42 patients just before instituting this new treatment?

Third, how do you determine when it is safe to reverse the ileostomy? Do you wait a minimum number of months, or do you continue to test these patients? When their *C. difficile* clears from either their ileostomy output or their colon, do you then consider it safe to reverse the patient's ileostomy?

Finally, you mentioned using this technique earlier in the course of the disease, which I think would be truly beneficial. Please tell us how you think this will alter your criteria for when to operate on these patients, assuming that they are referred to you soon enough? Also, do you envision using this technique in a patient who has chronic relapsing *C. difficile* disease but who is otherwise relatively stable?

Response from B. Zuckerbraun:

CT scanning alone is not very sensitive or specific for diagnosing *C. difficile* colitis. However, other tests available to confirm *C. difficile* are not timely enough to confirm the diagnosis in a deteriorating patient. We certainly have operated on patients on the basis of CT scan findings and history alone.

As far as choosing our historical controls, these were 42 consecutive patients before the institution of this therapy. Remarkably, the demographics in our patient population were quite similar.

In answer to your third question, regarding timing of the reversal of the ileostomy, this has been an ongoing process. Initially, when the idea was conceived with Dr Simmons and Dr Alverdy, the notion of, perhaps, reversing these patients early, even within the same hospital stay, was entertained, but we found these patients have too many comorbidities and could not consider doing a second operation early. Most of these patients require months to recover from the illness that brought them into the hospital in the first place, which oftentimes was not *C. difficile*. A fair number of these were patients on immunosuppression undergoing transplants. For the most part, the decision for ileostomy reversal was made in follow-up visits, ensuring that the patient is in a better nutritional state and is back on his or her feet.

You asked about utilizing this technique earlier. Most of these patients were critically ill and, most of them had been sent in from outlying institutions, already in extremis. We are finding, in our own institution, that we are becoming involved before these patients show any classical indication for surgical disease and we are happy to see these patients earlier. That way, when there are any signs of deterioration or patients meet any of these criteria, we can operate and intervene earlier. We look forward to changing the practice in the future.

As far as recurrent disease, 30% plus of these patients had recurrent disease at the time we operated on them. We saw only 1 recurrence after this procedure in our patient population. If you compare to that vancomycin therapy alone, the recurrence rate is up to 25%.

We were asked by infectious disease practitioners who are following patients as outpatients with 5, 10, etc, relapsing episodes of *C. difficile* to consider surgical therapy. We have done that for 2 patients, but this was not reported in this series. These patients are not in extremis; they are not acutely sick and they are tolerating a diet. They just keep getting diarrhea when they withdraw from their vancomycin. We have tried treating patients with a high volume of GoLYTELY lavage via nasogastric tube first, and we successfully eradicated *C. difficile* in a couple of patients and that has been reported in the literature. We did perform the operation on 2 desperate patients, one of which had 19 previous episodes.

DISCUSSANTS

D. Fry (Chicago, IL):

I am curious why you chose vancomycin as opposed to metronidazole. Using vancomycin in this topical fashion, with its

consequences relative to vancomycin-resistant organisms, raises the question of whether you are begging an epidemiological disaster in your intensive care unit, given that topical antibiotics are a long-proven strategy for encouraging resistance in a unit.

My second question is more of an epidemiological question in that the frequency of *C. difficile* in the US population is following in the footsteps of methicillin-resistant *Staphylococcus aureus* (MRSA), just 2 years out of step. That is, the frequency of MRSA in our hospitals is what *C. difficile* will be in 2 more years. We are at 1% of the total population of discharged patients with *C. difficile*–acquired infection in our hospitals in the United States. One of the alarming footstep phenomena is that *C. difficile* is now a community-acquired infection in patients who have not been in the hospital or have not even recently been challenged by antibiotics. Did you see any patients with community-acquired infections who came in the door with the problem, as opposed to patients who were strictly in the intensive care unit?

Response from B. Zuckerbraun:

The question regarding the choice of vancomycin as our topical antibiotic is an outstanding one. This was chosen purely based upon experience and reports utilizing vancomycin enemas as a topical therapy to instill and deliver vancomycin adequately to the colon and achieve an adequate MIC in order to kill *C. difficile*.

Regarding selection and creation of a VRE epidemic, both metronidazole and vancomycin have been associated with selecting for VRE, and this is a very real concern. This is a secondary research end point that we are examining, with continued culturing and swabbing of these patients. We have not followed this long enough to date, but it is a valid concern.

As far as the epidemiology of *C. difficile* in our patient population is concerned, yes, a fair number of these patients came from the community. All patients received antibiotics within 3 months before their episode of *C. difficile*, but some of these for relatively innocuous community-treated diseases, such as pneumonias and urinary tract infections.

