

# *Clostridium difficile* Infection in the Plastic Surgery Population: Lessons from the ACS NSQIP Database

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**Background:** *Clostridium difficile*-associated infections (CDI) have a significant impact on morbidity and mortality of hospitalized medical and surgical patients. There is a paucity of data regarding the incidence, impact, and modifiable risk factors in the plastic surgery population.

**Methods:** The ACS NSQIP database was retrospectively queried for all cases performed by plastic surgeons during 2016. All plastic surgery cases, combined cases, demographics, and baseline clinical characteristics were extracted from the database. The study population was divided into 2 groups based on the development of CDI. Independent variables for development of CDI were identified.

**Results:** During the study period, a total of 29,256 patients underwent a procedure by plastic surgery, with the most commonly performed procedures involving the breast (58%) and trunk (14%). Only 44 patients developed post-operative CDI (0.1%). Factors independently associated with development of CDI were wound classification at the end of the surgery, COPD, procedures involving the trunk, and surgery for reconstruction of pressure ulcers. Outpatient surgery was associated with decreased odds of developing CDI [AOR (95% CI):0.2 (0.1, 0.4), adj  $P < 0.001$ ]. Staying overnight did not increase the odds of developing CDI; however, staying for  $>1$  day in the hospital was associated with an increased risk of CDI development [AOR (95% CI): 1.03 (1.01, 1.13), adj  $P = 0.001$ ]. Combined cases, ASA, body mass index, diabetes, and active smoking were not associated with CDI.

**Conclusions:** CDI are rare in the plastic surgery population and are most associated with trunk/decubitus ulcer reconstructions, inpatient hospital stay, and contaminated wounds. The patients that usually fit in these categories have acutely or chronically infected wounds, which are often treated with systemic antibiotics. For patient with decubitus ulcers and other trunk reconstruction, the guidelines for pre and post-operative systemic antibiotic usage is not well defined. For patients who have had trunk reconstruction, development of evidence-based antibiotic stewardship guidelines may help these patients by limiting antibiotic usage and thereby reducing the incidence of CDI. (*Plast Reconstr Surg Glob Open* 2020;8:e3281; doi: 10.1097/GOX.0000000000003281; Published online 21 December 2020.)

## INTRODUCTION

*Clostridium difficile* Infections (CDI) have increased exponentially over the last years and, as a result, have become the center of attention for hospitals and physicians

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globally. CDI have become not only publicly reportable but also a quality measure that guides compensation and grading among different institutions. Furthermore, CDI can result in billions of dollars of added healthcare costs but can also cause a significant morbidity ranging from chronic diarrhea to devastating cases of toxic megacolon and, subsequently, death. For the above reasons, CDI have been in the spotlight of the literature, and several multimodal approaches for the prevention, diagnosis, and prompt treatment have been developed.<sup>1</sup>

In all surgical specialties, the procedures most commonly associated with CDI in surgery are lower-extremity amputation, bowel resection or repair, and

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gastric or esophageal surgeries and emergency surgeries.<sup>2,3</sup> Transmission of *Clostridium difficile* is usually hospital-acquired, with only 35% of all infections being community-acquired.<sup>4</sup>

Risk factors for CDI in general surgery patients are age > 65 years, inflammatory bowel disease, immunodeficiency, malnutrition, obesity, and low serum albumin. Comorbidities such as type 2 diabetes mellitus, sepsis, and use of proton pump inhibitors were also associated with CDI.<sup>5-7</sup> Situations that increase exposure to *C. difficile* includes length of stay in hospitals greater than 2 weeks.<sup>8</sup>

Although there has been a plethora of information regarding CDI, there is a paucity of data regarding the impact of CDI in the plastic surgery population. Patients undergoing plastic surgery represent a unique population, ranging from the healthy outpatient cosmetic surgery patients, to the medically compromised patients undergoing reconstruction following trauma, malignancy, or chronic disease. There are currently no data to help plastic surgeons when they counsel and treat patients with regard to CDI. In an era of antibiotic stewardship and strict oversight with the aim to avoid development of antibiotic resistant strains of bacteria, a closer look at CDI, their risk factors, and their impact is important. The present study aimed to assess the impact of CDI in the plastic surgery population and to identify patients at a higher risk for CDI, using a large population analysis.

