



# Total Abdominal Colectomy Versus Diverting Loop Ileostomy and Antegrade Colonic Lavage for Fulminant *Clostridioides Colitis*: Analysis of the National Inpatient Sample 2016–2019

Tyler McKechnie<sup>1</sup> · Jigish Khamar<sup>2</sup> · Yung Lee<sup>1,3</sup> · Léa Tessier<sup>2</sup> · Edward Passos<sup>1,2</sup> · Aristithes Doumouras<sup>1,2,4</sup> · Dennis Hong<sup>1,2,4</sup> · Cagla Eskicioglu<sup>1,2,4</sup> 

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## Abstract

**Background** When surgery is indicated for fulminant *Clostridioides difficile* infection (CDI), total abdominal colectomy (TAC) is the most common approach. Diverting loop ileostomy (DLI) with antegrade colonic lavage has been introduced as a colon-sparing surgical approach. Prior analyses of National Inpatient Sample (NIS) data suggested equivalent postoperative outcomes between groups but did not evaluate healthcare resource utilization. As such, we aimed to analyze a more recent NIS cohort to compare these two approaches in terms of both postoperative outcomes and healthcare resource utilization.

**Methods** A retrospective analysis of the NIS from 2016 to 2019 was conducted. The primary outcome was postoperative in-hospital morbidity. Secondary outcomes included postoperative in-hospital mortality, system-specific postoperative complications, total admission cost, and length of stay (LOS). Univariable and multivariable regressions were utilized to compare the two operative approaches.

**Results** In total, 886 patients underwent TAC and 409 patients underwent DLI with antegrade colonic lavage. Adjusted analyses demonstrated no difference between groups in postoperative in-hospital morbidity (aOR 0.96, 95%CI 0.64–1.44,  $p=0.851$ ) or in-hospital mortality (aOR 1.15, 95%CI 0.81–1.64,  $p=0.436$ ). Patients undergoing TAC experienced significantly decreased total admission cost (MD \$79,715.34, 95%CI 133,841–25,588,  $p=0.004$ ) and shorter postoperative LOS (MD 4.06 days, 95%CI 6.96–1.15,  $p=0.006$ ).

**Conclusions** There are minimal differences between TAC and DLI with antegrade colonic lavage for fulminant CDI in terms of postoperative morbidity and mortality. Healthcare resource utilization, however, is significantly improved when patients undergo TAC as evidenced by clinically important decreases in total admission cost and postoperative LOS.

**Keywords** Colorectal Surgery · General Surgery · *Clostridioides colitis* · *C. difficile* · Colectomy

## Introduction

*Clostridioides difficile* infection (CDI) affects nearly 500,000 Americans per year and has become increasingly prevalent over the past two decades.<sup>1</sup> Clinically, CDI severity ranges across a broad spectrum. Mild CDI can result in a patient experiencing watery diarrhea, whereas fulminant CDI can result in sepsis along with its sequelae.<sup>2</sup> First-line therapy consists of oral vancomycin, with newer medications such as fidaxomicin becoming increasingly relied upon.<sup>3</sup> In patients with fulminant CDI, medical management is successful in controlling disease in approximately 70–80% of cases.<sup>4,5</sup> The most common surgical approach for those that fail medical management is a total abdominal colectomy (TAC) with end ileostomy. This is a morbid procedure, with significant

✉ Cagla Eskicioglu  
eskicio@mcmaster.ca

<sup>1</sup> Division of General Surgery, Department of Surgery, McMaster University, Hamilton, ON L8N 4A6, Canada

<sup>2</sup> Michael G. DeGroot School of Medicine, McMaster University, Hamilton, Ontario, Canada

<sup>3</sup> Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA

<sup>4</sup> Division of General Surgery, Department of Surgery, St. Joseph's Healthcare, Hamilton, Ontario, Canada

associated mortality, and often leaves patients with a permanent end ileostomy.<sup>6,7</sup> As such, in 2011 Neal et al. proposed diverting loop ileostomy (DLI) with antegrade colonic lavage as a colon-preserving surgical alternative.<sup>8</sup>

The original description of DLI with antegrade colonic lavage is as follows: diagnostic laparoscopy/laparotomy to ensure colonic viability, abdominal washout, creation of a DLI, on table lavage with eight litres of warmed polyethylene glycol solution, and postoperative administration of 500 mg vancomycin enemas via the efferent limb every eight hours.<sup>8</sup> Neal et al. reported a significant reduction in overall postoperative mortality with this approach compared to TAC (19% vs. 50%).<sup>8</sup> They also reported a 79% rate of long-term colonic preservation in patients undergoing DLI with antegrade colonic lavage.<sup>8</sup> However, these impressive initial morbidity and mortality results have not been reliably reproduced.<sup>9–11</sup>

We performed the first systematic review and meta-analysis comparing TAC and DLI with antegrade colonic lavage in 2020, which pooled data from five studies (n = 3,683 patients).<sup>12</sup> There were no significant differences between approaches in terms of postoperative morbidity, mortality, or reoperation rate.<sup>12</sup> Subsequent systematic reviews and meta-analyses have demonstrated similar results.<sup>13,14</sup> One of the included studies was a retrospective database cohort derived from the United States (U.S.) National Inpatient Sample (NIS).<sup>10</sup> They analyzed over 2,000 patients from the 2011–2015 NIS, and again failed to demonstrate a difference in morbidity and mortality between groups.<sup>10</sup> While all previous data suggest equivalent outcomes between these two approaches, none of the large database studies have evaluated healthcare resource utilization.<sup>9,10</sup> As such, we aimed to analyze a more recent NIS cohort to compare these two approaches in terms of both postoperative outcomes and healthcare resource utilization.

