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Risk Factors and Costs Associated With *Clostridium difficile* Colitis in Patients With Prosthetic Joint Infection Undergoing Revision Total Hip Arthroplasty

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ABSTRACT

Background: With the increased demand for primary total hip arthroplasty (THA) and corresponding rise in revision procedures, it is imperative to understand the factors contributing to the development of *Clostridium difficile* colitis. We aimed to provide a detailed analysis of: (1) the incidence of; (2) the demographics, lengths of stay, and total costs for; and (3) the risk factors and mortality associated with the development of *C. difficile* colitis after revision THA.

Methods: The National Inpatient Sample database was queried for all individuals diagnosed with a periprosthetic joint infection and who underwent all-component revision THA between 2009 and 2013 (n = 40,876). Patients who developed *C. difficile* colitis during their inpatient hospital stay were identified. Multilevel logistic regression analysis was conducted to assess the association between hospital- and patient-specific characteristics and the development of *C. difficile* colitis.

Results: The overall incidence of *C. difficile* colitis after revision THA was 1.7%. These patients were significantly older (74 vs 65 years), had greater lengths of hospital stay (19 vs 9 days), accumulated greater costs ($51,641 vs $28,282), and were more often treated in an urban hospital compared to their counterparts who did not develop *C. difficile* colitis ($P < .001$ for all). Patients with colitis also had a significantly higher in-hospital mortality compared to those without (5.6% vs 1.4%; $P < .001$).

Conclusion: While *C. difficile* colitis infection is an uncommon event following revision THA, it can have potentially devastating consequences. Our analysis demonstrates that this infection is associated with a longer hospital stay, higher costs, and greater in-hospital mortality.

Periprosthetic joint infection (PJI) is a devastating complication after total hip arthroplasty (THA). Between 2000 and 2013, the percentage of revision THAs required secondary to PJI increased from 10.9%-13.7% [1]. In these cases, 2-stage revision THA in combination with prophylactic antibiotics is the gold standard treatment [2,3]. The addition of postoperative prophylactic antibiotics is a major factor in the considerable success of 2-stage revision THA in PJI eradication [4–6]. As such, the use of long-term antibiotics is expanding from the treatment of PJI to the routine prophylactic regimen after both septic and aseptic revision THAs [7]. However, this heightened use of antibiotics is not without its share of consequences.

Prolonged antibiotic use can predispose patients to native bacterial flora suppression and the subsequent development of *Clostridium difficile* colitis. *C. difficile* has become the most common healthcare-associated infection in hospitalized patients, accounting for 12.1% of healthcare-associated infections and affecting nearly 500,000 patients each year in the United States [8,9]. Among orthopedic surgery patients, the incidence of *C. difficile* colitis is estimated to range from 0.17% after primary THA or total knee arthroplasty (TKA) to 7.1% after fixation of an intertrochanteric

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femur fracture [10,11]. Although the number of total joint arthroplasties (TJAs) complicated by *C. difficile* colitis is low, the consequences of this illness can be severe. In addition to pseudomembranous colitis and its attributed profuse and/or bloody diarrhea, affected patients may experience severe sequelae such as toxic megacolon, bowel perforation, and death [6]. *C. difficile* infection is also associated with increased lengths of stay (LOSs) and increased total admission costs [12,13]. In fact, management of *C. difficile* infection in acute care facilities alone is estimated to cost the US healthcare system an additional $4.8 billion annually [14,15].

Although the risk factors for and outcomes of *C. difficile* infection in primary TJA patients have been investigated, there is a paucity of literature regarding *C. difficile* infection in revision THA patients [10,16,17]. As compared with primary THA patients, revision THA patients have an especially high risk of sustaining a PJI and often require longer courses of more potent antibiotics. This antibiotic regimen renders them highly susceptible to the development of *C. difficile* colitis. Therefore, we aimed to provide a detailed analysis of (1) the incidence of *C. difficile* colitis; (2) the demographics, LOS, and total costs for patients who developed *C. difficile* colitis; and (3) the risk factors and mortality associated with the development of *C. difficile* colitis in patients who underwent revision THA for PJI.

Methods

Database

The National Inpatient Sample (NIS) database was used to query patient discharge records which are between the years 2009 and 2013. Developed for the Healthcare Cost and Utilization Project and sponsored by the Agency for Healthcare Research and Quality, NIS data are intended to guide national-level, state-level, and community-level healthcare policies. The NIS is the largest publicly-available inpatient healthcare database in the United States, containing information from over 7 million hospital encounters annually as an unweighted data set and from over 35 million hospital encounters annually when weighted. This is estimated to represent more than 96% of the US population. As the NIS no longer contains state or hospital identifiers, institutional review board's approval was not necessary for this study [18].