## MATERIALS AND METHODS

This study utilized the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database. UT Health San Antonio IRB approval was obtained before proceeding this study. All patients who were coded as undergoing a surgical procedure via plastic surgery as the surgical specialty were selected. As a result, all patients who underwent plastic and reconstructive surgery in each participating hospital were included in the database regardless of their current procedural terminology code.

The following variables were extracted from the ACS NSQIP database for each patient: age, gender, race (if the surgery was performed in an outpatient setting), history of tobacco use, steroid use comorbidities, and history of open wound or wound infection. The current procedural terminology (CPT) codes were used to categorize the procedures in different groups, including flaps, pressure ulcer reconstruction, breast, and craniofacial. Combined cases with other specialties were identified. The wound classification at the end of the surgery and the American Society of Anesthesiology (ASA) class was also extracted from the database. The OR time for each case was documented in minutes. The weight and height were used to calculate the body mass index for each patient. Primary outcome was development of complications.

American College of Surgeons National Surgical Quality Improvement Program and the hospitals participating in the ACS NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

## STATISTICAL ANALYSIS

The study population was divided into 2 groups (CDI versus no CDI), and independent predictors were identified. A univariate comparison was performed to identify differences between the two groups. Categorical variables were compared using Pearson's chi square or Fisher's exact test as appropriate. Continuous variables were examined for normality of distribution using the Shapiro Wilks test. Normally distributed variables were compared using student's *t*-test, while non-normally distributed variables were compared using Mann-Whitney U test. Variables that were different at  $P < 0.2$  were entered in a forward stepwise logistic regression to identify the different predictors of CDI development. Adjusted odds ratios with 95% confidence intervals [AOR (95% CI)] were derived from the regression. SPSS 16 (IBM, Armonk, N.Y.) was used for statistical analysis.

## RESULTS

A total of 29,256 patients were identified in the 2016 data set. Out of those, only 44 (0.15%) developed CDI, while 29,302 did not. The mean age of the study group was 49 years, with a mean body mass index of 28. Men accounted only for 17% of the study population, while the most common race was white (85%), followed by black (12%). Outpatient surgery was the most common modality (75%). Thirteen percent of patients used nicotine products. The most common comorbidity was hypertension requiring medication, followed by presence of an open wound. Patients who developed CDI were more likely to be men (41% versus 17%,  $P < 0.001$ ), more likely to have a prior open wound (60% versus 6%,  $P < 0.001$ ) and use tobacco (27% versus 13%,  $P = 0.004$ ). Patients who underwent an outpatient procedure were significantly less likely to develop CDI (Table 1).

The most common procedure performed by plastic surgeons was non-autologous breast reconstruction (58%), followed by operation of the trunk and surgery of the upper extremity (14% and 10%, respectively). A total of 1198 patients (4%) were combined cases with other specialties and most of the wounds were clean (87%), with 4% of the cases being infected. The most common ASA classification was 2 and the mean OR time was 140 minutes. Patients who developed CDI were more likely to undergo a free flap reconstruction of the trunk, a pressure ulcer reconstruction, and have a higher ASA classification (Table 2).

A total of 6 independent predictors for CDI were identified. The predictors included the wound classification at the end of the surgery [AOR (95% CI): 6.1 (3.0, 12.2)], outpatient status of the surgery [AOR (95% CI): 0.2 (0.1, 0.4)], chronic obstructive pulmonary disease [AOR (95% CI): 3.6 (1.4, 9.5)], surgery of the trunk [AOR (95% CI): 3.4 (1.6, 7.2)], pressure ulcer reconstruction [AOR (95% CI): 5.4 (1.7, 16.7)], and total hospital length of stay [AOR (95% CI): 1.6 (1.4, 1.9)]. The c statistic for the model was 0.87 (0.74, 0.89),  $P < 0.001$  (Table 3). Patients with CDI were also more likely to have deep surgical site infections, UTI, and sepsis (Table 4).

