Risk for *Clostridium difficile* Infection after Radical Cystectomy for Bladder Cancer: Analysis of a Contemporary Series

Nick W. Liu[1], Kashyap Shatagopam[1], M. Francesca Monn[1], Hristos Z. Kaimakliotis[1], Clint Cary[1], Ronald S. Boris[1], Matthew J. Mellon[1], Timothy A. Masterson[1], Richard S. Foster[1], Thomas A. Gardner[1], Richard Bihrle[1], Michael G. House[2] and Michael O. Koch[1]

[1]Department of Urology, Indiana University School of Medicine, Indianapolis, Indiana

[2]Department of Surgery, Indiana University School of Medicine, Indianapolis, Indiana

Role of the Funding Source: None

Disclosure of Potential Conflicts of Interest: None

*Correspondence:
Nick W. Liu, M.D.
Department of Urology
Indiana University Health
535 Barnhill Drive, Suite 140
Indianapolis, IN 46202
Phone: (607) 316-0756
Fax: (317) 948-2619
Email: nickliu@gmail.com

Running head: Incidence and Risk Factors of Clostridium difficile in Radical Cystectomy Patients

Key Words: Clostridium difficile, infection, bladder cancer, radical cystectomy, urinary diversions

Abstract word count: 262
Total word count: 2499
Figures: 1 Tables: 4 References: 30

Risk for *Clostridium difficile* Infection after Radical Cystectomy for Bladder Cancer: Analysis of a Contemporary Series

Role of the Funding Source: None

Disclosure of Potential Conflicts of Interest: None

Running head: Incidence and Risk Factors of Clostridium difficile in Radical Cystectomy Patients

Key Words: Clostridium difficile, infection, bladder cancer, radical cystectomy, urinary diversions

Abstract word count: 262
Total word count: 2499
Figures: 1 Tables: 4 References: 30

Abbreviations

CDI – *Clostridium difficile* infection

RC – radical cystectomy

UTI – urinary tract infection

Abstract

Introduction: This study seeks to evaluate the incidence and associated risk factors for *Clostridium difficile* infection (CDI) in patients undergoing radical cystectomy (RC) for bladder cancer.

Methods: We retrospectively reviewed a single institution bladder cancer database including all patients who underwent RC between 2010 and 2013. CDI was diagnosed by detection of *Clostridium difficile* toxin B gene using polymerase chain reaction based stool assay in patients with clinically significant diarrhea within 90 days of the index operation. A multivariable logistic regression model was used to identify demographics and perioperative factors associated with developing CDI.

Results: Of the 552 patients who underwent RC, postoperative CDI occurred in 49 patients (8.8%) with a median time to diagnosis after RC of 7 days (IQR: 5-19). Of the 122 readmissions for postoperative complications, 10% (n=12) were related to CDI. Two patients died from sepsis directly related to severe CDI. On multivariate logistic regression, the use of chronic antacid therapy (OR: 1.9, 95% CI 1.02 – 3.68, p=0.04) and antibiotic exposure greater than 7 days (OR: 2.2, 95% CI: 1.11 – 4.44, p=0.02) were independently associated with developing CDI. The use of preoperative antibiotics for positive urine culture within 30 days prior to surgery was not statistically significantly associated with development of CDI (p = 0.06).

Conclusions: The development of CDI occurs in 8.8% of patients undergoing RC. Our study demonstrates that use of chronic antacid therapy and long duration of antimicrobial exposure are associated with development of CDI. Efforts focusing on minimizing antibiotic exposure in RC patients are needed and perioperative antimicrobial prophylaxis guidelines should be followed.

Introduction

In the United States, *Clostridium difficile*, a spore-forming, gram-positive anaerobic bacillus, is the leading cause of nosocomial infectious diarrhea.[1] Despite efforts on infection control and prudent antibiotic stewardship, the incidence of *Clostridium difficile* infection (CDI) continues to escalate in both the nosocomial and community settings.[2, 3] Since the emergence of the hypervirulent NAP1/027 strain in recent years, there has been an increase in the severity of CDI, with more patients failing medical therapy and requiring emergent colectomy.[2, 4, 5]

Recent epidemiologic data suggests that CDI is a growing burden among surgical patients and is associated with increased morbidity, mortality, hospital stay and health care costs.[6, 7] The risk of CDI is highest among patients requiring intestinal tract manipulation or reconstruction, a population very similar to patients undergoing radical cystectomy (RC).[6] Other major risk factors for CDI include advanced age and recent antibiotic exposure.[4, 8-10] Bladder cancer patients tend to be older and require frequent antimicrobial prophylaxis for pre- and perioperative urinary tract instrumentation, therefore placing them at a higher risk for development of CDI.