## Materials and Methods

### Data Source

A retrospective population-based cohort study was performed utilizing the January 1st, 2016 to December 31st, 2019 data from the Healthcare Cost and Utilization Project (HCUP) National Inpatient sample (NIS), managed by the Agency for Healthcare Research and Quality (AHRQ). The timeline was chosen to capture the years that NIS started utilizing the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes. The NIS is the largest public all-payer inpatient database in the U.S.; it approximates a 20% stratified sample of community hospital discharges, and its included hospitals cover more than 97% of the population, providing a nationally

representative sample of the patient population and hospital characteristics. The NIS records information on roughly 7 million hospitalizations annually, including weighted data to help make population estimates. Local ethics board approval was not required for this study.

### Cohort Selection

The NIS captures 30 admission diagnoses and 15 admission procedures through the ICD-10-CM codes. Corresponding ICD-10-CM codes were utilized to identify a cohort of adult patients ( $\geq 18$  years of age) admitted with an admission diagnosis of *Clostridioides difficile* colitis. The study group was further narrowed by identifying only those patients who underwent either surgery on the given admission. The specific operations coded for using the ICD-10-CM admission procedures were TAC and DLI. The diagnosis and procedure codes utilized were drawn from previous similar studies.<sup>10,15</sup> Admissions associated with both TAC and DLI were allocated to the TAC group. Patients were excluded if they had an admission diagnosis of the following diseases, as per previously defined ICD-10-CM coding, for which they may have undergone either TAC or DLI: inflammatory bowel disease, ischemic colitis, lower gastrointestinal bleeds, or colorectal cancer.<sup>16–18</sup> All patients who remained in the DLI group were assumed to have undergone DLI with antegrade colonic lavage for CDI. Please see Appendix 1 for detailed ICD-10-CM codes utilized to identify the cohort for this study. Patients with missing data pertaining to age, sex, type of hospital admission (i.e., elective vs. emergent), mortality, length of stay, and total in-hospital healthcare cost were excluded.

### Patient and Institution Characteristics

The patient characteristics included for analysis were age, sex, race category (White, Black, Hispanic, Asian or Pacific Islander, and others), body mass index (BMI), insurance status (Medicare, Medicaid, Private Insurance, Self-pay, and others), and income quartile. Comorbidities were assessed with the Charlson Comorbidity Index software for ICD-10-CM for each individual patient. The institutional characteristics included for analysis were teaching status, rural status, region (Northeast, Midwest, South, West), and bed size (small, medium, large).

### Outcomes

The primary outcomes were overall in-hospital postoperative morbidity and mortality. Postoperative morbidity was identified with ICD-10-CM diagnosis and procedure codes that explicitly identified individual postoperative outcomes. For postoperative morbidity that was not identifiable by individual ICD-10-CM codes, the AHRQ Patient Safety Indicators were used.<sup>19</sup>

The secondary outcomes included system-specific postoperative morbidity, postoperative length of stay, total in-hospital healthcare cost, and discharge disposition. System-specific complications included respiratory, cardiovascular, gastrointestinal, genitourinary, and infectious using previously utilized methods.<sup>20,21</sup> Healthcare utilization resources (i.e., length of stay, cost) are recorded in the HCUP NIS. Discharge disposition was categorized into home, short-term hospital, skilled-nursing facility, home healthcare, and others. Due to the nature of the NIS database not having patient identifiers or linkage with other administrative databases, only in-hospital outcomes could be captured and out of hospital outcomes could not be captured.

## Statistical Analyses

Patient characteristics are presented as frequencies (%) for categorical variables and means (standard deviations) for continuous variables. Statistical analyses for categorical and continuous variables were performed using the chi square test and two sample t-test, respectively. Univariable and multivariable logistic regression models were fit for the primary outcomes and dichotomous secondary outcomes according to type of operation performed (i.e., TAC vs. DLI). Univariable and multivariable linear regression models were fit for the continuous secondary outcomes according to type of operation performed. All multivariable models were determined a priori by experts in the field on the basis of clinical importance of the covariate. The final model included age, obesity status, Charlson Comorbidity Index, operative approach, number of days from admission to procedure, insurance status, income quartile, hospital

