Severe complicated *Clostridium difficile* infection: Can the UPMC proposed scoring system predict the need for surgery?

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INTRODUCTION: *Clostridium difficile* infection (CDI) is one of the most common health care–associated infections, and it continues to have significant morbidity and mortality. The onset of fulminant colitis often requires total abdominal colectomy with ileostomy, which has a mortality rate of 35% to 57%. University of Pittsburgh Medical Center (UPMC) developed a scoring system for severity and recommended surgical consultation for severe complicated disease. The aim of this study was to evaluate if the UPMC-proposed scoring system for severe complicated CDI can predict the need for surgical intervention.

METHODS: This is a retrospective review of all patients who developed severe complicated CDI at Geisinger Medical Center between January 2007 and December 2012 as defined by the UPMC scoring system. Main outcomes were the need for surgical intervention and 30-day mortality.

RESULTS: Eighty-eight patients had severe complicated CDI based on the UPMC scoring system. Fifty-nine patients (67%) required surgery and 29 did not. All patients had a diagnosis of CDI as shown by positive toxin assays. There was no difference between the groups with respect to age, sex, body mass index, or comorbidities. When comparing the surgical group to the nonsurgical cohort, the surgical cohort averaged 20 points on the scoring system compared to 9 in the nonoperative cohort. In patients with severe complicated CDI, 15 or more points predicted the need for surgery 75% of the time. Forty-two percent of the surgical cohort had respiratory failure requiring mechanical ventilation compared to 0% in the nonsurgical cohort ($p < 0.0001$). Forty-nine percent of the surgical cohort required vasopressors for septic shock before surgery compared to 0% in the nonsurgical cohort ($p < 0.0001$). Acute kidney injury was present in 92% of the surgical cohort versus 72% within the nonsurgical cohort ($p = 0.026$). Seventy-six percent of the surgical patients were admitted to the ICU before surgery. Within the nonsurgical cohort, only 24% of patients required ICU stay during admission. Overall, 30-day mortality in the surgical cohort was 30%, and there was no mortality in the nonsurgical cohort.

CONCLUSIONS: The UPMC scoring system for severe complicated CDI can help us predict patients who need a surgical consult and the need for surgical intervention. In patients with severe complicated CDI, evidence of end-organ failure predicts surgical intervention. (*J Trauma Acute Care Surg.* 2016;81: 221–228. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Prognostic study, level III; therapeutic study, level IV.

KEY WORDS: *Clostridium difficile*; colitis; indications; surgery.

Clostridium difficile is a spore-forming gram-positive bacteria first identified as the cause of antibiotic-associated diarrhea and colitis in the late 1970s.[1,2] *Clostridium difficile* infection (CDI) is the leading cause of nosocomial diarrhea in the United States. For most patients who acquire CDI, the infection seems to appear after usage of antibiotics, which have altered the normal colonic flora.[3] *Clostridium* produces two toxins that cause colonic inflammation that can range from mild colitis to life-threatening disease.[4] Toxin A is primarily an exotoxin affecting the colonic wall, and toxin B is primarily cytotoxic affecting the colon on a cellular level.[2] Recently, hypervirulent strains of *C. difficile* have emerged that are capable of producing toxins A and B in quantities 16- to 20-fold higher than less virulent strains.[2] Most cases of CDI respond to antibiotic therapy with metronidazole and/or vancomycin.[4] However, a small percentage of patients, approximately 3% to 10% will progress to a severe, complicated, or "fulminant" state of life-threatening systemic toxicity.[4] Severe complicated disease is ill defined but can be concluded as severe CDI resulting in clinical deterioration, such as multiorgan system failure, peritonitis, and/or sepsis.[5] The mortality rate of patients with severe complicated CDI has been reported to be 34% to 57% in most series.[6,7]