Recent studies utilizing data from community practice settings identified a CDI rate of 1.3 – 1.7% in patients undergoing RC.[10, 11] However, with RC becoming more regionalized to tertiary referral centers,[12] the complications and incidence associated with CDI after RC at referral centers are rarely reported. The purpose of this study is two-fold: to determine the incidence of CDI in a contemporary cohort undergoing RC at a high-volume tertiary referral center, and to identify the perioperative risk factors for development CDI in RC patients.

Materials and Methods

Following institutional review board approval, we conducted a retrospective review of patients undergoing RC between January 2010 and December 2013 at our institution for bladder cancer. Patients undergoing cystectomy for non-oncological indications or with a history of chronic antibiotic use were excluded. Patients with a preoperative urine culture demonstrating bacterial growth were treated with oral antibiotics within 30 days prior to RC. Mechanical bowel preparations were only done in patients undergoing continent catheterizable urinary reservoir diversion (Indiana pouch). Oral antibiotic prophylaxis sterilizing gut flora was not used.

All patients received a single-dose of cefoxitin within one hour of surgical incision. For patients with a penicillin allergy or positive preoperative urine culture resistant to cephalosporins, other antibiotic regimens with coverage for gram negatives and anaerobes were administered (typically a fluoroquinolone in combination with metronidazole). Perioperative antibiotic prophylaxis was extended beyond 24 hours postoperatively in select patients depending on surgeon preference. All patients that qualified received pre and postoperative alvimopan, a peripheral opioid antagonist. Postoperatively, patients were maintained on no oral intake on postoperative day 0 through 1 and given either proton-pump inhibitors or histamine-2 antagonists. Nasogastric tubes were removed on postoperative day 1 with allowance of limited clear liquids on postoperative day 2. An unlimited clear liquid diet was given on postoperative day 3 until flatus, at which point patients were transitioned to a regular diet.

The primary end point of this study was the development of CDI within 90 days of RC. CDI was diagnosed by detection of the *Clostridium difficile* toxin B gene using polymerase chain reaction based stool assay in patients with clinically significant diarrhea, which is defined as greater than three loose bowel movements in one day, or presence of pseudomembranous colitis

during exploratory laparotomy. Hospital-wide CDI occurrences during the studied period were obtained from our Department of Infectious Diseases. Examined clinical and perioperative variables included age, gender, body mass index, preoperative/neoadjuvant chemotherapy, medical comorbidities, prior gastrointestinal surgery, preoperative urinary tract infection (UTI) and antibiotic use (within 30 days prior to RC), Charlson comorbidity index, chronic antacid therapy (including proton-pump inhibitors and histamine antagonists), urinary diversion type, operative time, estimated blood loss, perioperative blood transfusion, and perioperative antibiotic duration (defined as days of antibiotics received starting in the preoperative setting and ending at hospital discharge).

Postoperative outcome variables included length of stay, readmission rate, need for postoperative antibiotics, septicemia/bacteremia, pyelonephritis/UTI, urinoma, hospital-acquired pneumonia, acute renal failure, prolonged ileus, wound infection/complication, intra-abdominal abscesses and death within 30 days of RC.

Univariate analysis between CDI and clinical variables was assessed using Student's t-test for continuous variables and Pearson's chi-square test for categorical variables. To determine independent risk factors for CDI, we performed forward and backward stepwise logistic regressions using $p \leq 0.2$ as the significance level required for inclusion. Variables identified as significant in the stepwise model were used in the final multivariate logistic regression model to examine the increased risk of CDI development. Statistical analysis was performed using Stata® version 13.1 (StataCorp, College Station, Texas) with $p<0.05$ considered statistically significant.

