

AGA Clinical Practice Update on Medical Management of Colonic Diverticulitis: Expert Review.

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Authors: University of North Carolina, Chapel Hill, North Carolina. Electronic address: anne_peery@med.unc.edu.

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03 12 2020 2 2021 160 3 375275 906 911.e1 06 12 2020 01 02 2022 01 02 2022 13 02 2021 16 06 2024 This file is available for text mining. It may also be used consistent with the principles of fair use under the copyright law. Colonic diverticulitis is a painful gastrointestinal disease that recurs unpredictably and can lead to chronic gastrointestinal symptoms. Gastroenterologists commonly care for these patients. The purpose of this clinical practice update is to provide practical and evidence-based advice for diverticulitis management. We reviewed systematic reviews, meta-analyses, randomized controlled trials, and observational studies to develop 14 best practices. In brief, computed tomography is often necessary to make a diagnosis. Rarely, a colon malignancy is misdiagnosed as diverticulitis. Whether patients should have a colonoscopy after an episode depends on the patient's history, most recent colonoscopy, and disease severity and course. In patients with a history of diverticulitis and chronic symptoms, alternative diagnoses should be excluded with both imaging and lower endoscopy. Antibiotic treatment can be used selectively, rather than routinely, in immunocompetent patients with mild acute uncomplicated diverticulitis. Antibiotic treatment is strongly advised in immunocompromised patients. To reduce the risk of recurrence, patients should consume a high-quality diet, have a normal body mass index, be physically active, not smoke, and avoid nonsteroidal anti-inflammatory drug use except aspirin prescribed for secondary prevention of cardiovascular disease. At the same time, patients should understand that genetic factors also contribute to diverticulitis risk. Patients should be educated that the risk of complicated diverticulitis is highest with the first presentation. An elective segmental resection should not be advised based on the number of episodes. Instead, a discussion of elective segmental resection should be personalized to consider severity of disease, patient preferences and values, as well as risks and benefits.

Colonic diverticulitis is a common gastrointestinal disease. Annually, in the United States (US), there are more than 1.9 million outpatient visits and 208,000 inpatient admissions for diverticulitis at a cost \$5.5 billion dollars. 1 The incidence of diverticulitis in the U.S. is 180/100,000 persons per

year. 2 While diverticulitis is most common in older adults, the relative increase in diverticulitis in recent decades has been greatest in younger adults. The incidence of diverticulitis in individuals 40–49 years old increased by 132% from 1980 through 2007. 2

Diverticulitis can be uncomplicated or complicated. Uncomplicated diverticulitis involves thickening of the colon wall and peri-colonic inflammatory changes. Complicated diverticulitis additionally includes the presence of abscess, peritonitis, obstruction, stricture and/or fistula. Only 12% of patients with diverticulitis present with complicated disease. 3 , 4 The most common complication is phlegmon or abscess followed by peritonitis, obstruction, stricture and fistula. 3 , 4 While the majority of individuals recover from an episode of acute uncomplicated diverticulitis, approximately 5% individuals will experience smoldering diverticulitis, characterized by abdominal pain and continued evidence of inflammation on CT scan. 5 , 6 Smoldering diverticulitis is a distinct diagnosis from segmental colitis associated with diverticular disease (SCAD). SCAD is a rare diagnosis characterized by diverticular colitis that spares the rectum. SCAD is likely on the spectrum of inflammatory bowel diseases. 7

The purpose of this American Gastroenterological Association (AGA) Clinical Practice Update (CPU) Expert Review is to provide practical and evidence-based advice for the clinicians who care for patients with diverticulitis. We reviewed systematic reviews, meta-analyses, randomized controlled trials, and observational studies to develop 14 best practices. This expert review was commissioned and approved by the AGA Institute Clinical Practice Updates Committee (CPUC) and the AGA Governing Board to provide guidance on a topic of clinical importance to the AGA membership, and underwent internal peer review by the CPUC and external peer review through standard procedures of Gastroenterology .

Computed tomography should be considered to confirm the diagnosis of diverticulitis in patients without a prior imaging-confirmed diagnosis and to evaluate for potential complications in patients with severe presentations. Imaging should also be considered in those who fail to improve with therapy, are immunocompromised, or who have multiple recurrences and are contemplating prophylactic surgery in order to confirm the diagnosis and location(s) of disease.

Abdominal pain, usually acute or subacute in onset and located in the left lower quadrant, is the most common presenting symptom. Other presenting signs and symptoms include fever, change in bowel habits, nausea without vomiting and an elevated white blood cell count and/or C-reactive protein (CRP). However, these features are not specific for diverticulitis. Clinical suspicion of diverticulitis alone is correct in only 40–65% of patients. 8 , 9 CT scan of the abdomen and pelvis with oral and intravenous contrast is highly accurate for diagnosing diverticulitis (sensitivity/specificity 95%) (Figure 1). 10 Abdominal ultrasonography is an alternative that avoids contrast and radiation exposure, but it is operator dependent and more frequently utilized in Europe. Magnetic Resonance Imaging is very sensitive but less specific than CT and is generally not used in the acute setting. 11 Plain radiographs cannot be used to confirm the diagnosis but are useful in assessing for complications such as perforation or obstruction.