In the literature to do, there are no precise indications for patients with CDI and surgical management.[8] As a general rule of thumb, most surgeons agree that surgical intervention is indicated in patients with worsening clinical examinations, peritonitis, or in shock.[8] In the United States, total abdominal colectomy with end ileostomy has been the operation of choice for severe complicated CDI. This operation has marginally improved survival compared to nonoperative management in these critically ill patients.[9,10] In 2011, the University of Pittsburgh Medical Center (UPMC) published a severity scoring system for patients with severe complicated CDI, as shown in Table 1.[1] The purpose of this scoring system would allow for earlier surgical consultation in patients with severe complicated CDI, facilitating earlier surgical intervention and improved outcomes.[1]

"Mortality rates in patients with severe complicated CDI are unacceptably high, and the question may arise whether these patients receive timely and appropriate treatment."[11] Olivas et al.[11] has elucidated factors that contribute to the unacceptably high postoperative mortality rate: surgical intervention too late in the course of the disease, lack of clearly defined guidelines for patient selection, and difficulty in predicting the clinical course of the disease. The timing of surgical intervention is key to survival in patients with severe complicated CDI.[12] The current study is a retrospective review of patients who had severe complicated CDI according to the criteria put forth by UPMC. We evaluated the UPMC scoring criteria for patients with severe complicated CDI to determine which criteria predict the need for surgery. Finally, we analyzed our population to try and identify risk factors for mortality.

MATERIALS AND METHODS

All patients who had a diagnostic code for CDI over a 5-year period from January 2007 to December 2012 were identified. Institutional guidelines require infectious disease (ID) and surgical consultation for any patient with worsening abdominal examination or evidence of end-organ failure and CDI. All patient charts with ID and surgical consultation were reviewed and patients with severe complicated disease were identified. All patients that were treated at Geisinger Medical Center (GMC) between January 2007 and December 2012 and met the diagnostic criteria of severe, complicated, or "fulminant" CDI as described by UPMC- Presbyterian Hospital were included in the study.[1] Overall hospital admissions and death rates were obtained to

TABLE 1. Proposed *C. difficile* 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 or pancolitis, ascites, and/or bowel wall thickening	2
White blood cell count >15,000 and/or band count >10%	2
Creatinine 1.5-fold > baseline	2
Abdominal peritoneal signs	3
Vasopressors required	5
Mechanical ventilation required attributed to C. *difficile*	5
Disorientation, confusion, or decreased consciousness	5

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calculate the incidence of *C. difficile* colitis. The patients were divided into surgical and nonsurgical groups. The UPMC guidelines were used, and all patients with severe, complicated CDI had scores calculated. The surgical group score was calculated on the day of surgery. The nonsurgical group score was the highest calculated score within 72 hours of surgery consultation. The study was independently approved by the respective institutional review boards. The characteristics of the study population were described using mean ± SD for continuous data, median (IQR) for nonparametric data, and frequencies (%) for categorical data. Characteristics were compared between groups using the χ^2 or Fisher exact test for categorical data, two sample *t*-tests for continuous, and Wilcoxon rank-sum test for nonparametric data. An exact logistic regression model was developed to test the associations of age and the proposed *C. difficile* severity scoring system on the need for surgery. Receiver operating characteristic analysis was used to test model accuracy. A logistic model was used to determine the predicted event probability of needing surgery given a specific point on the scoring system. A *p* value less than 0.05 was considered statistically significant. Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

From January 2007 to December 2012, 3,713 patients had a diagnosis of *C. difficile* infection at Geisinger Medical Center. Of those, 3,625 patients were excluded from this study because they did not meet the criteria for severe complicated disease according to the UPMC scoring system. Eighty-eight patients did meet the criteria for severe complicated disease, which was 2% of the total population. Fifty-nine patients required surgical intervention, and 29 were managed medically. All 59 patients in the surgery group underwent total abdominal colectomy with end ileostomy.

The overall trend of severe complicated CDI from 2007 to 2012 has increased, as there were only 17 patients within the first two years of the study compared to 47 patients within the last two years of the study. Surgical management of the disease has increased over time, and the nonsurgical management has trended downward. Comparing the surgical group and the nonsurgical group, the only statistical difference between the groups with regard to demographics or comorbidities was that the nonsurgical group had a higher incidence of diabetes. There was no difference when looking at imaging modalities and the use of positive toxin assay for the diagnosis of *C. difficile*. In the nonsurgical group, however, there were more CT scans performed.