Results

Of the 552 patients who underwent RC at our institution, 49 (8.8%) patients developed CDI. The rate of CDI in RC patients increased from 6.4 per 1000 patients in 2010 to 16.5 per 1000 patients in 2013 (Figure 1) and a small increase in hospital-wide CDI rate was also observed in the same time period (Table 1). Of the 115 patients with clinically significant diarrhea, 42.6% tested positive for CDI. The number of patients presenting with clinically significant diarrhea also increased between 2010 and 2013 (Table 1). Median time to CDI diagnosis from RC was 7 days (IQR: 5-19). Twelve patients (24.4%) developed CDI after discharge from their index hospitalizations.

Table 2 describes the clinical characteristics of the cohort. Patients with CDI were more likely to use chronic antacid therapy and have a longer duration of perioperative antibiotic use but were less likely to undergo orthotopic neobladder diversion. The rate of preoperative antibiotic use was higher in patients with CDI than those without CDI, but this difference was not statistically significant ($p=0.06$).

The most common initial presenting symptom of CDI was diarrhea in 48 patients (97.9%). Thirty-three patients (67.3%) were treated with either intravenous or oral metronidazole, and the remaining patients were treated with a combination of metronidazole and oral vancomycin. Two patients with severe CDI and a history of fecal diversion were treated with vancomycin lavage via their end colostomies.

In the stepwise logistic regression model, preoperative hemoglobin, chronic antacid therapy, perioperative antibiotic duration and urinary diversion type were considered significant ($p<0.2$), and therefore were included in the final multivariable logistic regression model. Patients on chronic antacid therapy had a 1.9 times increased odds of CDI when adjusting for preoperative hemoglobin, urinary diversion type, and duration of perioperative antibiotics

received (p=0.04, Table 3). Additionally, patients who received more than 7 days of antibiotics (starting in the preoperative setting) had a 2.2 times increased odds of CDI when compared to patients who received no more than one day of antibiotics (p=0.02). Since only patients with an Indiana pouch received mechanical bowel preparation, urinary diversion type was not significantly associated with CDI. This suggests that mechanical bowel preparation is unlikely an inciting factor for CDI.

Patients with CDI were more likely to have a longer hospital stay and higher readmission rate (Table 4). Of the 122 readmissions, 10% (n=12) were readmitted for CDI. The rate of postoperative antibiotic use during hospitalization was higher in patients with CDI than those without CDI but this did not reach statistical significance (p=0.08). Patients with CDI had substantially more postoperative complications including urinoma, acute renal failure, wound infections and intra-abdominal abscesses. Two deaths (4%) occurred as a result of CDI. One patient developed severe sepsis and end-organ failure from both CDI and other competing infections leading to withdrawal of care. The second patient died of severe pseudomembranous colitis 3 days after RC.

Discussion

This study provides contemporary data on the incidence and risk factors associated with CDI in patients undergoing RC. At high-volume centers, the incidence of CDI in patients undergoing RC is largely unknown. In a recent review of 5,425 patients undergoing RC from more than 2,900 community hospitals, Calvert et al. identified a CDI incidence of 1.7%, which is higher than patients undergoing radical prostatectomy (0.02%) or nephrectomy (0.23%) but comparable to those undergoing colorectal procedures (1.5%).[10, 13] A retrospective review of 180 patients undergoing RC at a high-volume institution reported a higher CDI rate of 7.2% within 30 days of surgery.[14] Our study found that 8.8% of patients undergoing RC for bladder cancer developed CDI within 90 days of surgery. Additionally, we demonstrated that nearly 10% of patient readmissions for postoperative complications were related to CDI, emphasizing the significant morbidity associated with this disease.

Antimicrobial exposure is the most commonly cited risk factor for CDI development in surgical patients and the risk of CDI increases with longer duration of exposure.[4, 9, 15, 16] A recent study from the Netherlands showed that the risk of CDI development is the highest during therapy and in the first month following antibiotic use.[17] In congruence with these published findings, our study showed that the risk of CDI is highest after having received more than 7 days of perioperative antibiotics (HR: 2.2, p=0.02) compared to those who received only one day or less of antibiotics. Our findings highlight the importance of minimizing antimicrobial exposure in RC patients and should serve as an important reminder to follow appropriate prophylaxis guidelines.