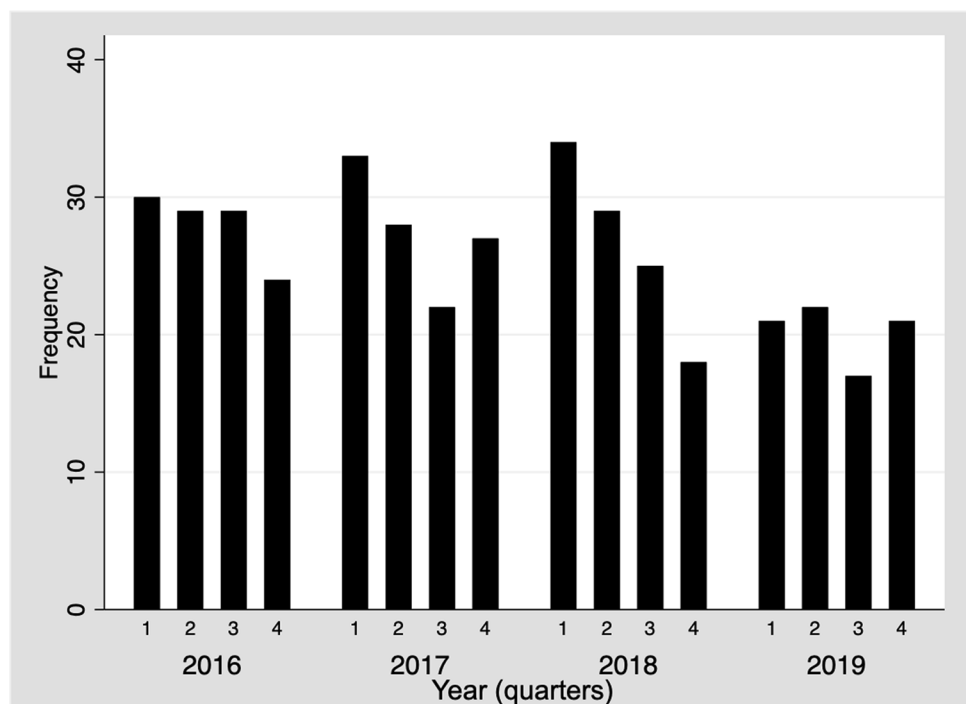
bed size, and hospital location. A multivariable logistic model was fit to identify predictors of undergoing DLI with antegrade colonic lavage. For each independent variable in the models, the variation inflation factor (VIF) was calculated to exclude multicollinearity. An a priori subgroup was planned for patients undergoing surgical intervention within three days of admission. This subgroup analysis was based on similar analyses conducted by Juo et al. and the rationale that earlier intervention is associated with improved outcomes.<sup>10</sup> All statistical tests were two-sided with the threshold for significance set at  $p < 0.05$ . Discharge-level weight provided by HCUP was used to calculate national estimates. All statistical analysis was performed using STATA (StataCorp version 15; College Station, TX).

## Results

### Patient Demographics and Hospital Characteristics

The NIS sample population included 886 patients (mean age: 64.9 [15.9], 56.4% female) undergoing TAC and 409 patients (mean age: 60.7 [18.6], 56.2% female) undergoing DLI with antegrade colonic lavage. From this sample, the data were extrapolated to the entire U.S. population, resulting in an estimated 4,430 patients undergoing TAC and 2,045 patients undergoing DLI with antegrade colonic lavage. Figure 1 presents the number of patients undergoing DLI with antegrade colonic lavage per year. There was no significant difference in the observed proportion of patients undergoing DLI with antegrade colonic

**Fig. 1** Bar chart of frequency of DLI with antegrade colonic lavage for fulminant CDI per quarter per year, National Inpatient Sample 2016–2019 (1 = first quarter, 2 = second quarter, 3 = third quarter, 4 = fourth quarter)



**Table 1** Univariate comparison of baseline patient, disease, and hospital characteristics between total abdominal colectomy (TAC) and diverting loop ileostomy (DLI) with antegrade colonic lavage, Nationwide Inpatient Sample January 2016–December 2019

<i>n</i> (sample size) <i>N</i> (weighted population estimate)	TAC <i>n</i> = 886 <i>N</i> = 4430	DLI with Colonic Lavage <i>n</i> = 409 <i>N</i> = 2045	<i>p</i>
<b>Patient Characteristics, n (%)</b>			
Female Sex	500 (56.4)	230 (56.2)	0.95
Age (mean [SD])	64.94 (15.88)	60.66 (18.63)	< <b>0.001</b>
Age ≥ 65 years	517 (58.4)	201 (49.1)	<b>0.002</b>
<b>Race</b>			
White	663 (74.8)	281 (68.7)	<b>0.021</b>
Black	94 (10.6)	56 (13.7)	0.11
Hispanic	68 (7.7)	33 (8.1)	0.81
Asian or pacific islander	15 (1.7)	10 (2.4)	0.36
Others	18 (2.0)	11 (2.7)	0.46
<b>BMI (kg/m<sup>2</sup>)</b>			
< 30	817 (92.2)	368 (90.0)	0.18
≥ 30	69 (7.8)	41 (10.0)	0.18
<b>Insurance</b>			
Medicare	547 (61.7)	220 (53.8)	<b>0.007</b>
Medicaid	110 (12.4)	59 (14.4)	0.32
Private Insurance	184 (20.8)	113 (27.6)	<b>0.006</b>
Self-pay	17 (1.9)	9 (2.2)	0.74
Others	27 (3.0)	6 (1.5)	0.093
<b>Residential Income</b>			
First Quartile (lowest)	240 (27.1)	108 (26.4)	0.80
Second Quartile	222 (25.1)	115 (28.1)	0.24
Third Quartile	245 (27.7)	90 (22.0)	<b>0.031</b>
Fourth Quartile (highest)	168 (19.0)	90 (22.0)	0.20
<b>Charlson Comorbidity Index (Median [IQR])</b>			
< 3	422 (47.6)	219 (53.5)	<b>0.048</b>
4–6	374 (42.2)	138 (33.7)	<b>0.004</b>
≥ 7	90 (10.2)	52 (12.7)	0.17
<b>Treatment Characteristics, n (%)</b>			
<b>Year Treated</b>			
2016	268 (30.2)	112 (27.4)	0.29
2017	231 (26.1)	110 (26.9)	0.75
2018	201 (22.7)	106 (25.9)	0.20
2019	186 (21.0)	81 (19.8)	0.62
Time to 1 <sup>st</sup> Procedure (median [IQR])	2 (1, 7)	3 (0, 7)	0.96
<b>Surgical Approach</b>			
Open	844 (95.3)	310 (75.8)	< <b>0.001</b>
Minimally invasive	45 (5.1)	99 (24.2)	< <b>0.001</b>
<b>Hospital Characteristics, n (%)</b>			
<b>Hospital bed size</b>			
Small	129 (14.6)	64 (15.6)	0.61
Medium	261 (29.5)	105 (25.7)	0.16
Large	496 (56.0)	240 (58.7)	0.36
<b>Teaching status</b>			
Non-teaching	32 (3.6)	7 (1.7)	0.063
Teaching	854 (96.4)	402 (98.3)	0.063
<b>Hospital location</b>			
Urban	854 (96.4)	402 (98.3)	0.063

