

## Is a diverting loop ileostomy and colonic lavage an alternative to colectomy for the treatment of severe *Clostridium difficile*-associated disease?

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The term “evidence-based medicine” was first coined by Sackett and colleagues as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.”<sup>1</sup> The key to practising evidence-based medicine is applying the best current knowledge to decisions in individual patients. Medical knowledge is continually and rapidly expanding. For clinicians to practise evidence-based medicine, they must have the skills to read and interpret the medical literature so that they can determine the validity, reliability, credibility and utility of individual articles. These skills are known as critical appraisal skills, and they require some knowledge of biostatistics, clinical epidemiology, decision analysis and economics, and clinical knowledge.

Evidence Based Reviews in Surgery (EBRS) is a program jointly sponsored by the Canadian Association of General Surgeons (CAGS) and the American College of Surgeons (ACS). The primary objective of EBRS is to help practising surgeons improve their critical appraisal skills. During the academic year, 8 clinical articles are chosen for review and discussion. They are selected for their clinical relevance to general surgeons and because they cover a spectrum of issues important to surgeons, including causation or risk factors for disease, natural history or prognosis of disease, how to quantify disease, diagnostic tests, early diagnosis and the effectiveness of treatment. A methodological article guides the reader in critical appraisal of the clinical article. Methodological and clinical reviews of the article are performed by experts in the relevant areas and posted on the EBRS website, where they are archived indefinitely. In addition, a listserv allows participants to discuss the monthly article. Surgeons who participate in the monthly packages can obtain Royal College of Physicians and Surgeons of Canada Maintenance of Certification credits and/or continuing medical education credits for the current article only by reading the monthly articles, participating in the listserv discussion, reading the methodological and clinical reviews and completing the monthly online evaluation and multiple choice questions.

We hope readers will find EBRS useful in improving their critical appraisal skills and in keeping abreast of new developments in general surgery. Four reviews are published in condensed versions in the *Canadian Journal of Surgery*, 4 are published in the *Journal of the American College of Surgeons* and 4 are published in *Diseases of the Colon and Rectum*. For further information about EBRS, please refer to the CAGS or ACS websites. Questions and comments can be directed to the program administrator, Marg McKenzie, at mmckenzie@mtsinai.on.ca.

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1. Evidence-Based Medicine Working Group. Evidence-based medicine. *JAMA* 1992; 268:2420-5.

## SELECTED ARTICLE

Neal MD, Alverdy JC, Hall DE, et al. Diverting loop ileostomy and colonic lavage. An alternative to total abdominal colectomy for the treatment of severe, complicated *Clostridium difficile* associated disease. *Ann Surg* 2011;254:423–29.

## ABSTRACT

**Objective:** To determine whether a colon-sparing diverting ileostomy with colonic lavage reduces mortality in patients with severe *Clostridium difficile*-associated disease (CDAD) when compared with colectomy. **Design:** Retrospective cohort study. **Setting & patients:** Forty-two patients with diagnosed severe, complicated CDAD who were treated at the University of Pittsburgh Medical Center or VA Pittsburgh Health Care System between June 2009 and January 2011 with diverting loop ileostomy and colonic lavage (warmed polyethylene glycol 3350/electrolyte solution via the ileostomy and postoperative antegrade instillation of vancomycin flushes via the ileostomy). Patients were compared with a historical control group of 42 patients who had a colectomy. **Main outcome:** Resolution of CDAD. **Results:** There was no significant difference in age, sex, pharmacologic immunosuppression and Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scores between the current cohort and historical controls. In the ileostomy group, surgery was performed laparoscopically in 35 patients (83%). This treatment strategy resulted in reduced mortality compared with the historical population (19% v. 50%; odds ratio [OR] 0.24,  $p = 0.006$ ). Preservation of the colon was achieved in 39 of 42 patients (93%). **Conclusion:** Loop ileostomy and colonic lavage are an alternative to colectomy in the treatment of severe, complicated CDAD, resulting in reduced morbidity and preservation of the colon.

## COMMENTARY

There has been a steady increase in the incidence of CDAD over the last 10 years owing in part to increased awareness and the availability of more sensitive testing. Of the more than 22 000 cases of CDAD reported last year, approximately 3%–15% would be expected to progress to the “fulminant” state, a severe form of the disease unresponsive to medical therapy.<sup>1</sup> Surgical intervention has been on the rise, and the preferred treatment in these critically ill patients has been a colectomy and ileostomy.