Antibiotic stewardship programs have been shown to decrease overall CDI rates,[18, 19] but could a similar strategy be adopted in patients undergoing RC? For patients undergoing urinary

diversions, the American Urological Association recommends the use of antimicrobial prophylaxis for no more than 24 hours after surgery.[20] Our study showed that only 49% of patients followed the appropriate guidelines on antimicrobial prophylaxis. While the compliance rate at our institution seems low, the study by Calvert et al. also showed a comparable compliance rate of 44% in RC patients.[10] Reasons for deviation from antimicrobial prophylaxis guidelines in RC patients include increased patient comorbidities, preoperative bacteriuria, difficult operations associated with fecal contamination, and indwelling hardware such as ureteral stents, catheters and/or surgical drains.[21] Limiting antibiotic use in the postoperative setting seems logical but is difficult to apply universally as the incidence of postoperative infectious complications after RC patients remains high, and is reported in 16% to 38% of patients.[22, 23]

Limiting the use of preoperative antimicrobials in RC patients should be a priority. Approximately 30% of patients in our series received antibiotics for bacteriuria identified on preoperative urine cultures. Though the 2005 guideline from Infectious Diseases Society of America recommends routine treatment of asymptomatic bacteriuria in patients undergoing urological procedures[24], recent data from patients undergoing stone surgery have questioned the value of preoperative urine culture, as asymptomatic bacteriuria is a poor predictor of postoperative infection.[25] Furthermore, several studies have shown that treatment of asymptomatic bacteriuria in bladder cancer patients undergoing outpatient urological procedures (ie. cystoscopy and intravesical therapy) is unnecessary as these patients did not have an increased risk of UTI.[26, 27] A prospective trial on the utility of preoperative urine culture in patients undergoing RC is needed to fully address this issue.

Diarrhea in the immediate postoperative period is a common phenomenon after urinary diversion, however for patients undergoing a continent urinary reservoir procedure, this is often a result of anatomic loss of the ileocecal valve along the alimentary tract. Since the most common trigger to test for CDI is diarrhea, we have found that less than half of our patients complaining of diarrhea had CDI. Despite appropriate hand hygiene and implementation of CDI preventive measures at our institution, our study still demonstrated an increased incidence of CDI. With the incidence of community-acquired CDI on the rise in recent years[3], it is possible that some patients in our series are asymptomatic carriers of nontoxigenic *Clostridium difficile*. Whether treatment is necessary for an asymptomatic carrier of *Clostridium difficile* remains controversial.[28] One study has suggested that screening asymptomatic carriers at admission may lower in-hospital transmission rates of CDI.[29] Thus, a prospective study for screening of asymptomatic carriers of *Clostridium difficile* at the time of radical cystectomy is warranted.

The use of gastric acid reducers, such as histamine-2 antagonists or proton-pump inhibitors, has been suggested as a potential risk factor for the development of CDI.[28, 30] A potential mechanism is that a vegetative form of *Clostridium difficile* spores is sensitive to gastric acid and an elevated gastric pH facilitates passage of spores to the colon.[30] Our study also found that chronic antacid therapy was an independent risk factors for CDI within 90 days of RC (HR: 1.9, p=0.04). This result should be interpreted with caution as one potential confounder is that all patients were treated with perioperative antacids - especially in patients with prolonged nasogastric decompression. Nevertheless, in light of these findings, our institution has shifted away from giving patients perioperative antacids routinely since the completion of this study.

The development of CDI in the postsurgical setting is associated with significant hospital morbidity and resource utilization.[6, 16] In a study assessing the outcomes of hospital acquired adverse events in radical cystectomy patients, Kim et al. found that patients with CDI had a longer hospital stay by 9 days, and an increase in total hospitalization cost by $21,000 compared to those without adverse events.[11] Similarly, our study found that CDI was associated with longer hospital stays, increased hospital-acquired infections, additional surgical and pharmacotherapies, and higher readmission rates. Based on these findings, it is fair to assume that CDI leads to longer stay or higher overall postoperative complication rates, but the development of CDI may also be a consequence of these factors. Therefore, it is difficult to identify a causality between CDI and postoperative complications with adequate certainty.