**Table 1** (continued)

<i>n</i> (sample size) <i>N</i> (weighted population estimate)	TAC <i>n</i> =886 <i>N</i> =4430	DLI with Colonic Lavage <i>n</i> =409 <i>N</i> =2045	<i>p</i>
Rural	32 (3.6)	7 (1.7)	0.063
Hospital region			
Northeast	189 (21.3)	93 (22.7)	0.57
Midwest	195 (22.0)	98 (24.0)	0.44
South	334 (37.7)	143 (35.0)	0.34
West	168 (19.0)	75 (18.3)	0.79

All *n* are analytic sample; all % and means (SD) are survey-weighted to reflect national estimates. Percentages may not add up to 100% due to rounding

Bolded data = statistically significant (i.e.,  $p < 0.05$ )

lavage between years ( $p = 0.517$ ). Patients in the DLI with antegrade colonic lavage group were significantly younger ( $p < 0.001$ ), less comorbid according to the median Charlson

Comorbidity Index ( $p = 0.021$ ), and more likely to be privately insured ( $p = 0.006$ ) than the patients in the TAC group. Patients in the DLI with antegrade colonic lavage

**Table 2** In hospital mortality and morbidity by surgical approach, Nationwide Inpatient Sample January 2016–December 2019

<i>n</i> (sample size) <i>N</i> (weighted population estimate)	TAC <i>n</i> =886 <i>N</i> =4430	DLI with Colonic Lavage <i>n</i> =209 <i>N</i> =2045	Unadjusted OR (95%CI)	<i>p</i>	Adjusted OR* (95%CI)	<i>p</i>
In-hospital mortality, <i>n</i> (%)	227 (25.6)	82 (20.0)	1.37 (1.00, 1.89)	0.051	1.15 (0.81, 1.64)	0.436
Post-operative ICU admission, <i>n</i> (%)	350 (39.5)	150 (36.7)	1.13 (0.86, 1.49)	0.394	1.03 (0.76, 1.39)	0.843
Composite system-specific complications, <i>n</i> (%)						
Any	763 (86.1)	332 (81.2)	1.44 (1.01, 2.04)	<b>0.042</b>	0.96 (0.64, 1.44)	0.851
Respiratory	491 (55.4)	213 (52.1)	1.14 (0.88, 1.49)	0.323	0.89 (0.66, 1.20)	0.429
Pneumonia	177 (20.0)	90 (22.0)	0.88 (0.64, 1.23)	0.469	0.77 (0.54, 1.10)	0.154
Cardiovascular	41 (4.6)	16 (3.9)	1.19 (0.62, 2.28)	0.595	0.97 (0.46, 2.07)	0.946
Stroke	11 (1.2)	3 (0.7)	1.70 (0.40, 7.33)	0.475	1.49 (0.26, 8.48)	0.652
MI	26 (2.9)	8 (2.0)	1.52 (0.60, 3.81)	0.377	1.47 (0.50, 4.38)	0.485
Gastrointestinal	194 (21.9)	109 (26.7)	0.77 (0.57, 1.05)	0.096	0.76 (0.54, 1.07)	0.114
Ileus	126 (14.2)	62 (15.2)	0.93 (0.64, 1.35)	0.694	1.01 (0.66, 1.55)	0.952
Anastomotic leak	83 (9.4)	-	-	-	-	-
Genitourinary	596 (67.3)	242 (59.2)	1.42 (1.08, 1.87)	<b>0.013</b>	1.15 (0.84, 1.58)	0.377
Acute kidney injury	517 (58.4)	201 (49.1)	1.45 (1.11, 1.89)	<b>0.006</b>	1.21 (0.90, 1.64)	0.209
Urinary retention	31 (3.5)	12 (2.9)	1.20 (0.55, 2.61)	0.645	1.09 (0.47, 2.54)	0.839
Urinary tract infection	184 (20.8)	82 (20.0)	1.05 (0.75, 1.46)	0.793	1.00 (0.69, 1.44)	0.983
Infectious	61 (6.9)	55 (13.4)	0.48 (0.31, 0.74)	<b>0.001</b>	0.42 (0.26, 0.68)	<b>&lt; 0.001</b>
Wound	32 (3.6)	8 (2.0)	1.88 (0.77, 4.60)	0.167	1.90 (0.66, 5.43)	0.231
Post-procedural shock	12 (1.4)	4 (1.0)	1.39 (0.38, 5.02)	0.615	1.65 (0.43, 6.29)	0.461
Discharge Disposition, <i>n</i> (%)						
Home	93 (10.5)	60 (14.7)	0.68 (0.46, 1.02)	0.061	1.05 (0.64, 1.73)	0.844
Short-term hospital	21 (2.4)	7 (1.7)	1.39 (0.52, 3.72)	0.506	1.13 (0.40, 3.16)	0.818
Skilled nursing facility	403 (45.5)	163 (39.9)	1.26 (0.96, 1.65)	0.092	1.03 (0.77, 1.39)	0.830
Home healthcare	139 (15.7)	95 (23.2)	0.62 (0.44, 0.86)	<b>0.004</b>	0.70 (0.47, 1.03)	0.073
Other	229 (25.8)	84 (20.5)	1.35 (0.98, 1.86)	0.066	1.15 (0.81, 1.65)	0.433