Multiple significant differences were found between the surgical and nonsurgical groups when evaluating the UPMC severe complicated criteria (Table 2). The surgical group was

TABLE 2. Comparison of Surgery Versus No Surgery

	No Surgery n = 29	Surgery n = 59	*p* Value
Age, years	69.1 ± 11.8	65.4 ± 12.6	0.19
WBC >15,000 and/or band count >10%	16 (55.2%)	45 (76.3%)	0.04
Peritonitis	7 (24.1%)	45 (76.27%)	<0.0001
Worsening abdominal distention/pain	27 (93.1%)	59 (100%)	0.11
Fever >38.5°C	13 (44.8%)	32 (54.2%)	0.41
Mechanical ventilation	0 (0%)	25 (42.37%)	<0.0001
Vasopressor requirement	0 (0%)	29 (49.15%)	<0.0001
Disorientation, confusion, or decreased consciousness	10 (34.5%)	43 (72.88%)	0.0005
Hypoalbuminemia (<3 g/dL)	17 (58.6%)	48 (81.4%)	0.02
Creatinine, 1.5 fold > baseline	21 (72.4%)	54 (91.5%)	0.03
Immunosuppression and/or chronic medical condition	26 (89.7%)	59 (100%)	0.03
30-day mortality	0 (0%)	18 (30.51%)	0.0009
Total points	9 (7–12)	20 (14–25)	<0.001

TABLE 3. Comparison of Mortality in Surgical Group

	No Mortality n = 41	Mortality n = 18	*p* Value
Age	63.8 ± 13.7	69.1 ± 8.8	0.14
WBC >15,000 and/or band count >10%	29 (70.7%)	16 (88.9%)	0.19
Peritonitis	33 (80.5%)	12 (66.7)	0.32
Worsening abdominal distention/Pain	41	18	n/a
Fever >38.5°C	25 (61%)	7 (38.9%)	0.12
Mechanical ventilation	13 (31.7%)	12 (66.7%)	0.01
Vasopressor requirement	19 (46.3%)	10 (55.6%)	0.51
Disorientation, confusion, or decreased consciousness	28 (68.3%)	15 (83.3%)	0.34
Hypoalbuminemia (<3 g/dL)	32 (78.1%)	16 (88.9%)	0.48
Creatinine 1.5 fold > baseline	38 (92.7%)	16 (88.9%)	0.64
Immunosuppression and/or chronic medical condition	41	18	n/a
Days from diagnosis to OR	8.0 (2.2–17.6)	3.5 (0.5–5.5)	0.01
Total points	19 (14–24)	22 (16–25)	0.99

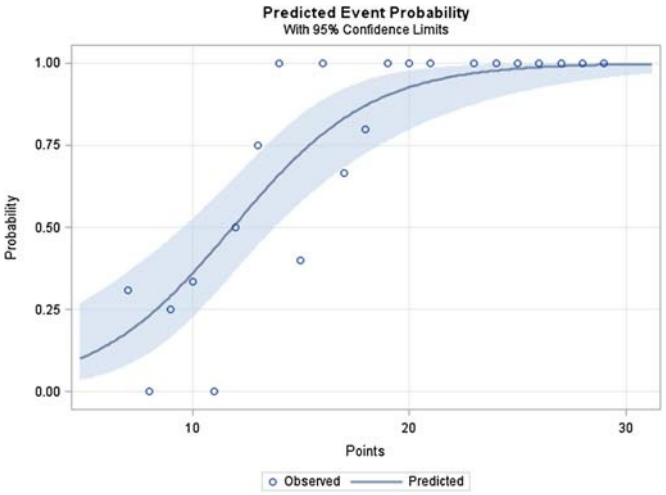

Figure 1. Probability that a patient with severe *C. difficile* infection will need surgery.

