Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Timing and type of surgical treatment of *Clostridium difficile*-associated disease: a practice management guideline from the Eastern Association for the Surgery of Trauma.

Bibliographic Source(s)

Ferrada P, Velopulos CG, Sultan S, Haut ER, Johnson E, Praba-Egge A, Enniss T, Dorion H, Martin ND, Bosarge P, Rushing A, Duane TM. Timing and type of surgical treatment of Clostridium difficile-associated disease: a practice management guideline from the Eastern Association for the Surgery of Trauma. J Trauma Acute Care Surg. 2014 Jun;76(6):1484-94. [59 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The strength of recommendation (strong or weak/conditional) and levels of evidence (high, moderate, low or very low) are defined at the end of the "Major Recommendations" field.

1. In adult patients with *Clostridium difficile*-associated disease (CDAD), the panel strongly recommends that patients undergo surgery early, that is, before the development of shock or the need for vasopressors. This recommendation is based on very low quality evidence but considers that individual patients will place a high value on the overall benefit (reduced mortality rates).
2. In adult patients with CDAD undergoing surgery, the panel conditionally recommends total or subtotal colectomy (vs. partial colectomy or other surgery). This recommendation is based on very low-quality evidence but places a high value on patient preferences for a definitive surgical intervention that may more effectively reduce mortality rates.

Definitions:

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Methodology Levels for Rating the Quality of Evidence

Quality Level	Definitions
High	Very confident that the true effect lies close to estimate of effect.

Quality Level	Definitions
Moderate	Moderate effect; true effect is likely close to estimate of effect but may be substantially different.
Low	Limited confidence; true effect may be substantially different from estimate of effect
Very Low	Little confidence; true effect likely substantially different from estimate of effect.

GRADE â€‹â€‹Definition of Strong and Weak Recommendation

	Strong Recommendation	Weak/Conditional Recommendation
For patients	Most patients would want the recommended course of action.	Most patients would want the recommended course of action, but many would not.
For clinicians	Most patients should receive the recommended course of action.	Different choices will exist for different patients, and clinicians should help patients decide.
For policy makers	Recommended course should be adopted as policy.	Considerable debate and stakeholder involvement needed to make policy.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Clostridium difficile-associated disease (CDAD)

Guideline Category

Management

Treatment

Clinical Specialty

Colon and Rectal Surgery

Gastroenterology

Infectious Diseases

Internal Medicine

Surgery

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide evidence-based recommendations that may be used to direct the decision-making processes related to the care of patients with severe *Clostridium difficile*-associated disease (CDAD) that may require surgical intervention
- To evaluate whether surgical timing (early vs. late) and type (total abdominal colectomy [TAC] vs. other surgical options) are associated with better outcomes in patients with severe CDAD

Target Population

Adult patients with *Clostridium difficile*-associated disease (CDAD)

Interventions and Practices Considered

1. Early surgery
2. Total or subtotal colectomy

Major Outcomes Considered

- Length of stay
- Intensive care unit (ICU) length of stay
- Cost
- Ventilator-free days
- Renal failure
- Respiratory failure

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Inclusion Criteria for This Review

Study Types

For the purpose of making recommendations, studies included randomized controlled trials, prospective observational or retrospective studies, and case control studies. Meta-analyses, case reports, letters, and reviews containing no original data or comments were excluded.

Participant Types

The panel included studies of adult patients without restricting sex, ethnicity, or degree of comorbidity. Only studies pertaining to the treatment of hospitalized patients with *Clostridium difficile*-associated disease (CDAD) were included. CDAD was defined as severe *Clostridium difficile* infection (CDI) resulting in clinical deterioration, such as multiorgan system failure, peritonitis, and/or sepsis as a consequence of the disease.

Intervention Type

The panel included studies in which total abdominal colectomy (TAC) or subtotal colectomy (each defined as removal of most of the colon excluding the rectum) was performed compared with other procedures such as segmental colectomy, exploratory laparotomy without colectomy, or ostomy formation.

Outcome Measure Types

Outcomes were chosen by the team and rated in importance from 1 to 9, with scores of 7 to 9 representing critical outcomes. The following outcomes were considered by the committee members: length of stay, intensive care unit (ICU) length of stay, cost, ventilator-free days, renal failure, and respiratory failure. However, all of these criteria were deemed noncritical for the decision-making process within the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. In addition, the available literature did not provide sufficient or consistent measurements across the studies, specifically if the onset of related conditions such as renal or respiratory failure occurred before or after surgical intervention. Only a reduction in mortality was deemed a critical outcome for the decision-making process, and this was chosen as the primary outcome measure.