\*Adjusted by age, obesity status, Charlson Comorbidity Index, operative approach (i.e., minimally invasive vs. open), number of days from admission to procedure, insurance status, income quartile, hospital bed size, and location of hospital (i.e., urban vs. rural)

All *n* are analytic sample; all % and means (SD) are survey-weighted to reflect national estimates

OR = Odds ratio

Bolded data = statistically significant (i.e.,  $p < 0.05$ )

**Table 3** Healthcare utilization by surgical approach, Nationwide Inpatient Sample January 2016–December 2019

<i>n</i> (sample size) <i>N</i> (weighted population estimate)	TAC <i>n</i> = 886 <i>N</i> = 4430	DLI with Colonic Lavage <i>n</i> = 209 <i>N</i> = 2045	Unadjusted mean difference (95%CI)	<i>p</i>	Adjusted mean difference* (95%CI)	<i>p</i>
Cost, median (IQR), USD	196,838 (128,212, 616,097)	232,020 (128,212, 616,097)	-68,373.7 (-119,041.3, -17,706.11)	<b>0.008</b>	-79,715.34 (-133,841.9, 25,588.79)	<b>0.004</b>
Total length of stay, median (IQR), days	16 (9, 24)	19 (11, 29)	-4.50 (-7.42, -1.58)	<b>0.003</b>	-4.88 (-8.05, -1.71)	<b>0.003</b>
Postoperative length of stay, median (IQR), days	11 (6, 18)	14 (7, 23)	-4.22 (-6.87, -1.56)	<b>0.002</b>	-4.06 (-6.96, -1.15)	<b>0.006</b>

\* Adjusted by sex, age, race, class of obesity, insurance status, income quartile, Elixhauser comorbidities score, complicated diverticulitis type, minimally invasive surgery status, teaching status of the hospital, and rural status of the hospital

Bolded data = statistically significant (i.e.,  $p < 0.05$ )

group were significantly more likely to undergo a minimally invasive operation ( $p < 0.001$ ). The detailed demographic data according to group are reported in Table 1.

### Postoperative Morbidity and Mortality

In-hospital postoperative morbidity was 86.1% and 81.2% in the TAC and DLI with antegrade colonic lavage groups, respectively. In-hospital postoperative mortality was 25.6% and 20.0% in the TAC and DLI with antegrade colonic lavage groups, respectively (Table 2). Adjusted analyses did not demonstrate significant differences between groups with regards to in-hospital postoperative morbidity (aOR 0.96, 95%CI 0.64–1.44,  $p = 0.851$ ) or in-hospital postoperative mortality (aOR 1.15, 95%CI 0.81–1.64,  $p = 0.436$ ). There were no significant differences between groups in any system-specific postoperative morbidity aside from an increased risk of infectious morbidity in the patients undergoing DLI with antegrade colonic lavage (aOR 0.42, 95%CI 0.26–0.68,  $p < 0.001$ ).

### Length of Stay

The median length of stay was 16 days (IQR 9–24) and 19 days (IQR 11–29) in the TAC and DLI with antegrade colonic lavage groups, respectively (Table 3). Total length of stay was significantly lower in the TAC group than the DLI with antegrade colonic lavage group by a mean of 4.88 days (95%CI -8.05 to -1.71 days,  $p = 0.003$ ). When corrected for days to procedure in order to calculate postoperative length of stay, there remained a significant reduction in the TAC group by 4.06 days (95%CI -6.96 to -1.15 days,  $p = 0.006$ ).

### Cost

The median total hospitalization costs were \$196,838 (IQR \$128,212–616,097) and \$232,020 (IQR \$128,212–616,097)

in the TAC and DLI with antegrade colonic lavage groups, respectively (Table 3). Total cost was significantly lower in the TAC group than the DLI with antegrade colonic lavage group by a mean of \$79,715.34 (95%CI -133,841 to -25,589,  $p = 0.004$ ). Detailed information pertaining to the items included within the cost allocation (e.g., laparoscopic equipment) was not available in the NIS database.

### Discharge Disposition

Patients were most commonly discharged to a skilled nursing facility in both groups (TAC: 45.5%; DLI: 39.9%). On adjusted analyses, there was no difference between patients undergoing TAC and patients undergoing DLI with antegrade colonic lavage in terms of discharge disposition (Table 2).

### Factors Associated with DLI with Antegrade Colonic Lavage

On multivariate logistic regression, younger patient age (aOR 0.98, 95%CI 0.97–0.99,  $p = 0.003$ ) and receiving care at a teaching hospital (aOR 3.38, 95%CI 1.15–9.97,  $p = 0.027$ ) were significantly associated with an increased odds of undergoing DLI with antegrade colonic lavage (Table 4).