statistically more likely to have white blood cell count (WBC) greater than 15,000 and/or bands greater than 10%, peritonitis, respiratory failure requiring mechanical ventilation, vasopressor requirements, altered mental status, hypoalbuminemia, acute renal failure, and immunosuppression. Importantly, 42% of the surgical group had respiratory failure requiring mechanical ventilation compared to 0% in the nonsurgical group ($p < 0.0001$). Forty-nine percent of the surgical group required vasopressors for septic shock before surgery compared to 0% in the nonsurgical group ($p < 0.0001$). Acute kidney injury was present in 92% of the surgical group versus 72% within the nonsurgical group ($p = 0.026$). Seventy-six percent of the surgical patients were admitted to the ICU before surgery. Within the no-surgical group, only 24% of patients required ICU stay during admission. The average total points for patients within the nonsurgical group were 9 versus 20 within the surgical group. Overall, 30-day mortality in the surgical group was 30%, and there was no mortality in the nonsurgical group.

The surgical group was further analyzed by comparing the mortality group to the no mortality group (Table 3). There was no statistical difference between white blood cell count/bandemia, peritonitis, fever, vasopressor requirement, or altered mental status between the two groups. In the surgical mortality group, more patients had respiratory failure requiring mechanical ventilation, $p = 0.01$. The number of patients with septic shock requiring vasopressor support was similar between the two groups. However, nine of the ten patients within the mortality group required two or more vasopressors to maintain adequate blood pressure before surgery. Most of the no mortality group required only one vasopressor at the time of surgery. The mortality group had a much shorter time from diagnosis to OR compared to the no mortality group (3.5 versus 8.0 days). The surgical mortality group averaged 22 points on the UPMC scoring system compared to 19 points within the no surgical mortality. This did not reach statistical significance.

As seen in Figure 1, a logistic model was used to predict the probability of receiving surgery given a specific UPMC score. In this study, a patient with 11 or more points had a 50% probability of having surgery. A patient with 15 or more points had a 75% probability of receiving surgery. Finally, 100% of patients with 22 or more points required surgery.

A multivariate model was created to predict the need for surgery. In addition to the individual UPMC variables, this model included age 70 years or older, as this has previously been shown to predict poor outcomes. Using these variables, only peritonitis had a significant association with the need for surgery (odds ratio, 5.4 [95% confidence interval, 1.2–30.9]). The ROC analysis for this model found an area under the curve (AUC) of 0.9342 (Fig. 2).

The second model tested age 70 years or older and the UPMC point value to predict the need for surgery. It was found that the point value had a significant association with the need for surgery (odds ratio, 1.4 [95% confidence interval, 1.2–1.6]). The ROC analysis for this model found an AUC of 0.8895 (Fig. 3).

DISCUSSION

Consistent with previous studies, which have reported a rising incidence of severe complicated CDI in the United States,[13–16] the results of our study demonstrate that the incidence of severe complicated CDI continues to increase among hospitalized patients. This seems to be a worldwide health concern, as reports from Japan,[17] Europe,[18–21] and Canada[18] are also documenting rising trends of severe complicated CDI cases. The more concerning facts are the rising numbers of colectomies performed for severe complicated CDI, which seem again as a continuation of a previously observed trend that started in the mid-1990s.[13] This could be a marker of more severe disease associated with the emergence of hypervirulent strains such as the PCR ribotype 001 and 010, 106,[22] BI/NAP1/027[23,24] and strains carrying the binary toxin gene.[24] All of these strains have been shown to be associated with failure of medical management, multidrug resistance, and increased recurrence rates.[25] During the current study period, GMC was not

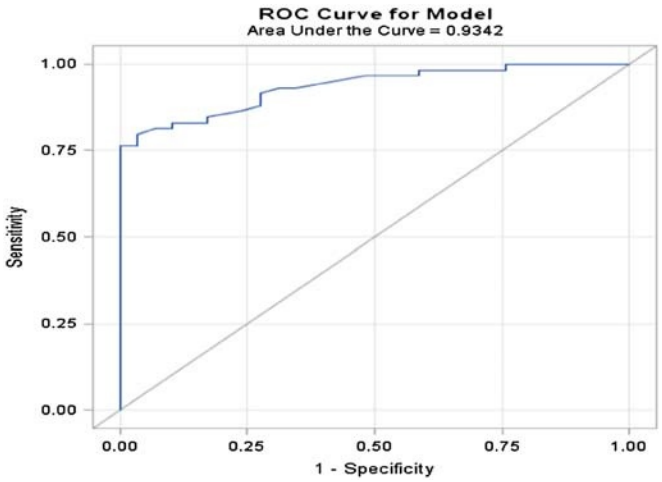

Figure 2. Exact logistic regression of UPMC variables and age for patients having surgery.