Several limitations of this study are noteworthy for discussion. This study was conducted at a high-volume tertiary referral center for bladder cancer so the findings may not be applicable to other settings. The increased incidence of CDI found in the present study may be a result of increased vigilance during the studied period or a reflection of increasing hospital-wide CDI occurrence. These findings highlight the need to identify the incidence of CDI in the preoperative setting. Additionally, RC in this study were performed by multiple experienced surgeons with different practice patterns and views regarding the use of perioperative antibiotics. Such factors may have contributed to the high incidence of CDI, but we did not study the individual rates of CDI related to each surgeon. One major strength of the study is the detailed information available for each patient (ie. timing of preoperative, perioperative and postoperative antibiotics), which cannot be achieved by extracting data from large prospective databases. We recognize that outcomes related to CDI cannot be randomized, but a prospective trial involving multiple referral centers for bladder cancer may overcome the limitations of the current study.

Conclusion

We found that the rate of CDI in patients undergoing RC and urinary diversion for bladder cancer is higher than previously reported. Additionally, the current study demonstrated that chronic antacid therapy and long duration of antibiotic exposure in the perioperative setting are independent predictors of CDI development in RC patients. Efforts focusing on minimizing antibiotic exposure in RC patients are needed and perioperative antimicrobial prophylaxis guidelines should be followed. These data also support future endeavors focusing on improving patient safety and reducing CDI in RC patients.

References

1. Polage, C. R., Solnick, J. V., Cohen, S. H.: Nosocomial diarrhea: evaluation and treatment of causes other than Clostridium difficile. Clin Infect Dis, **55:** 982, 2012
2. McDonald, L. C., Killgore, G. E., Thompson, A. et al.: An epidemic, toxin gene-variant strain of Clostridium difficile. N Engl J Med, **353:** 2433, 2005
3. Khanna, S., Pardi, D. S., Aronson, S. L. et al.: The epidemiology of community-acquired Clostridium difficile infection: a population-based study. Am J Gastroenterol, **107:** 89, 2012
4. Gerding, D. N., Lessa, F. C.: The Epidemiology of Clostridium difficile Infection Inside and Outside Health Care Institutions. Infect Dis Clin North Am, 2015
5. See, I., Mu, Y., Cohen, J. et al.: NAP1 strain type predicts outcomes from Clostridium difficile infection. Clin Infect Dis, **58:** 1394, 2014
6. Zerey, M., Paton, B. L., Lincourt, A. E. et al.: The burden of Clostridium difficile in surgical patients in the United States. Surg Infect (Larchmt), **8:** 557, 2007
7. Krapohl, G. L., Morris, A. M., Cai, S. et al.: Preoperative risk factors for postoperative Clostridium difficile infection in colectomy patients. Am J Surg, **205:** 343, 2013
8. Eyre, D. W., Walker, A. S., Wyllie, D. et al.: Predictors of first recurrence of Clostridium difficile infection: implications for initial management. Clin Infect Dis, **55 Suppl 2:** S77, 2012
9. Stevens, V., Dumyati, G., Fine, L. S. et al.: Cumulative antibiotic exposures over time and the risk of Clostridium difficile infection. Clin Infect Dis, **53:** 42, 2011
10. Calvert, J. K., Holt, S. K., Mossanen, M. et al.: Use and outcomes of extended antibiotic prophylaxis in urological cancer surgery. J Urol, **192:** 425, 2014

11. Kim, S. P., Shah, N. D., Karnes, R. J. et al.: The implications of hospital acquired adverse events on mortality, length of stay and costs for patients undergoing radical cystectomy for bladder cancer. J Urol, **187:** 2011, 2012

12. Hollenbeck, B. K., Taub, D. A., Miller, D. C. et al.: The regionalization of radical cystectomy to specific medical centers. J Urol, **174:** 1385, 2005

13. Damle, R. N., Cherng, N. B., Flahive, J. M. et al.: Clostridium difficile infection after colorectal surgery: a rare but costly complication. J Gastrointest Surg, **18:** 1804, 2014

14. Large, M. C., Kiriluk, K. J., DeCastro, G. J. et al.: The impact of mechanical bowel preparation on postoperative complications for patients undergoing cystectomy and urinary diversion. J Urol, **188:** 1801, 2012

