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The morbidity of *Clostridium difficile* infection after elective colonic resection—results from a national population database

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Abstract

BACKGROUND: *Clostridium difficile* (CD), a gram-positive rod bacterium, resides normally within the human colon. Antibiotic treatment alters normal colonic flora, potentiating abnormal overgrowth of CD.

METHODS: This study examined the 2004 to 2006 Nationwide Inpatient Sample to determine outcomes of CD colitis after 695,010 elective colonic resections.

RESULTS: CD infection, occurring in 1.4% of patients, was associated with higher pulmonary (12.1% vs 6.4%) and gastrointestinal (12.8% vs 10.5%) complications as well as an increased length of stay (22.6 vs 10.9 days) and mortality (16.2% vs 4.9%; all $P < .001$). CD colitis patients more frequently held Medicare insurance (68% vs 51%) and underwent small segmental colonic resection as opposed to a defined anatomic resection (20.0% vs 9.9%; $P < .001$). An underlying diagnosis of colon cancer was associated with a lower incidence of CD colitis (odds ratio, .71; 95% confidence interval, .59–.84; $P < .001$).

CONCLUSIONS: CD colitis is associated with worse outcomes after elective colonic resection. Published by Elsevier Inc.

Clostridium difficile (CD) is a gram-positive rod bacterium that resides within the human colon. After antibiotic treatment, alterations of the normal colonic flora occur. This allows pre-existing colonization of CD to overgrow, become pathologic, and result in CD colitis.[1] Symptoms of this infection result from toxins released by the bacteria. Toxin A acts as a chemoattractant for neutrophils and causes inflammation and fluid secretion of the colonic mucosa, whereas both toxins A and B activate inflammatory cytokine release from monocytes.[2] Symptoms of the disease vary on a spectrum ranging from abdominal pain, distention, and diarrhea, to sepsis and toxic megacolon requiring colectomy, or even hemodynamic instability and death. Although the bacteria is present in stool cultures of approximately 3% of normal healthy adults and up to 16% to 35% of hospitalized patients, increasing rates are now reported after prolonged duration of exposure to antibiotics, and in those with a severe underlying disease.[3,4] Although any single antibiotic can cause the change in bacterial milieu leading to the pathologic state, certain drugs such as penicillins, clindamycin, fluoroquinolones, and third-generation cephalosporins traditionally are associated more commonly with development of CD colitis.[5]

The views expressed are those of the authors and do not reflect the official policy of the Department of the Army, the Department of Defense, or the US Government.

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Cases of CD colitis in the United States increased 200% between 2000 and 2005.[6] This recent increase in the rate of CD colitis in hospitalized patients, along with the increased virulence of particular strains, has lead to a greater concern about this disease worldwide.

One such strain, known as B1/NAP/027, has shown capacity for hypersporulation, increased resistance to fluoroquinolones, a 16 to 23-fold increase in toxin production, and a severe disease pattern, leading more frequently to pseudomembranous colitis.[7–9]

Alarming trends in CD colitis occurrence after preoperative prophylactic antibiotics was illustrated in a large cohort study from a tertiary care hospital in Quebec showing an increase from .7 cases per 1,000 from 1999 to 2002 to 14.9 cases per 1,000 from 2003 to 2005.[10] A large body of literature exists documenting poor outcomes associated with CD infections in hospitalized patients in the absence of surgery. In addition, population-based series have reported similarly increasing prevalence, mortality, and need for colectomy after development of CD colitis.[11] Although indications for surgical management of CD colitis have been well documented, including severe disease refractory to medical management and the development of life-threatening complications such as perforation or toxic megacolon, large-scale data regarding the morbidity and mortality with the secondary development of CD after colonic resection is lacking. More concerning, this evolution of CD resistance to first-line therapy such as metronidazole and higher recurrence rates suggest development of this disease may carry a much more morbid outcome than previously reported.[12] As such, the purpose of our study was to examine the national trends in incidence and outcomes associated with the secondary development of CD colitis after colonic resection.

Materials and Methods

Data for this study were collected from the Nationwide Inpatient Sample (NIS), an administrative database provided by the Department of Health and Human Services and a product of the Health Care Utilization Project, sponsored by the Agency for Healthcare Research and Quality The NIS is the largest inpatient, all-payer database in the United States. It contains information on patient demographics and comorbidities, admission and discharge diagnoses, and multiple outcome measures for approximately 8 million hospital admissions each year. This database uses a stratified sampling frame and discharge weights to create accurate national estimates from an approximate 20% sample of all nationwide discharges. During our study period, between 986 and 1,004 hospitals from 33 to 37 states were sampled by the NIS. States excluded from each year group were not identical from year to year. The NIS also contains multiple validated severity adjustment measures to estimate patient disease severity used for clinical comparisons.

Patients included in the study were identified within the NIS dataset for the period of 2004 through 2006 using the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) procedure and diagnostic codes. Initial inclusion criteria involved patients who underwent colonic resection during hospital admission.

Procedures included in our query were cecectomy (45.72), right hemicolectomy (45.73), transverse colectomy (45.74), left hemicolectomy (45.75), sigmoidectomy (45.76), total abdominal colectomy (45.8), and partial or segmental colectomy (45.79). Patients then were identified as having an infection with CD during their admission by ICD-9-CM diagnosis code (08.45). Because our goal was to focus on the outcomes with the secondary development of CD, those patients with a primary diagnosis of CD were excluded from the cohort.

Definition of variables

The primary variable in this study was the presence of CD infection during admission, defined by secondary diagnostic code (ICD-9-CM code 08.45). Demographic variables examined included age (years), sex, race, calendar year (2004–2006), pre-existing comorbidities, insurance status (Medicare, Medicaid, private insurance, or other), and type of colonic resection (as described earlier). Diagnoses included in our analysis were colon cancer (153.0–153.9); bowel obstruction, including adhesive disease, volvulus, and incarcerated hernia (552.8–552.9, 560.0–560.9); diverticulitis (562.1); lower gastrointestinal bleeding (578.0–578.9, 772.4); and inflammatory bowel disease (Crohn's disease, 555.0, 555.1, 555.9; ulcerative colitis, 556.8–556.9). Other variables included in our analysis were the number of diagnoses included in the hospital record, number of procedures performed during admission, and NIS specific markers of disease severity, principle stage, and mortality score.

Race

The NIS database categorizes ethnicity as Caucasian, African American, Hispanic, Asian, Native American, and other. For the purpose of our analysis, ethnicity was dichotomized to Caucasian and non-Caucasian for comparison of outcomes variables. Patients with missing data in the category of race were excluded from this portion of our analysis only.

Admission type. The admission type category classifies admission status as either elective or nonelective. For the purpose of our analysis, we combined both NIS categories of urgent and emergent into 1 variable, to define our admission status as one elective group and a separate nonelective group.