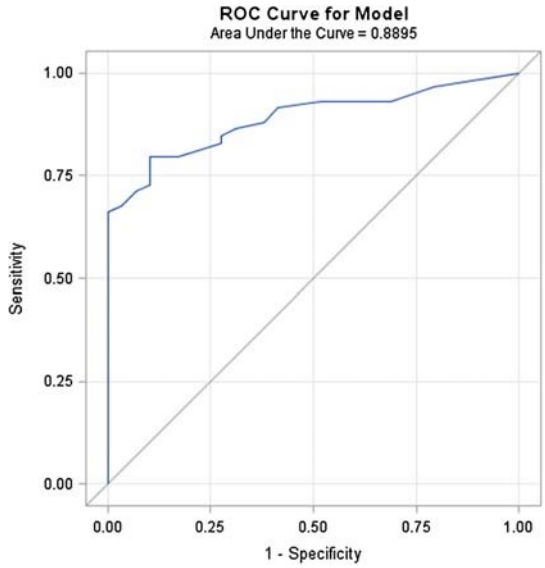

Figure 3. Exact logistic regression of UPMC point value and age for patients having surgery.

testing for these strains and cannot comment on the incidence within our study population.

The mortality rate of 30% in the current study for patients undergoing surgery for severe complicated CDI, although high, is consistent with previous studies.[26] Also consistent with previous studies was the high correlation of mortality with septic shock, renal failure, and respiratory failure.[26,27] We hypothesize that mortality from surgery remains high because clinicians await the development of signs of cardiopulmonary collapse and/or other organ failure as signs of failure of medical therapy and indications for surgery. These are late indications for surgical intervention. However, to improve outcomes and patient survival from severe complicated CDI, the indications for surgery should be reliable and easy to apply in the clinical setting before the onset of organ failure. Although classified as severe complicated *C. difficile* colitis, 33% of the patients required no surgical intervention in this study. No mortality was found in the nonsurgical group. Importantly, none of these patients developed respiratory failure or septic shock. Acute kidney injury was a common zfinding in both the surgical and nonsurgical groups and should not be used as the sole indication for surgery.

Surgical patients at GMC who died from severe CDI had increased respiratory failure requiring mechanical ventilation, but there was no statistical difference between any of the other UPMC criteria. Interestingly, the mortality group had a much shorter time from diagnosis to operative intervention compared to the no mortality group (3.5 versus 8 days), suggesting a more fulminant course. On closer evaluation, differences were found in the number of vasopressors that patients required before surgery. Nine of the 10 patients within the mortality group required two or more vasopressors to maintain adequate perfusion before surgery. Most of the no mortality group only required one vasopressor at the time of surgery. The actual concentration of each vasopressor requirement at the time of surgery could not be determined owing to the retrospective nature of the study. Likely, patients requiring multiple vasopressors did require higher concentrations based on current management of septic shock. A combination of increased incidence of respiratory failure, higher overall points on the UPMC scoring system, and a higher number of vasopressor requirements found in the mortality group supports a more fulminant course. These findings of a more severe fulminant course potentially explain the earlier operative intervention found in the mortality group. Additionally, these findings within the mortality group confirm that surgical intervention should be performed earlier in the disease process, before the development of multiorgan failure. Potentially with the UPMC scoring system in place, earlier surgical consultation will lead to earlier surgical intervention and improved mortality rates. Perhaps if there were a larger population of surgical patients, we could see more criteria trending toward significance in the mortality group.