### Early Operative Intervention

In the subgroup analysis of patients undergoing operative intervention within three days of admission, there were 508 patients in the TAC group and 224 patients in the DLI with antegrade colonic lavage group (Table 5). Patients undergoing operative intervention on post-admission day one ( $p = 0.001$ ) and post-admission day two ( $p = 0.025$ ) were significantly more likely to be undergoing TAC than DLI with antegrade colonic lavage (Fig. 2). Overall in-hospital postoperative morbidity was 88.4% and 81.2% in the early intervention TAC and DLI with antegrade

**Table 4** Multivariate logistic regression estimating the predictors of undergoing diverting loop ileostomy with antegrade colonic lavage according to Nationwide Inpatient Sample January 2016–December 2019

	Adjusted OR (95% CI)	P value
Female	1.03 (0.80, 1.33)	0.826
Age	0.98 (0.97, 0.99)	<b>0.003</b>
BMI (kg/m <sup>2</sup> )		
< 30	Reference	
≥ 30	1.41 (0.90, 2.19)	0.130
Charlson Comorbidity Index	1.06 (0.99, 1.13)	0.075
Year		
2016	Reference	
2017	1.13 (0.80, 1.6)	0.483
2018	1.35 (0.96, 1.91)	0.087
2019	1.13 (0.78, 1.62)	0.517
Race		
White	Reference	
Black	1.23 (0.83, 1.82)	0.296
Hispanic	1.07 (0.67, 1.71)	0.762
Asian or pacific islander	1.68 (0.71, 3.93)	0.235
Other	1.49 (0.65, 3.42)	0.344
Insurance		
Medicare	Reference	
Medicaid	0.94 (0.60, 1.48)	0.802
Private Insurance	1.34 (0.95, 1.91)	0.098
Self-pay	0.89 (0.32, 2.46)	0.825
Other	0.47 (0.17, 1.31)	0.150
Residential income		
First Quartile (lowest)	Reference	
Second Quartile	0.53 (0.17, 1.65)	0.273
Third Quartile	0.37 (0.12, 1.16)	0.087
Fourth Quartile (highest)	0.56 (0.18, 1.76)	0.324
Teaching status		
Non-teaching	Reference	
Teaching	3.38 (1.15, 9.97)	<b>0.027</b>
Hospital bed size		
Small	Reference	
Medium	0.74 (0.50, 1.11)	0.151
Large	0.95 (0.66, 1.36)	0.765
Hospital region		
Northeast	Reference	
Midwest	1.05 (0.72, 1.53)	0.819
South	0.91 (0.64, 1.29)	0.610
West	0.82 (0.55, 1.22)	0.334
Days from admit to surgery	1.00 (0.99, 1.02)	0.887

OR = Odds ratio

Bolded data = statistically significant (i.e.,  $p < 0.05$ )

colonic lavage groups, respectively. Overall in-hospital postoperative mortality was 26.0% and 22.3% in the early intervention TAC and DLI with antegrade colonic lavage

groups, respectively. On adjusted analyses, there were no significant differences between groups with regards to in-hospital morbidity, mortality, or system-specific morbidity. Mean postoperative length of stay remained significantly lower in the TAC group (-4.42 days, 95%CI -7.47 to -1.36 days,  $p = 0.005$ ), as well as mean total in-hospital cost (-\$90,066.30, 95%CI -161,045 to -19,087,  $p = 0.005$ ).

## Discussion

In congruence with the current scientific literature, the present study was unable to reliably reproduce the initial findings from Neal et al.<sup>8</sup>. Our NIS cohort failed to show a difference between the two surgical approaches with regards to in-hospital postoperative morbidity or mortality. Total and postoperative length of stays were approximately four days shorter in patients undergoing TAC with an associated cheaper total hospitalization cost by \$79,715.34. Earlier operative intervention did not significantly alter the observed results. Younger patients and patients receiving care at a teaching hospital were significantly more likely to undergo DLI with antegrade colonic lavage.

Six previously published studies have compared TAC and DLI with antegrade colonic lavage.<sup>8–11,22,23</sup> Similar to our study, three studies found no significant differences in mortality between both interventions.<sup>9,10,23</sup> The landmark study by Neal et al. noted the most drastic decrease in mortality (19% DLI vs. 50% TAC,  $p = 0.006$ ) with no studies being able to replicate the same therapeutic advantage of DLI with antegrade colonic lavage.<sup>8</sup> Abou-Khalil et al. noted a similar trend with regards to in-hospital mortality (27.7% DLI vs. 34.5% TAC,  $p = 0.004$ ) and Ferrada et al. calculated an adjusted mortality favouring DLI with antegrade colonic lavage (17.2% DLI vs. 39.7% TAC,  $p = 0.002$ ).<sup>11,22</sup> All systematic reviews and meta-analyses have shown no significant difference in mortality between treatment modalities.<sup>12–14</sup> Recently, the Surgical Infection Society published a guideline recommending TAC for fulminant, non-perforated CDI.<sup>24</sup> The decision to maintain TAC as the continuing gold standard likely stems from the significant clinical equipoise in the literature and observational nature of the evidence.<sup>24</sup>

Our study was the first to investigate healthcare resource utilization between both treatment modalities. The cost savings by opting to use TAC are statistically significant and is likely at least partially explained by the decreased length of stay in this group. The acuity of these patients usually requires costly ICU care postoperatively and therefore a four-day decreased length of stay can have a significant economic benefit.<sup>25–30</sup> No previous studies have shown a significant difference in length of stay between the two interventions.<sup>9–11</sup> It is possible that the prolonged postoperative length of stay in the present study is due to the required vancomycin enema administration in the DLI group or possibly the increased

**Table 5** In hospital mortality and morbidity by surgical approach, Nationwide Inpatient Sample January 2016–December 2019