**Table 1. Patient Demographics and Clinical Characteristics**

	Overall (n = 29,256)	CDAI (n = 44)	No CDAI (n = 29,302)	P
Age	48.8 ± 15.0	49.1 ± 15.2	48.7 ± 14.9	0.869
Body mass index	28.1 ± 7.8	27.2 ± 9.4	28.5 ± 7.5	0.246
Male gender	17.2 (5038)	40.9 (18)	17.1 (5020)	<0.001
Race				
American Indian	0.3 (102)	4.5 (2)	0.3 (100)	
Asian	2.2 (656)	2.3 (1)	2.2 (655)	
Black	12.1 (3549)	11.4 (5)	12.1 (3544)	
Pacific Islander	0.2 (72)	0 (0.0)	0.2 (72)	
White	85.1 (24,967)	81.9 (36)	85.1 (24,931)	<0.001
Outpatient surgery	74.8 (21,954)	18.2 (8)	74.9 (21,946)	<0.001
Tobacco use	12.9 (3788)	27.3 (12)	12.9 (3776)	0.004
COPD	1.6 (470)	11.4 (5)	1.6 (465)	<0.001
HTN	25.6 (7514)	25.0 (11)	25.6 (7503)	0.927
On dialysis	0.6 (163)	9.1 (4)	0.5 (159)	<0.001
Open wound/infection	6.2 (1820)	59.1 (26)	6.1 (1794)	<0.001
Steroid use	2.1 (623)	6.8 (3)	2.1 (620)	0.066
Bleeding disorders	1.5 (444)	9.1 (4)	1.5 (440)	<0.001

**Table 2. Case Categories**

	Overall (n = 29,256)	CDAI (n = 44)	No CDAI (n = 29,302)	P
Free flap of head and neck	2.1 (611)	4.5 (2)	2.1 (609)	0.233
Free flap of lower extremity	0.9 (233)	2.3 (1)	0.9 (252)	0.317
Free flap of the trunk	2.2 (631)	15.9 (7)	2.1 (624)	<0.001
Free flap of the upper extremity	0.3 (90)	0.0 (0)	0.3 (90)	1
Upper extremity other than free flap	10.4 (3054)	2.3 (1)	10.4 (3053)	0.083
Head and neck other than free flap	0.5 (139)	2.3 (1)	0.5 (138)	0.189
Lower extremity other than free flap	0.4 (120)	2.3 (1)	0.4 (119)	0.165
Pressure ulcer	0.7 (202)	11.4 (5)	0.7 (197)	<0.001
Sex reassignment	0.1 (44)	0.0 (0)	0.2 (44)	1
Trunk other than free flap	13.8 (4057)	40.9 (18)	13.8 (4039)	<0.001
Breast	58.3 (17,112)	13.6 (6)	58.4 (17,106)	<0.001
Craniofacial	2.6 (767)	2.3 (1)	2.6 (766)	1
DIEP	4.3 (1256)	2.3 (1)	4.3 (1255)	1
Breast flap other than DIEP	2.2 (631)	0.0 (0)	2.1 (631)	1
Other	1.3 (379)	0.0 (0)	1.3 (379)	1
Combined case with other specialty	4.1 (1198)	6.8 (3)	4.1 (1195)	0.427
Wound classification at end of surgery				
Clean	87.0 (25,522)	38.6 (17)	87.0 (25,505)	
Clean/contaminated	5.8 (1699)	11.4 (5)	5.8 (1694)	
Contaminated	3.1 (904)	11.4 (5)	3.1 (899)	
Infected	4.2 (1,221)	38.6 (17)	4.1 (1,204)	<0.001
ASA				
1	17.3 (5088)	0.0 (0)	17.4 (5088)	
2	56.7 (16,625)	34.1 (15)	56.7 (16,610)	
3	24.3 (7137)	52.3 (23)	24.3 (7114)	
4	1.7 (496)	13.6 (6)	1.7 (490)	<0.001
OR time (min)	140 ± 103	147 ± 126	139 ± 102	0.647