In patients with severe *C. difficile*, there is a lack of a validated scoring system to help aid health care professionals in the care of these patients.[4,7,26] The scoring systems currently in the literature are limited.[1] They often cannot predict which patients will respond to antibiotic treatment verse failure and need for surgery.[1] The UPMC scoring system was developed for early surgical consultation for patients with severe CDI and can be used to predict the need for surgical intervention. As most CDI patients are not admitted to surgery, it is imperative to have a system in place for early consultation, as early intervention has been shown to improve outcomes. Overall, 67% of patients with severe complicated disease required surgery. As expected, the higher the score on the UPMC scoring system, the higher the probability of receiving surgery. Patients with 11 or more points had a 50% probability of receiving surgery, 15 or more points predicted the need for surgery 75% of the time, and finally, 100% of patients with 22 or more points underwent surgery.

From the current study, two multivariate models were created using age ≥ 70 and the factors that make up the UPMC *C. difficile* severity scoring system. Looking at the individual variables in the models, only peritonitis and point value had a significant association with the need for surgery. However, using all the variables combined in the models, there was an excellent correlation for predicting the need for surgery, AUC, 0.934 and 0.889, respectively (Fig. 2, Fig. 3).

There are several limitations to this analysis. Given that this is a series from a single institution and retrospective, conclusions regarding the broad application of this technique to the general medical population are limited. Our sample size was small, and it may lack the power to detect subtle differences within the surgical group with regard to mortality.

Lack of evidence-based data for the management of severe complicated CDI makes developing definitive recommendations difficult. Early identification of patients who have severe complicated CDI, and specific guidelines for indications for surgery are needed. As seen in this retrospective study, mortality for severe complicated CDI remains high. The UPMC scoring system is easy to calculate, can quickly be performed at the bedside, and can help facilitate operative decision making. This scoring system needs further validation. Patients calculated to have severe complicated CDI and early clinical signs of respiratory or cardiovascular failure should undergo prompt surgical intervention.

AUTHORSHIP

All the authors above made substantial contributions to the conception or design of the work, analysis, and interpretation of data for the work. All worked on drafting the work or revising it critically for important intellectual content, and final approval of the version to be published. They made an agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DISCLOSURE

The authors declare no conflicts of interest.

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DISCUSSION

Dr. Brian Zuckerbraun (Pittsburgh, Pennsylvania): I am pleased to see that our proposed scoring system correlated with outcomes in this retrospective study, especially since we devised this scoring system based upon experience from our center and the consideration from other published series with factors that were associated with poor outcomes.

For sure and by no means are we married to this set of criteria. And we would urge change and refinement with experience over time.

Importantly, you mentioned the benefits of using such a scoring system to prompt surgical consultation. I agree and encourage the use of simple criteria with a relatively low threshold to get the surgery team involved, so as to not complicate issues for those working outside of the surgical unit.

However, I would take some opposition to the statement that when most patients with severe complicated *C. diff* require surgery, they would require total abdominal colectomy. Our group believes that most can be treated adequately with loop ileostomy and colonic lavage, but that remains to be validated as well.

One thing the UPMC score did not take into account was any measure of patient characteristics that are associated with frailty or increased risk. Realizing that frail patients are predisposed to reach the clinical criteria that were used in the scoring system, would adding any patient characteristics or frailty increase the sensitivity of a scoring system based upon your evaluation of the data?

Do you have any plans to prospectively validate this or another scoring system? Given that the number of patients at your facility, this would take a fair amount of time—perhaps a collaborative, multi-institutional approach would be called for. Maybe a joint effort between an organization such as the AAST and other organizations that are interested in this disease such as the Surgical Infection Society, and if so, I would be happy to participate.

Thirdly, how do you plan on using this score in clinical practice to guide management? Can it tell practitioners who to operate on? Will you set a threshold based upon the score to prompt operation, what operation to perform or, perhaps, on whom an operation may be futile?

Again, congratulations and thank you for the opportunity to discuss this paper.

Dr. H. Gill Cryer (Los Angeles, California): I enjoyed the study and I think it's really important. A couple of questions, though.

First of all you said, "required surgery." What were the actual indications for surgery? How did you decide to operate versus not operate?