<i>n</i> (sample size) <i>N</i> (weighted population estimate)	TAC <i>n</i> = 508 <i>N</i> = 2540	DLI with Colonic Lavage <i>n</i> = 224 <i>N</i> = 1120	Unadjusted OR (95%CI)	<i>p</i>	Adjusted OR* (95%CI)	<i>p</i>
In-hospital mortality, n (%)	132 (26.0)	50 (22.3)	1.22 (0.78, 1.92)	0.382	1.03 (0.63, 1.68)	0.909
Post-operative ICU admission, n (%)	208 (40.9)	93 (41.5)	0.98 (0.66, 1.44)	0.905	0.86 (0.57, 1.31)	0.494
Composite system-specific complications, n (%)						
Any	449 (88.4)	182 (81.2)	1.76 (1.05, 2.93)	<b>0.031</b>	1.13 (0.63, 2.03)	0.688
Respiratory	288 (56.7)	115 (51.3)	1.24 (0.85, 1.80)	0.257	0.93 (0.61, 1.42)	0.730
Pneumonia	102 (20.1)	46 (20.5)	0.97 (0.61, 1.56)	0.907	0.87 (0.53, 1.42)	0.572
Cardiovascular	28 (5.5)	6 (2.7)	2.12 (0.85, 5.31)	0.109	2.05 (0.69, 6.10)	0.199
Stroke	6 (1.2)	1 (0.4)	2.67 (1.05, 6.80)	<b>0.040</b>	1.35 (0.32, 5.58)	0.681
MI	18 (3.5)	3 (1.3)	2.71 (0.58, 12.68)	0.206	3.78 (0.65, 21.96)	0.139
Gastrointestinal	98 (19.3)	50.0 (22.3)	0.83 (0.53, 1.32)	0.431	0.84 (0.50, 1.43)	0.524
Ileus	63 (12.4)	29 (12.9)	0.95 (0.53, 1.70)	0.867	1.08 (0.56, 2.1)	0.811
Anastomotic leak	50 (9.8)	-	-	-	-	-
Genitourinary	358 (70.5)	144 (64.3)	1.33 (0.89, 1.98)	0.165	1.05 (0.67, 1.66)	0.819
Acute kidney injury	311 (61.2)	124 (55.4)	1.27 (0.87, 1.87)	0.219	1.05 (0.68, 1.61)	0.837
Urinary retention	19 (3.7)	7 (3.1)	1.20 (0.41, 3.51)	0.733	1.08 (0.33, 3.52)	0.899
Urinary tract infection	107 (21.1)	48 (21.4)	0.98 (0.62, 1.54)	0.925	0.84 (0.51, 1.40)	0.502
Infectious	37.0 (7.3)	27 (12.1)	0.57 (0.30, 1.08)	0.085	0.56 (0.27, 1.17)	0.124
Wound	16 (3.1)	5 (2.2)	1.42 (0.40, 5.05)	0.583	1.26 (0.37, 4.26)	0.708
Post-procedural shock	7 (1.4)	3 (1.3)	1.03 (0.20, 5.29)	0.972	1.68 (0.22, 12.71)	0.617
Discharge Disposition, n (%)						
Home	57 (11.2)	31 (13.8)	0.79 (0.44, 1.40)	0.411	1.59 (0.74, 3.41)	0.237
Short-term hospital	9 (1.8)	4 (1.8)	0.99 (0.24, 4.18)	0.991	0.66 (0.15, 2.98)	0.586
Skilled nursing facility	239 (47.0)	89 (39.7)	1.35 (0.91, 1.99)	0.133	1.09 (0.71, 1.66)	0.698
Home healthcare	70 (13.8)	50 (22.3)	0.56 (0.34, 0.90)	<b>0.017</b>	0.57 (0.33, 0.99)	<b>0.047</b>
Other	133 (26.2)	50 (22.3)	1.23 (0.79, 1.94)	0.358	1.04 (0.63, 1.70)	0.886
Cost, median (IQR), USD	168,628 (96,040, 274,455)	185,851 (104,816, 364,055)	-78,301.2 (-144,664, -11,938.41)	<b>0.021</b>	-90,066.3 (-161,045.5, -19,087.12)	<b>0.013</b>
Total length of stay, median (IQR), days	14 (8, 25)	13 (7, 19)	-4.04 (-7.02, -1.07)	<b>0.008</b>	-4.42 (-7.47, -1.36)	<b>0.005</b>
Postoperative length of stay, median (IQR), days	13 (7, 24)	11 (6, 18)	-4.28 (-7.27, -1.29)	<b>0.005</b>	-4.42 (-7.47, -1.36)	<b>0.005</b>

\* Adjusted by sex, age, race, class of obesity, insurance status, income quartile, Elixhauser comorbidities score, complicated diverticulitis type, minimally invasive surgery status, teaching status of the hospital, and rural status of the hospital. For discharge disposition, hospital region and bed size was added to the multivariate analysis as a covariate

All *n* are analytic sample; all % and means (SD) are survey-weighted to reflect national estimates