Review Methods

Search Strategy

With the assistance of an information specialist, the panel conducted a systematic search of the PubMed, EMBASE, and Cochrane Library databases for studies published from 1992 to January 2014. The search used the following MeSH terms alone or in combination: *Clostridium difficile*, *colitis*, *colectomy*, *surgery*, and *mortality*. The panel used the "Related Articles" function to broaden the search and scan all citations for relevance. The panel used only articles available in English. In addition to the electronic search, they manually searched the bibliographies of recent reviews and articles.

Study Selection

After completing the literature search, two independent reviewers screened the titles and abstracts; any disagreement on inclusion was resolved through consensus. They excluded case reports and narrative review articles. The resulting studies were subjected to full-text review by two independent reviewers.

Results

The original search yielded 62 studies; after the elimination of studies that did not contain the original data, only 38 were deemed appropriate for full-text review. The panel further excluded six studies: one excluded study included a pediatric population, another was descriptive in nature, and four did not address the specific questions outlined in our review.

Number of Source Documents

32 studies were included in this guideline for recommendation. Of these articles, there were no randomized trials; two were prospective studies, while the remaining were retrospective (see Table 1 in the original guideline document).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Methodology Levels for Rating the Quality of Evidence

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Quality Level	Definitions
Low	Limited confidence; true effect may be substantially different from estimate of effect
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Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction and Management

Using a form developed by the team, two independent reviewers extracted data from the individual studies into Microsoft Excel, using double data entry for accuracy. They entered these data into Review Manager X.6 (Review Manager [RevMan][Computer program], Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012), including information on the authors, study number, country of origin, study methodology, population, intervention, and relevant outcome measures.

Methodological Quality Assessment

The articles were evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, which describes four levels of quality of evidence: high, moderate, low, and very low (see the "Rating Scheme for the Strength of the Evidence" field). Quality of evidence is reflected as the extent to which one can be confident that an estimate of effect is correct and includes an explicit consideration of the following domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The data were entered into GRADEpro for the generation of evidence tables.

Measures of Treatment Effect

The reviews reported the dichotomous outcome of mortality as a risk ratio (RR) with associated 95% confidence intervals (CIs) and *p* values since the baseline incidence of the primary outcome was thought to be relatively high in this population (>20%). The unit of analysis was individual patients.

Assessment of Heterogeneity

Potential heterogeneity exists because of population differences, different types of surgery performed, and how patients are defined. The workgroup examined these differences across studies to assess the clinical and methodological heterogeneity. For the meta-analysis, the reviewers used RevMan to calculate the Q statistic, and then the I^2 statistic (%) was used to determine the proportion of variation between studies attributable to heterogeneity and categorized as "low" (25%-49%), "moderate" (50%-74%), or "high" (74%-100%). They also used the x^2 test for heterogeneity and examined the CIs for overlap, with decreasing overlap representing increasing heterogeneity.

Data Synthesis (Meta-analysis)

The reviews performed a meta-analysis of the outcome of mortality rate for each population, intervention, comparison, and outcome (PICO) question by using the RevMan software. They used the DerSimonian and Laird random-effects model method because the included studies did not share a common effect size and unknown influential factors could vary across studies (unknown confounders). This allowed the reviewers to incorporate both the intrastudy and interstudy variability along a distribution of the "true" effects, which weighs larger and smaller studies more evenly. Potential heterogeneity across studies was assessed using the Q statistic, I^2 statistic (%), and x^2 test for heterogeneity. If heterogeneity was "moderate" to "high," they did not consider pooling the data; rather, they performed a qualitative narrative summary of the results only.

Sensitivity Analysis

The reviews conducted a sensitivity analysis for PICO Question 2 to investigate the implications of the ultimate surgery type performed compared with the first surgery since some patients underwent more than one procedure. A further analysis was performed to examine only those studies that reported their conversion rates from other procedures to total abdominal colectomy (TAC).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Recommendations are based on the overall quality of evidence with implicit consideration of the risk-benefit ratio and patients' values and preferences. Strong recommendations are prefaced by the statement "the panel strongly recommends," while weak recommendations are prefaced by the statement "the panel suggest" or "the panel conditionally recommend" as per the GRADE methodology (see the "Rating Scheme for the Strength of the Recommendations" field).