DISCUSSANTS

S. Wren (Palo Alto, CA):

Why not go even more toward a minimally invasive technique and place a colonic decompression tube right up the ileocecal valve and perform colonic irrigations? This has been described and has been successful in some reports. Why not use, as the treatment algorithm, colonic irrigation first followed by loop ileostomy as a secondary option?

Response from B. Zuckerbraun:

There have been reports describing placement of long decompression tubes via colonoscopy and instilling vancomycin that way. Additionally, in an initial iteration in which we wanted to utilize a less-invasive approach in patients who were not improving on standard medical therapy, we tried placing a cecostomy tube in one patient and an appendicostomy tube in another to deliver vancomycin and attempted to irrigate the colon. Both patients, in our experience, improved, but I was very dissatisfied with this approach.

Again, the reason why our current ilesostomy and lavage approach is effective is unclear at this point. We do believe it is multifactorial, and it is not just the delivery of the antibiotic alone. We feel that the combination of diversion—which has surely been used in toxic megacolon—lavage, vancomycin, and perhaps changing colonic oxygen tension all contribute to the effect. The Turnbull/Blowhole procedure in a toxic megacolon context has also been shown to benefit patients who were not great operative candidates in the past. So, we feel it is multifactorial, but the future will shed further insight.

DISCUSSANTS

M. T. Dayton (Buffalo, NY):

If time bears out the results of your study, this will be a simpler and more effective way to handle these complicated patients. Anyone who has ever operated on many of these patients knows that these patients have thick, boggy, edematous colons that seem to be very amotile. In fact, they often seem to have a profound ileus.

Is there any technical difficulty in getting the lavage to traverse the entire colon to travel distally to the sigmoid and to the rectum areas? And, if so, how did you monitor that?

Response from B. Zuckerbraun:

These colons are very thick, and what we actually find, although we have no proof, is that it seems the thicker they are, the more rigid of a tube and the faster or lower the required volume will be until we begin to see return of that effluent from the rectal tube. Furthermore, because they are so thick, the concern about perforating the colon is minimal.

We usually see return of effluent through the rectal tube at somewhere between 1 and 1.5 L after that volume has been instilled by the ileostomy. We monitor the output to make sure that we get close to 8 L returned. We actually leave the laparoscopic trocars in until the completion of lavage and we look to make sure that there is not excessive fluid in the belly.

Because the colon is so thick, there is some challenge to performing the operation laparoscopically, but placing the patient in steep Trendelenburg position, to move everything toward the head and away, allows us to easily identify the terminal ileum, and the operation can be readily accomplished.

DISCUSSANTS

O. Kirton (Hartford, CT):

We still need to understand which patient population can actually benefit from this procedure, other than suspicion of *C. difficile* colitis, because several of the patients in your study did not present positive toxin assays, or critical illness.

How do you decide when to proceed to colectomy? Second, what is the antibiotic regimen that should be utilized in the perioperative period, and finally, should colonic endoscopy be performed in all patients before you proceed to lavage?

Response from B. Zuckerbraun:

Previously, we utilized colectomy in patients we thought were failing. Of note, in all the patients, even in the patients who died, we saw resolution of their white count; we have autopsies on 2 of those patients, which showed resolution of their colitis. We believe they died secondary to their comorbid diseases and the insult from the severity of illness associated with their *C. difficile*–associated disease.

We chose the patients who received colectomies in this series based on clinical judgment. As we advance in our experience, it seems less likely that we will be performing colectomies on these patients unless indicated by findings of necrosis or perforation, which is rare.

As for antibiotics, we initially treated these patients with concurrent intravenous metronidazole as an additive effect, but we moved away from this in general.

DISCUSSANTS

E. Moore (Denver, CO):

When we adopt a new procedure, there will likely be patients who are relegated to this unnecessarily, but more concerning is those who will receive this procedure when it may not be appropriate. In reviewing your mortality, although laudable at only 20%, were

there any patients, in retrospect, in whom the colon should have been removed earlier? Clearly, the infected colon is a major source of systemic inflammation and could be the threshold to drive multiple organ failure.

Response from B. Zuckerbraun:

That is an ongoing question. We find that we are leaving this inflamed, boggy colon that is neutrophil laden, with an ongoing SIRS response. Although we do see an almost, immediate partial resolution of laboratory results, such as white counts and clinical status with decreased pressor requirements, we do see that critical illness extends for several cases. If we perform a colectomy, the inflammation may be reversed more rapidly. However, we feel the magnitude of colectomy also poses other challenges to these critically ill patients.

Regarding the decision as to when to perform a colectomy, we believe strongly, at this point, that if the colon is not perforated or is not necrotic, this operation can be utilized in all settings. However, experience at other centers and further experience in our own center will prove whether this is true or not.