OR = Odds ratio

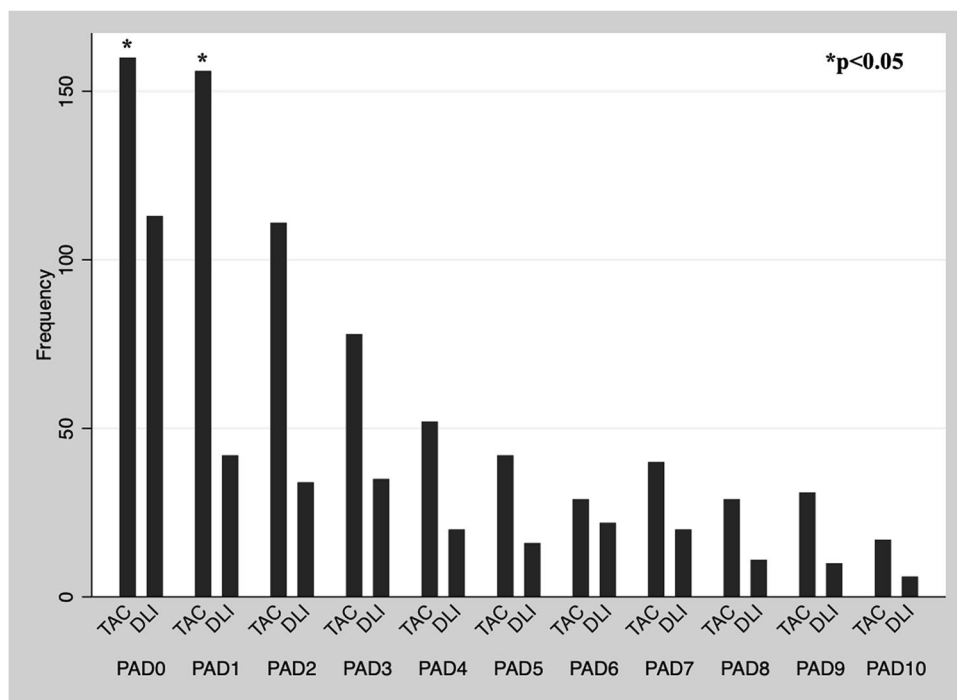
Bolded data = statistically significant (i.e.,  $p < 0.05$ )

infectious morbidity in this group. Additionally, privately insured patients tend to have longer length of stay, and within this study, the DLI group had a larger proportion of patients who were privately insured.<sup>31</sup> Patients undergoing TAC did have a reduced incidence of wound infections which may also contribute to reduced postoperative costs and length of stay. Traditionally, wound infections have been noted to be minimized in minimally invasive surgery.<sup>32</sup> The increased usage of minimally invasive techniques in the DLI with antegrade colonic lavage group in the present study is thus

discordant with the incidence of postoperative infection in our study. Juo et al. found a similar result with wound infections being more common in the DLI with antegrade colonic lavage group (8.9% DLI vs. 3.6% TAC,  $p = 0.01$ ).<sup>10</sup> They attributed this finding to a limitation in the NIS database with regards to inconsistent definitions of complications.<sup>10</sup> Further investigation with regards to surgical site infections following these two operative approaches for patients with fulminant CDI in the form of granular, outcome-adjudicator assessed outcome data is required.



**Fig. 2** Bar chart of frequency of TAC and DLI with antegrade colonic lavage for fulminant CDI per day admitted to hospital, National Inpatient Sample 2016–2019



The primary strengths of this study include a large sample size, thorough statistical analyses, and subgroup analyses conducted based on duration of admission. Furthermore, the NIS is a robust database and provides a reliable sample that is representative of the U.S. patient population. However, this study has several limitations. Firstly, the observational nature of the data makes it vulnerable to selection bias. Factors such as surgeon preference and institutional guidelines can impact choice of surgical approach for certain patients. Moreover, preoperative factors such as hemodynamic stability and preoperative imaging may have resulted in the inclusion of patients with more severe disease in the TAC group. We attempted to control for this through multivariable regression. Nonetheless, the findings are at risk of residual confounding due to unmeasured variables in the NIS database. Next, there is no specific ICD-10-CM code for antegrade colonic lavage, therefore, this study assumed that all DLI performed without an associated colectomy was for the purpose of antegrade lavage. Furthermore, while ICD-10-CM procedure coding is performed according to the temporality of the procedures, it is possible that patients included in the TAC group had previously undergone DLI with antegrade colonic lavage but failed and thus required TAC. We were limited in the patients we could include since patients with concurrent colon pathologies had to be excluded in order to ensure that the surgical interventions were solely for CDI. Since CDI can occur alongside other gastrointestinal conditions, our sample is restricted in its

ability to represent the full spectrum of CDI patients undergoing surgical intervention. Lastly, this study only investigated in-hospital data, and therefore no long-term analyses of colonic preservation were conducted which is a potential advantage of DLI with antegrade colonic lavage.<sup>8–11,22,23</sup> Importantly, there are significant costs associated with a permanent stoma from a TAC such as the supplies, nursing visits, complications, and hospitalizations for a potential ileostomy reversal which could not be modelled due to the restriction of the dataset to the index hospitalization.<sup>33–36</sup> Thus while the data from the present study suggest that TAC offers an advantage in terms of healthcare resource utilization with equivalent short-term postoperative outcomes, it is possible that longer term outcomes such as colonic preservation, stoma-free survival, and reoperation may favor DLI with antegrade colonic lavage.<sup>8</sup> Further prospective studies with high-quality, long-term data are required.

## Conclusion

As the medical and economic burden of CDI continues to rise, strategies for surgical management must be available to handle patients with fulminant disease. The present study demonstrates that there is not a significant difference in postoperative morbidity or mortality between TAC and DLI with antegrade colonic lavage. However, patients undergoing TAC have lower total costs with an associated four-day

shorter length of stay. Due to ongoing clinical equipoise, the choice of surgical approach should still be based upon individual patient factors such as age, comorbidities, CDI associated end-organ damage, patient expectations, surgeon preference, and resource availability.

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Acquisition of data – McKechnie, Lee.

Analysis and interpretation of data – All authors.

Drafting and revision of the manuscript – All authors.

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## Declarations

**Conflict of Interest Statement** None declared.

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