Neal and colleagues<sup>2</sup> reported on the use of diversion and colonic lavage as a minimally invasive surgical approach for the management of CDAD with excellent outcomes. The authors’ hypotheses for the success of colonic lavage and diversion were 1) a diverting loop

ileostomy with colonic lavage through a minimally invasive approach poses minimal stress for the already critically ill patient and 2) the fecal stream is diverted and the luminal flora is deprived of nutrition, such that mechanical lavage and topical vancomycin administration should remove the causative bacteria and toxin with ultimate reversal of the pathologic process. Although novel to the recent era of increasingly prevalent and hypervirulent CDAD, a similar surgical approach has been advocated in the past. In 1971, Turnbull and colleagues<sup>3</sup> described colonic decompression and diversion in the form of a skin-level colostomy and a loop ileostomy for fulminant toxic megacolon in patients with inflammatory bowel disease (IBD). The Turnbull-Blowhole colostomy was used to bridge the patient over the critical illness to a time when a definitive, elective procedure could be safely performed. However, with improved medical care of patients with IBD, refined operative approaches and extensive perioperative supportive resources, the blowhole procedure is now rarely performed.

Neal and colleagues presented the results of 42 patients prospectively enrolled and treated with colonic lavage with 8 L of warmed polyethylene glycol 3350/electrolyte solution through an antegrade catheter placed via a diverting loop ileostomy. The loop ileostomy was created laparoscopically in 83% of patients. The patients in this study were critically ill before surgery, as demonstrated by intensive care unit (ICU) admission (90%), mechanical ventilation (64%), vasopressor support (74%), mean white blood cell count of  $25.4 \times 10^9/L$  and a mean APACHE-II score of 29.7 at the time of surgical evaluation. Furthermore, this cohort included immunocompromised (45%) and elderly patients (mean age 65 yr). The authors compared the outcomes of the prospectively followed group to a historical control group of 42 consecutive patients with similar demographic characteristics and degree of critical illness who underwent total abdominal colectomy and an end ileostomy.

The primary outcome of the study was resolution of CDAD, as documented by resolution of symptoms (which was not defined by the authors) and normalization of leukocytosis. The secondary outcomes were mortality and morbidity. The authors reported “all patients who underwent diversion and lavage had resolution of leukocytosis and clinical signs of CDAD.” However, they did not explicitly report this outcome in the colectomy cohort. There was a single patient in whom recurrent *C. difficile* infection occurred, but it is not clear how the authors monitored the other patients for this outcome or whether follow-up was complete in all patients. The secondary outcome of mortality was reported in both groups: 8 of 42 (19%) in the ileostomy group versus 21 of 42 (50%) in the historic colectomy group ( $p = 0.006$ ).

This cohort study has numerous methodological weaknesses that could confound the outcomes and undermine

the validity of the findings. First, the authors did not report important information regarding the total number of hospitalized patients with diagnosed *C. difficile* colitis. There is evidence that high mortality in patients with CDAD is correlated to specific strains of *C. difficile* that result in higher rates of surgery and worse outcomes.<sup>1</sup> The NAP1 strain is known to be hypervirulent and has been associated with outbreaks.<sup>4</sup> Thus, it would be important to determine whether there was a difference in strain types between the case series and historical cases. Viral strain analysis would be ideal but is often not available. Information about the proportion of patients needing ICU admission related to the overall incidence of *C. difficile* infection would provide a surrogate for this information, but the authors did not report this information. Recent National Surgical Quality Improvement Program and meta-analysis data suggest 30%–40% mortality in patients treated with colectomy for CDAD, although the range includes the 50% that this group reports.<sup>5,6</sup> The authors themselves state that because this strategy is less invasive, they are using it earlier in patients with CDAD. Thus, while the 2 cohorts appear to be similar, there may be some differences in disease severity that account for the differences in outcome.

In addition, the temporal protocol change introduces bias related to cointerventions. There are few details about the perioperative management during the era in which colectomy was the procedure of choice. Were all patients treated with appropriate perioperative antibiotics? Were they treated with appropriate deep vein thrombosis prophylaxis? What were the indications for surgery? When was surgery performed in relation to the start of the patients' symptoms? The introduction of the protocol described by the authors includes regimented perioperative management that may have contributed substantially to the survival improvement. Furthermore, we don't know if there were patients in the colectomy era treated with segmental colectomy or other lesser surgeries. This might suggest that only

patients with the most dire clinical conditions were treated with colectomy, and this might not be the best comparison cohort.

Despite these limitations, the authors present compelling data that suggest a colon-preserving alternative to colectomy may be an effective option in patients with fulminant CDAD. In addition to the mortality benefits, the authors report a 79% rate of ileostomy reversal at 6 months. This compares favourably to the reported 20% gastrointestinal continuity restoration after colectomy.<sup>7</sup> Long-term follow-up in order to assess the rate of recurrent disease in this group of patients will be important to ensure that this approach has durability. The strategy has biologic plausibility, and further study via a randomized controlled trial is necessary before it replaces the current standard colectomy in patients with severe CDAD.

**Competing interests:** None declared.

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