15. Shah, K., Pass, L. A., Cox, M. et al.: Evaluating contemporary antibiotics as a risk factor for Clostridium difficile infection in surgical trauma patients. J Trauma Acute Care Surg, **72:** 691, 2012

16. Keshavamurthy, S., Koch, C. G., Fraser, T. G. et al.: Clostridium difficile infection after cardiac surgery: prevalence, morbidity, mortality, and resource utilization. J Thorac Cardiovasc Surg, **148:** 3157, 2014

17. Hensgens, M. P., Goorhuis, A., Dekkers, O. M. et al.: Time interval of increased risk for Clostridium difficile infection after exposure to antibiotics. J Antimicrob Chemother, **67:** 742, 2012

18. Valiquette, L., Cossette, B., Garant, M. P. et al.: Impact of a reduction in the use of high-risk antibiotics on the course of an epidemic of Clostridium difficile-associated disease caused by the hypervirulent NAP1/027 strain. Clin Infect Dis, **45 Suppl 2:** S112, 2007

19. Muto, C. A., Blank, M. K., Marsh, J. W. et al.: Control of an outbreak of infection with the hypervirulent Clostridium difficile BI strain in a university hospital using a comprehensive "bundle" approach. Clin Infect Dis, **45:** 1266, 2007

20. Wolf, J. S., Jr., Bennett, C. J., Dmochowski, R. R. et al.: Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol, **179:** 1379, 2008

21. Mossanen, M., Calvert, J. K., Holt, S. K. et al.: Overuse of Antimicrobial Prophylaxis in Community Practice Urology. J Urol, 2014

22. Nazmy, M., Yuh, B., Kawachi, M. et al.: Early and late complications of robot-assisted radical cystectomy: a standardized analysis by urinary diversion type. J Urol, **191:** 681, 2014

23. Bochner, B. H., Dalbagni, G., Sjoberg, D. D. et al.: Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: A Randomized Clinical Trial. Eur Urol, 2014

24. Nicolle, L. E., Bradley, S., Colgan, R. et al.: Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis, **40:** 643, 2005

25. Eswara, J. R., Shariftabrizi, A., Sacco, D.: Positive stone culture is associated with a higher rate of sepsis after endourological procedures. Urolithiasis, **41:** 411, 2013

26. Herr, H. W.: Outpatient urological procedures in antibiotic-naive patients with bladder cancer with asymptomatic bacteriuria. BJU Int, **110:** E658, 2012

27. Herr, H. W.: The Risk of Urinary Tract Infection after Flexible Cystoscopy in Patients with Bladder Tumor Who Did Not Receive Prophylactic Antibiotics. J Urol, 2014

28. Cohen, S. H., Gerding, D. N., Johnson, S. et al.: 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, **31:** 431, 2010

29. Lanzas, C., Dubberke, E. R.: Effectiveness of screening hospital admissions to detect asymptomatic carriers of Clostridium difficile: a modeling evaluation. Infect Control Hosp Epidemiol, **35:** 1043, 2014

30. Dial, S., Delaney, J. A., Barkun, A. N. et al.: Use of gastric acid-suppressive agents and the risk of community-acquired Clostridium difficile-associated disease. JAMA, **294:** 2989, 2005

Figure 1. Incidence of CDI in RC patients by year of surgery

Table 1. RC patient and hospital-wide CDI rate by year

Year	No. of RC patients	No. of stool toxin test sent (%)	No. of CDI in RC patients (%)	Hospital-wide CDI rate
2010	150	21 (14)	9 (6)	1.0%
2011	136	28 (21)	7 (5)	1.0%
2012	130	26 (20)	12 (9)	1.2%
2013	136	40 (26)	21 (15)	1.4%