**Table 3. Predictors of CDAI Development**

Step	Variable Entered	AOR (95% CI)	Adjusted P	Cumulative R2
1	Wound infection	6.1 (3.0, 12.2)	<0.001	0.176
2	Outpatient surgery	0.2 (0.1, 0.4)	<0.001	0.184
3	COPD	3.6 (1.4, 9.5)	0.01	0.191
4	Trunk	3.4 (1.6, 7.2)	0.001	0.198
5	Pressure ulcer	5.4 (1.7, 16.7)	0.004	0.206
6	Hospital length of stay	1.6 (1.4, 1.9)	0.004	0.209

Outpatient surgery was used as the reference point for examination of the association of hospital length of stay and the probability of developing CDI. Overnight stay was not associated with an increased probability of CDI development [AOR (95% CI): 0.9 (0.5, 1.5), adjusted  $P = 0.631$ ]. When patients had a LOS of 2 days, there was a significant increase in the probability of developing CDI [AOR (95% CI): 1.4 (1.2, 4.3), adjusted  $P = 0.031$ ]. Increasing HLOS resulted in increased odds of developing CDI in the study population (Table 5).

## DISCUSSION

The incidence of CDI in plastic surgery patients has not been previously evaluated, likely due to the low incidence of CDI in plastic surgery, as shown already. There is a significant difference and increased risk for CDI in the following instances: increased length of stay, decubitus ulcers, wound classification of III or IV, surgery of the trunk, high ASA, and COPD. These risk factors are similar to those seen in general surgery cases. In general, patients with increasing complexity, chronicity, and co-morbidities have the highest rates of CDI.

**Table 4. Outcomes**

	Overall (n = 29,256)	CDAI (n = 44)	No CDAI (n = 29,302)	P
Superficial surgical site infection	1.9 (558)	4.5 (2)	1.9 (556)	0.204
Deep surgical site infection	0.7 (200)	9.1 (4)	0.7 (196)	<0.001
Organ space surgical site infection	0.7 (212)	2.3 (1)	0.7 (211)	0.273
Dehiscence	0.9 (250)	4.5 (2)	0.8 (248)	0.054
Pneumonia	0.3 (75)	2.3 (1)	0.3 (74)	0.107
Pulmonary embolism	0.1 (41)	0 (0.0)	0.1 (41)	1
Acute kidney injury	0.1 (12)	0 (0.0)	0.1 (12)	1
UTI	0.5 (134)	11.4 (5)	0.4 (129)	<0.001
Myocardial infarction	0.1 (17)	0 (0.0)	0.1 (17)	1
Deep venous thrombosis	0.2 (56)	0 (0.0)	0.2 (56)	1
Sepsis	3.1 (168)	11.4 (5)	0.6 (163)	<0.001
Septic shock	0.1 (35)	6.8 (3)	0.1 (32)	<0.001

**Table 5. Association of Hospital Length of Stay and CDAI Development**

HLOS	AOR (95% CI)	Adjusted P
0	<i>Reference</i>	<i>Reference</i>
1	0.9 (0.5, 1.5)	0.631
2	1.4 (1.2, 4.3)	0.031
3	2.5 (1.4, 6.7)	0.027
4	1.7 (1.2, 10.5)	0.001
5	3.1 (2.3, 9.1)	<0.001
>5	10.4 (4.1, 13.2)	<0.001

In this study, wound classification at the end of surgery, inpatient admission to the hospital, trunk and pressure sore reconstruction, and COPD were associated with the increased risk of developing CDI. COPD has been found in other studies to be associated with the increased risk of developing CDI due to more frequent hospitalizations, use of antibiotics for lung infections, and higher use of antacid medications.<sup>9,10</sup> Although this article did not have the information regarding the specific antibiotics used in the cohort of patients, it is the first in the plastic surgery literature to examine the prevalence of CDI in our specialty.