Rating Scheme for the Strength of the Recommendations

Grading of Recommendations Assessment Development, and Evaluation (GRADE) â€‹â€‹Definition of Strong and Weak Recommendation

	Strong Recommendation	Weak/Conditional Recommendation
For patients	Most patients would want the recommended course of action.	Most patients would want the recommended course of action, but many would not.
For clinicians	Most patients should receive the recommended course of action.	Different choices will exist for different patients, and clinicians should help patients decide.
For policy makers	Recommended course should be adopted as policy.	Considerable debate and stakeholder involvement needed to make policy.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

All authors participated in the critical review of all versions of the article.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with *Clostridium difficile*-associated disease (CDAD)

Potential Harms

Despite the overall quality of evidence being very low, the panel considered that most patients would place a high value on the potential 50% reduction in mortality and that the potential benefit outweighs any potential harm in performing surgery early.

Qualifying Statements

Qualifying Statements

- The Eastern Association for the Surgery of Trauma (EAST) is a multi-disciplinary professional society committed to improving the care of injured patients. The Ad hoc Committee for Practice Management Guideline Development of EAST develops and disseminates evidence-based information to increase the scientific knowledge needed to enhance patient and clinical decision-making, improve health care quality, and promote efficiency in the organization of public and private systems of health care delivery. Unless specifically stated otherwise, the opinions expressed and statements made in this publication reflect the authors' personal observations and do not imply endorsement by nor official policy of EAST.
- "Clinical practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."* These guidelines are not fixed protocols that must be followed, but are intended for health care professionals and providers to consider. While they identify and describe generally recommended courses of intervention, they are not presented as a substitute for the advice of a physician or other knowledgeable health care professional or provider. Individual patients may require different treatments from those specified in a given guideline. Guidelines are not entirely inclusive or exclusive of all methods of reasonable care that can obtain/produce the same results. While guidelines can be written that take into account variations in clinical settings, resources, or common patient characteristics, they cannot address the unique needs of each patient nor the combination of resources available to a particular community or health care professional or provider. Deviations from clinical practice guidelines may be justified by individual circumstances. Thus, guidelines must be applied based on individual patient needs using professional judgment.

* Institute of Medicine. Clinical practice guidelines: directions for a new program. MJ Field and KN Lohr (eds) Washington, DC: National Academy Press. 1990: pg 39.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

Ferrada P, Velopulos CG, Sultan S, Haut ER, Johnson E, Praba-Egge A, Enniss T, Dorion H, Martin ND, Bosarge P, Rushing A, Duane TM. Timing and type of surgical treatment of Clostridium difficile-associated disease: a practice management guideline from the Eastern Association for the Surgery of Trauma. J Trauma Acute Care Surg. 2014 Jun;76(6):1484-94. [59 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Jun

Guideline Developer(s)

Eastern Association for the Surgery of Trauma - Professional Association

Source(s) of Funding

Eastern Association for the Surgery of Trauma (EAST)

Guideline Committee

Eastern Association for the Surgery of Trauma (EAST) Practice Management Guidelines Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

The authors declare no conflicts of interest.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the Eastern Association for the Surgery of Trauma (EAST) Web site .

Print copies: Available from the Eastern Association for the Surgery of Trauma Guidelines, c/o Paula Ferrada, MD, VCU Surgery, Trauma, Critical Care and Emergency Surgery, West Hospital, 15th Floor, East Wing, 1200 E Broad St, Richmond, VA 23298, PO Box 980454, Richmond, VA 23298-0454; email: pferrada@mcvh-vcu.edu.

Availability of Companion Documents

The following is available:

- Kerwin AJ, Haut ER, Burns JB, Como JJ, Haider A, Stassen N, Dahm P, Eastern Association for the Surgery of Trauma Practice Management Guidelines Ad Hoc Committee. The Eastern Association of the Surgery of Trauma approach to practice management guideline development using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. J Trauma Acute Care Surg. 2012 Nov;73(5 Suppl 4):S283-7. Electronic copies: Available from the Eastern Association for the Surgery of Trauma (EAST) Web site .

In addition, a continuing medical education (CME) activity for this guideline is available in the original guideline document .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on February 13, 2015.

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