Table 2. Patient and procedure characteristics

Variable	No CDI N=503	CDI N=49	P-value
Median age at surgery (IQR)	68 (58 – 76)	67 (60 – 75)	0.96
No. Male gender (%)	399 (79.3)	35 (71.4)	0.20
Median BMI, kg/m^2 (IQR)	27.6 (24.2 – 31.5)	28.4 (24 – 34)	0.27
No. urothelial bladder histology (%)	489 (97.2)	46 (93.8)	0.19
No. preoperative chemotherapy (%)	127 (25.2)	10 (20.4)	0.60
Median preoperative creatinine, mg/dL (IQR)	1.11 (0.9 – 1.32)	1.05 (0.85 – 1.3)	0.40
No. preoperative hemoglobin, g/dL (IQR)	12 (10.5 – 13.3)	12.6 (10.9 – 13.7)	0.27
No. prior gastrointestinal surgery (%)	75 (15.0)	9 (18.4)	0.53
No. chronic antacid therapy (%)	106 (21.1)	18 (36.7)	0.01
No. preoperative UTI (%)	137 (27.2)	17 (34.7)	0.32
No. preoperative antibiotics	129 (25.7)	19 (38.8)	0.06
Comorbidities			
No. stage III/IV chronic kidney disease (%)	47 (9.3)	7 (14.3)	0.31
No. chronic obstructive pulmonary disease (%)	56 (11.1)	8 (16.3)	0.35
No. hypertension (%)	313 (62.2)	32 (65.3)	0.67
No. diabetes (%)	130 (25.8)	13 (26.5)	0.92
No. coronary artery disease (%)	86 (17.1)	12 (24.5)	0.20
No. Charlson comorbidity index > 3(%)	79 (15.7)	12 (24.4)	0.11
Median hours operative time (IQR)	4.8 (3.5 – 6.2)	4.6 (3.5 – 6.3)	0.86
Median ml estimated blood loss (IQR)	500 (300 – 700)	500 (300 – 800)	0.24
Diversion Type			0.04
No. ileal conduit (%)	286 (56.9)	32 (65.3)	
No. Indiana pouch (%)	103 (20.5)	13 (26.5)	
No. orthotopic neobladder (%)	114 (22.7)	4 (8.2)	
Perioperative blood transfusion			0.28
No. none (%)	287 (57.1)	22 (44.9)	
No. intraoperative only (%)	98 (19.5)	13 (26.5)	
No. postoperative only (%)	72 (14.3)	7 (14.3)	
No. intraoperative and postoperative (%)	46 (9.2)	7 (14.3)	
Days of antibiotics received*			0.005
No. 1 day or less (%)	250 (49.7)	19 (38.8)	
No. 2 to 7 days (%)	179 (35.6)	14 (28.6)	
No. greater than 7 days (%)	74 (14.7)	16 (32.6)	

Table 3. Multivariable logistic regression of clinical characteristics associated with CDI

Variable	Hazard Ratio	95% CI	p Value
Diversion Type			
Ileal conduit	Reference		
Indiana pouch	1.2	0.63 – 2.56	0.5
Orthotopic neobladder	0.3	0.11 – 1.01	0.05
Preoperative hemoglobin	1.1	0.98 – 1.33	0.09
Preoperative antacid use	1.9	1.02 – 3.68	0.04
Days of antibiotics received			
1 day or less	Reference		
2 to 7 days	0.8	0.34 – 1.81	0.6
Greater than 7 days	2.2	1.11 – 4.44	0.02

Table 4. Postoperative outcomes of patients with and without CDI

Variable	No CDI N=503	CDI N=49	p Value
Median days length of stay (IQR)	7 (6 – 10)	9 (7 – 15)	<0.001
No. readmission (%)	102 (20.3)	20 (40.8)	0.002
No. postoperative antibiotics (%)	154 (30.6)	21 (42.9)	0.08
Complications			
No. septicemia/bacteremia (%)	46 (9.2)	10 (20.4)	0.02
No. pyelonephritis/UTI (%)	43 (8.6)	14 (28.6)	<0.001
No. urinoma (%)	4 (0.8)	6 (12.2)	<0.001
No. hospital acquired pneumonia (%)	27 (5.4)	2 (4.1)	0.52
No. acute renal failure (%)	27 (5.4)	11 (22.5)	<0.001
No. prolonged ileus (%)	90 (17.9)	11 (22.5)	0.43
No. wound infection (%)	61 (12.1)	11 (22.5)	0.04
No. intra-abdominal abscess (%)	25 (5.0)	8 (16.3)	0.001
No. death within 30 days (%)	6 (1.2)	2 (4.1)	0.15