Letters

RESEARCH LETTER

ASSOCIATION OF VA SURGEONS

Increasing Incidence of and Increased Mortality Associated With *Clostridium difficile*-Associated Megacolon

The symptoms of *Clostridium difficile* infection range from diarrhea to the rare, but potentially fatal, toxic megacolon. The aim of this study is to determine the changes in the incidence and outcomes of *C difficile*-associated megacolon over a 10-year period.

Methods | Using the Nationwide Inpatient Sample (2000-2010) and *International Classification of Diseases, Ninth Revision (ICD-9)* codes, we identified patients with both *C difficile* infection and megacolon. Patients without both diagnoses were excluded. The study cohort included patients who were managed with surgery and those who were managed without surgery. This study used deidentified data and is exempt from institutional review board approval. The outcome measures were length of stay, inflation-adjusted cost of hospitalization, transitional care needs, and in-hospital mortality.¹ Analyses were performed with χ^2 tests and analysis of variance. *P* > .05 was considered statistically significant.

Results | In 2000, there were 28 219 cases of *C* difficile infection (0.38% of all hospitalized patients), and by 2010, there were 68 645 cases (0.88% of all hospitalized patients). The overall incidence of megacolon among all hospitalized patients remained 0.02% from 2000 to 2010. In contrast, the percentage of cases of megacolon due to *C* difficile infection was 3.61% in 2000 and 9.39% in 2010 (P < .05).

Compared with patients with megacolon but without *C difficile* infection, patients with *C difficile*-associated megacolon are significantly older, are more likely to have an urgent or emergent admission, are more likely to be admitted from the emergency department or transferred from another hospital, and are more likely be treated at large, urban, teaching hospitals (**Table 1**). Among patients with *C difficile*associated megacolon, the mean (SD) length of hospital stay was 16.13 (16.55) days, the mean (SD) cost of hospitalization was \$41 968 (\$51 518), 50.7% required transitional care after hospital discharge, and the overall in-hospital mortality rate was 24.45% (**Table 2**). When examining mortality trends over the decade, the mortality rate associated with *C difficile*associated megacolon increased from 13.56% in 2000 to 24.45% in 2010, with a peak of 30.03% in 2007 (*P* < .05).

Discussion | The incidence of *C difficile*-associated megacolon has nearly tripled, and the mortality rate associated with this condition has nearly doubled, over the past decade. This increased incidence could be due in part to improvements in the

Table 1. Demographic Characteristics of 1051 Patients With Toxic Megacolon in the United States, 2000-2010

	% of Patients With Toxic Megacolon				
Characteristic	All	Without CDI	With CDI	P Value	
Age, mean (SD), y	63.57 (20.86)	63.22 (21.02)	68.90 (18.22)	<.001	
Race/ethnicity					
White	74.99	74.56	81.41		
Black	13.02	13.38	7.75	<.001	
Hispanic	7.63	7.67	7.03		
Asian	1.42	1.44	1.07		
Native American	0.55	0.57	0.24		
Other	2.40	2.39	2.50		
Urgent or emergent admission	82.89	82.66	86.43	.01	
Admission source					
Emergency department	60.07	59.97	61.89		
Transfer from another hospital	3.39	3.22	6.26		
Transfer from another facility (long-term care)	4.16	4.02	6.54	<.001	
Prison	0.01	0.07	0.00		
Routine (home)	32.32	32.71	25.31		
Insurance status					
Medicare	63.35	62.91	70.23		
Medicaid	9.73	9.98	5.82	<.001	
Private/HMO	22.64	22.86	19.37		
Uninsured	2.07	2.11	1.53		
Other	2.21	2.15	3.05		
Hospital size					
Small	15.08	15.21	13.13		
Medium	26.93	27.17	23.31	.001	
Large	57.99	57.63	63.56		
Location					
Rural	17.54	17.94	11.51	<.001	
Urban	82.46	82.06	88.49		
Teaching hospital	37.81	37.24	46.53	<.001	
Hospital region					
Northeast	18.54	18.26	22.84	<.001	
Midwest	23.65	23.48	26.26		
South	40.35	40.74	34.35		
West	17.45	17.51	16.56		

Abbreviations: CDI, *Clostridium difficile* infection; HMO, health maintenance organization.

detection of *C difficile*. However, this increase correlates with the work performed by the Agency for Healthcare Research and Quality, which showed a 74% increase in the overall number of hospital discharges of patients with *C difficile* infection from 1993 to 2001.²

jamasurgery.com

Outcome	% of Patients With Toxic Megacolon				
	All	Without CDI	With CDI	P Value	
Mortality	7.26	6.14	24.45	<.001	
Discharge disposition					
Routine (home)	48.85	50.45	24.45		
Short-term hospital	2.65	2.57	3.90		
Skilled nursing facility	28.85	28.37	36.16	. 0.01	
Home with home health care	11.87	11.95	10.66	- <.001	
Other	0.52	0.53	0.39		
Died in hospital	7.26	6.14	24.45		
Cost, mean (SD), \$	20 250 (30 633)	18718 (27963)	41 968 (51 518)	<.001	
LOS, mean (SD), d	9.36 (10.72)	8.92 (10.07)	16.13 (16.55)	<.001	
Colectomy performed	10.79	10.30	18.36	<.001	