NIS data elements include patient demographic characteristics—such as sex, age, race, comorbidities, median household income, and insurance payor—as well as hospital demographic characteristics—such as geographic region, ownership, teaching status, and bed size. Total hospital charges, patient discharge status, and LOS are also available. Each individual entry can contain up to 25 International Classification of Disease (ICD) diagnosis codes, and up to 15 ICD procedure codes.

Patient Selection

The NIS database was queried for all individuals with a primary diagnosis of PJI using the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) code 996.66 and who underwent all-component revision THA (ICD-9-CM code 00.70) between January 1, 2009 and December 31, 2013. The subset of patients who developed *C. difficile* colitis (ICD-9-CM code 008.45) during their inpatient hospital stay was also identified. This selection yielded 40,876 patients, of which 698 (1.7%; mean age 73.5 years) developed *C. difficile* colitis and 40,178 (98.3%; mean age 65.2 years) did not develop *C. difficile* colitis (see Table 1).

Table 1
Incidence and Demographics of Revision THA Patients With PJI.

	C. difficile	No *C. difficile*	*P* Value
Total number	698 (1.7%)	40,178 (98.3%)	
Age, y (SD)	73.5 (10.9)	65.2 (13.2)	<.001
Length of stay, d (SD)	18.9 (19.5)	8.8 (9.3)	<.001
Gender			
Male (%)	322 (46.1%)	19,895 (49.5%)	.07
Female (%)	377 (53.9%)	20,279 (50.5%)	
Charlson/Deyo comorbidity score			
0	39 (5.6%)	3671 (9.1%)	<.001
1	611 (87.4%)	36,096 (89.8%)	
2	30 (4.3%)	166 (0.4%)	
≥3	19 (2.7%)	245 (0.6%)	
In-hospital mortality	5.6%	1.4%	<.001
Total costs	$51,641	$28,282	<.001

PJI, periprosthetic joint infection; SD, standard deviation; THA, total hip arthroplasty.

Predictor Variables

Several factors were used as predictor variables in the statistical analysis. These included patient demographics (age, gender, race, and insurance status); hospital characteristics (rural, urban nonteaching, or urban teaching; small, medium, and large bed size); hospital ownership (federal; nonfederal [public]; private, not-for-profit [voluntary]; investor-owned (proprietary); or private); and patient comorbidities. Patient race was categorized as White, Black, Hispanic, Asian or Pacific Islander, Native American, or Other.

Statistical Analysis

Patient comorbidity severity level was calculated by using the listed patient comorbidities to obtain the Charlson/Deyo comorbidity index. An independent samples *t* test and a chi-squared analysis were performed to assess continuous and categorical variables, respectively. Multilevel logistic regression analysis was conducted to assess the association between hospital-specific and patient-specific characteristics and the development of *C. difficile* colitis. A 2-tailed *P* value <.05 was designated as statistical significance. All statistical analyses were performed with SPSS, version 24 (IBM Corporation, Armonk, NY).

Results

During the study period, 698 patients developed *C. difficile* colitis and 40,178 patients did not develop *C. difficile* colitis. This yielded an overall incidence of *C. difficile* colitis of 1.7% in patients undergoing revision THA after the treatment of PJI. The group of patients who developed *C. difficile* colitis comprised 46.1% men and 53.9% women, whereas the group of patients who did not develop *C. difficile* colitis comprised 49.5% men and 50.5% women ($P = .07$; see Table 1).

Patients who developed *C. difficile* were significantly older (73.5 vs 65.2 years; $P < .001$) and had significantly greater LOSs (18.9 vs 8.8 days; $P < .001$) than those who did not develop *C. difficile* infection. In addition, the patients with *C. difficile* colitis had significantly higher comorbidity severity scores (2.7% vs 0.6% of patients with Charlson/Deyo comorbidity index ≥3; $P < .001$), higher in-hospital mortality rates (5.6% vs 1.4%; $P < .001$), and higher total costs ($51,641 vs $28,282; $P < .001$) (see Table 1).

In this study, revision THA patients who developed *C. difficile* colitis were more likely to fall into the “Other” race category ($P < .001$) and more likely to be treated in an urban hospital than rural or community hospital ($P < .001$) (see Table 2).