The common factor between CDI in plastic surgery procedures and procedures from other surgical specialties is the presence of chronic wounds, such as decubitus ulcers. These wounds often have a history of chronic antibiotic usage, one of the main risk factors for developing CDI. Plastic surgery patients are often optimized before surgery, and many of the other risk factors identified in general surgery patients such as malnutrition, albumin and obesity can be mitigated before large reconstructive procedures. However, the optimization of the patient before reconstruction in the emergency or oncologic setting is not always possible. Suljagic et al examined CDI at their institution and separated out plastic surgery and burn procedures. The study showed that Plastic Surgery and Burns patients had one of the highest incidences of CDI of new cases per 100,000 patients second to cardiothoracic surgery (4.6/10,000 versus 6.5/10,000).<sup>11</sup> Unfortunately, the type of plastic surgery procedure is not differentiated into groups of patients such as was done in this study, and burn patient data were incorporated into the plastic surgery data set.<sup>11</sup>

The use of antibiotics in plastic surgery has been studied, and development of evidence-based recommendations has been attempted. The American Association of Plastic Surgeons published recommendations for

antibiotic prophylaxis, in 2015. Systemic antibiotic prophylaxis is recommended for clean breast surgeries and contaminated hand, head, and neck surgeries. It is not recommended for clean hand, skin, head and neck, or abdominoplasty procedures.<sup>12</sup> There are no antibiotic recommendations for pressure sore reconstruction. Despite these guidelines, the use of systemic antibiotic therapy in areas such as breast reconstruction continues to be controversial, especially in the setting of implant-based reconstruction and use of drains.<sup>13,14</sup> Even the proper use of surgical antibiotic prophylaxis has been questioned due to the lack of Level 1 evidence.<sup>15</sup>

Antibiotic usage in patients who specifically undergo decubitus ulcer reconstruction has not been reported extensively in the plastic surgery literature, and there are currently no universal guidelines for systemic antibiotics therapy before or after reconstruction. A Cochrane review from 2016 evaluated topical and systemic antibiotics for pressure sores before reconstruction. The review revealed that there is no consistent evidence of benefit of using antibiotics and there are no trials that looked at systemic antibiotics. There are no recommendations for post-operative antibiotic regimen or duration at this time.<sup>16</sup> Although there are no recommendations for post-operative antibiotics for the types of plastic surgery procedures highlighted in this study as high-risk for CDI, there are recommendations for prevention and treatment of CDI.

There are several limitations to the study due to following factors: the type of database used; details such as prior illness, prior CDI, and specific antibiotic use; type and duration being unknown. Furthermore, any details regarding each occurrence of CDI (such as duration), and treatment are not known. We were not able to differentiate between hospital- and community-acquired CDI. Patients who developed CDI after discharge were also not captured. This information would be important to determine more factors that put these patients at a higher risk of developing CDI. Finally, the decision regarding the duration and the type of antibiotic that is administered is based on the surgeon's preference rather than on the evidence-based medicine in most instances.

## CONCLUSIONS

CDI are rare in the plastic surgery population and are most associated with decubitus ulcer reconstructions, inpatient hospital stay, and contaminated wounds. The

patients who usually fit in these categories have acutely or chronically infected wounds, which are often treated with systemic antibiotics. For patients with decubitus ulcers and other trunk reconstruction, the guidelines for pre and post-operative systemic antibiotic usage are not well defined. For patients who have had trunk reconstruction, development of evidence-based antibiotic stewardship guidelines may help these patients by limiting antibiotic usage and therefore reducing the incidence of CDI. Multidisciplinary studies to develop evidence-based guidelines for antibiotic treatment after surgical intervention for patients with pressure sores are needed.

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