The increase in mortality could be attributed to changes in the virulence of the *C* difficile strains, although we are unable to determine this owing to the limitations of the data set. We were unable to examine variables such as antibiotic regimen, severity of disease, physical examination findings, immunosuppression, presence of end-organ failure, patient frailty status, Acute Physiology and Chronic Health Evaluation score, and signs of sepsis and leukocytosis, which have been identified as factors associated with mortality in prior published reports.³ Another limitation of this database is the use of ICD-9 codes rather than the use of clinical and radiographic criteria, which are not available in this database. The mortality rates associated with *C difficile*-associated megacolon have been reported to range from 38% to 80%, with early diagnosis crucial in improving mortality, but they are based on case studies and case series.⁴⁻⁶ The Nationwide Inpatient Sample database is limited to single admissions; further study is needed to examine long-term survival among these patients.

By using a national data set spanning a decade (2000-2010), we were able to study the largest group to date. This study draws attention to the tremendous burden of *C difficile* on patient mortality, health care costs and resources, and transitional care and the need for aggressive prevention of this iatrogenic disease. Despite the rarity of *C difficile*-associated megacolon, our findings suggest that health care professionals should have a heightened suspicion of megacolon in patients with *C difficile* infection and a lower threshold for transferring infected patients to intensive care units, where goaldirected resuscitation is most feasible.

SreyRam Kuy, MD, MHS Peter Jenkins, MD Ramon A. L. Romero, MD Navdeep Samra, MD SreyReath Kuy, DPM

Author Affiliations: Surgical Service, The Center for Innovations in Quality, Outcomes, and Patient Safety, Overton Brooks Veterans Affairs Medical Center, Abbreviations: CDI, *Clostridium difficile* infection; LOS, length of stay.

Shreveport, Louisiana (SreyRam Kuy, Romero); Department of Surgery, Louisiana State University School of Medicine, Shreveport (SreyRam Kuy, Romero); Regenstrief Institute, Division of Trauma and Surgical Critical Care, Department of Surgery, University of Indiana, Indianapolis (Jenkins); Department of Surgery, Louisiana State University School of Medicine, Shreveport (Samra); Wound Care Center, University General Hospital, Houston, Texas (SreyReath Kuy).

Corresponding Author: SreyRam Kuy, MD, MHS, Surgical Service, The Center for Innovations in Quality, Outcomes, and Patient Safety, Overton Brooks Veterans Affairs Medical Center and Department of Surgery, Louisiana State University School of Medicine, 1501 Kings Hwy, Shreveport, LA 71130 (sreyram@gmail.com).

Published Online: October 7, 2015. doi:10.1001/jamasurg.2015.2677.

Author Contributions: Dr SreyRam Kuy had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: SreyRam Kuy, SreyReath Kuy. *Acquisition, analysis, or interpretation of data:* SreyRam Kuy, Jenkins, Romero, Samra.

Drafting of the manuscript: SreyRam Kuy.

Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: SreyRam Kuy.

Administrative, technical, or material support: SreyRam Kuy, SreyReath Kuy. Study supervision: SreyRam Kuy, Jenkins, Samra, SreyReath Kuy.

Conflict of Interest Disclosures: None reported.

Previous Presentation: This paper was presented at the 39th Annual Meeting of the Association of VA Surgeons; May 4, 2015; Miami Beach, Florida.

1. Kuy S, Roman SA, Desai R, Sosa JA. Outcomes following thyroid and parathyroid surgery in pregnant women. *Arch Surg.* 2009;144(5):399-406.

2. Elixhauser A, Jhung M. Healthcare Cost and Utilization Project statistical brief 50: Clostridium difficile-associated disease in US hospitals, 1993-2005. http: //www.ncbi.nlm.nih.gov/books/NBK54554/. Published April 2008. Accessed September 10, 2015.

3. Autenrieth DM, Baumgart DC. Toxic megacolon. *Inflamm Bowel Dis*. 2012;18 (3):584-591.

4. Byrn JC, Maun DC, Gingold DS, Baril DT, Ozao JJ, Divino CM. Predictors of mortality after colectomy for fulminant *Clostridium difficile* colitis. *Arch Surg.* 2008;143(2):150-154.

5. Miller AT, Tabrizian P, Greenstein AJ, Dikman A, Byrn J, Divino C. Long-term follow-up of patients with fulminant *Clostridium difficile* colitis. *J Gastrointest Surg.* 2009;13(5):956-959.

6. Longo WE, Mazuski JE, Virgo KS, Lee P, Bahadursingh AN, Johnson FE. Outcome after colectomy for *Clostridium difficile* colitis. *Dis Colon Rectum*. 2004;47(10):1620-1626.