And then, secondly, when was the score determined? Is this when a patient shows up? Is this when you are deciding whether to operate or not?

I mean most of these patients have quite a long, prolonged course, trial of various antibiotics and care before we actually decide whether they need an operation or not. So I'm just interested in what that timing of when you create, when you score them to determine whether they need an operation. Thank you.

Dr. David A. Spain (Stanford, California): Similar to what Dr. Cryer said, in a retrospective study I'd be careful about saying "needed an operation" versus "got an operation." In your study, did you look at those patients who had a score greater than 15 but didn't get an operation and compare their outcomes to those who did get an operation?

Dr. George Velmahos (Boston, Massachusetts): Congratulations, very well presented. Two quick questions.

First, how do you use your three most dominant criteria—peritonitis, vasopressors, and intubation—in patients who are already intubated and on vaspressors for another disease and now have a positive *C. diff* culture? And, number 2, when you use more objective criteria, like white blood cell count, it all depends on your threshold. If you set the threshold low, like at 15,000, as you did, then you find no discriminatory value. But my fulminant *C. diff* colitis patients have white blood cell counts in the order of 20,000 to 40,000. If you set your threshold much higher, then you may find a difference.

Dr. Lawrence Diebel (Detroit, Michigan): Very nice presentation. One question and one comment. Was the score used to decide surgery, yes or no?

One of the problems with this scoring system—and all of the scoring systems that have been used for *C. diff* infection—is it's a single-time determination. Someone in the audience had the question of when was it determined. And I think what we need is a serial scoring system.

All the bad parameters are systemic parameters so we need some kind of biomarker from the systemic circulation, whether it is pro-inflammatory mediator levels or markers of *C. diff* toxemia to better discriminate who is getting bad on our therapies.

Dr. Michelle C. Julien (Danville, Pennsylvania): Thank you. These were all very good questions. I'd just like to start out by asking, would adding different patient characteristics make a difference? And I think that it would.

If we have a bigger patient population, whether that is collaborating with other facilities, I think that we would see that probably certain immuno-suppressions or, for example, patients with cancer, possibly, would have a different course than someone who did not.

As far as a prospective analysis, at Geisinger we do have a scoring system. Unfortunately, we don't use it as much as we should as far as every patient that has *C. diff* that we are consulted on.

I think doing a prospective analysis would be great. I think that it would help clinicians. I think it would help us as surgeons. And I think that it would help our patients and their families to be able to decide if it does come to the point of needing surgery or not as far as what the decision would be and the best decision for the patient.

As far as using the score in practice, I think that being able to tell a patient—and if I couldn't tell the patient because they were intubated or on pressors, severely ill, at least being able to tell their family and loved ones that they have a certain score—I will pick, for example, and say a score of 15 and their probability of about 75% of needing surgery, so I would be talking about that mortality associated with that and what would come after.

This was a retrospective review. We looked at all patients that had *C. diff*. The way that I was able to see if patients moved on for this study or were discarded, basically, was dependent on if they had a consult with infectious disease, which most of these patients do as soon as they meet the SIRS criteria.

After they meet a SIRS criteria at Geisinger, then they go on to have a surgical consult, whether that is the colorectal team or the acute care team, depending on the day and the workload in the operating room.

And after that, since it was a retrospective review, it was really up to the surgeon's discretion and the team at that time if the patient needed to go on to surgery or if they wanted to see if medical therapy was to be continued.

I think that setting the criteria higher is a good idea. I do agree with the white blood cell count. On average we see 30s or above, most definitely. I think that having it set at 15 you have a lot more patients that initially start within the scoring system but I think a lot of them drop off as you need higher points.

So I think maybe setting the bar in the future for severe complicated disease as far as scoring goes higher than seven points, as we saw with our patients they average about nine points.

And the surgical patients averaged 20 so I think taking a look at a different total score possibly in between those two numbers to set criteria a little bit higher would be something to think about as well.

And the comment about the CT scan, we used just strictly based off of what the paper had talked about. We did have the radiologist look at it for, since it was a retrospective just to make sure that they had clinical signs based on CT scan findings of *C. diff* infection.

Thank you.