Whether patients should have a colonoscopy after an episode of diverticulitis depends on the patient's history, most recent colonoscopy, and disease severity and course. Colonoscopy is advised after an episode of complicated diverticulitis and after a first episode of uncomplicated diverticulitis but may be deferred if a recent (within 1 year) high-quality colonoscopy was performed.

After an acute episode of diverticulitis colonoscopy should be delayed by 6–8 weeks or until complete resolution of the acute symptoms, whichever is longer. Colonoscopy should be considered sooner if alarm symptoms are present.

A malignancy can be misdiagnosed as diverticulitis. Colonoscopy after an episode of diverticulitis depends on the patient's history, most recent colonoscopy, and course of the disease (Figure 1). In a meta-analysis of 31 studies and 50,445 patients, the pooled prevalence of colon cancer was

1.9% among patients with diverticulitis. 12 The risk of colon cancer was higher in patients with complicated diverticulitis (7.9%) compared with patients with uncomplicated diverticulitis (1.3%). The prevalence of advanced adenomas was 4.4% and adenomas 14.2% among those who underwent lower endoscopy. In a randomized trial of comparing observation to antibiotic treatment for uncomplicated diverticulitis, 1.2% patients were diagnosed with colon cancer within 3 months of randomization. 6 Based on this evidence, colonoscopy is advised after an episode of complicated diverticulitis and after a first episode of uncomplicated diverticulitis but may be deferred if a recent (within 1 year) high-quality colonoscopy was performed and there were no findings warranting short interval follow up. Patients with recurrent uncomplicated diverticulitis should follow routine colorectal cancer screening and surveillance intervals unless alarm symptoms are present. Alarm symptoms include change in stool caliber, iron deficiency anemia, blood in stool, weight loss, and abdominal pain. During the recovery period after an episode of acute diverticulitis, colonoscopy theoretically increases the risk of perforation, is more technically difficult, and patients can experience more discomfort. Therefore, colonoscopy should be delayed 6 to 8 weeks unless alarm symptoms are present.

In patients with a history of diverticulitis and chronic symptoms, ongoing inflammation should be excluded with both imaging and lower endoscopy. If there is no evidence of diverticulitis, visceral hypersensitivity should be considered and managed accordingly.

Ongoing gastrointestinal symptoms are common after an episode of acute diverticulitis. Periodic abdominal pain was reported by ~45% of patients at 1-year follow up in a trial of acute uncomplicated diverticulitis. 13 While visceral hypersensitivity is the likely cause in the majority of cases, ongoing diverticular inflammation, a diverticular stricture or fistula, and alternative diagnoses like ischemic colitis, constipation, and inflammatory bowel disease should be excluded with both imaging (CT scan abdomen/pelvic with oral and intravenous contrast) and lower endoscopy. In our practice, patients are reassured to know that ongoing symptoms are common and often attributable to visceral hypersensitivity. This conversation is particularly important after a negative work up. If needed, ongoing abdominal pain can be treated with a low to modest dose of a tricyclic antidepressant. 14

A clear liquid diet is advised during the acute phase of uncomplicated diverticulitis. Diet should advance as symptoms improve.

Patients with acute uncomplicated diverticulitis commonly present with anorexia and malaise. While a small study suggests that a liquid diet is not necessary in the acute phase of diverticulitis, many patients report greater comfort on a clear liquid diet. 15 This is potentially because diverticulitis can cause a mechanical obstruction and/or may be secondary to the systemic inflammation associated with this disease. It is reasonable to advise a clear diet during the acute phase of uncomplicated diverticulitis with the goal of patient comfort. Some patients want to advance their diet more quickly and that is also acceptable. If a patient is unable to advance their diet after 3–5 days, they should follow up immediately.

Antibiotic treatment can be used selectively, rather than routinely, in immunocompetent patients with mild uncomplicated diverticulitis.

Antibiotic treatment is advised in patients with uncomplicated diverticulitis who have comorbidities or are frail, who present with refractory symptoms or vomiting, or who have a CRP >140 mg/L or baseline white blood cell count > 15 × 10⁹ cells per liter. Antibiotic treatment is advised in patients with complicated diverticulitis or uncomplicated diverticulitis with a fluid collection or longer segment of inflammation on CT scan.

Guidelines recommend antibiotics be used selectively, rather than routinely, in patients with acute uncomplicated diverticulitis (Figure 1). 16 – 19 While antibiotics have long been first-line therapy for acute uncomplicated diverticulitis, recent evidence suggests there is no benefit in

immunocompetent patients with mild acute uncomplicated diverticulitis. In a systematic review and meta-analysis of 9 studies that included 2,505 patients with acute uncomplicated diverticulitis, there was no difference in time to resolution or risk of readmission, progression to a complication, or need for surgery among patients treated with antibiotics compared to those not treated with antibiotics. 20 Importantly, these studies were limited to immunocompetent patients without evidence of sepsis.

Patients who are immunocompromised are high risk for complications and should be treated with antibiotics. Likewise, antibiotics are mandatory for the treatment of diverticulitis complicated by evidence for systemic inflammation, abscess, perforation, or obstruction. Among patients with acute uncomplicated diverticulitis, the risk of progression to complicated diverticulitis is 5%. 21 Risk factors for progression include baseline ASA score III or IV, duration of symptoms longer than 5 days prior to presentation, presence of vomiting, CRP >140 mg/L, and baseline white blood cell count > 15×10^9 cells per liter. 21 The presence of a fluid collection or longer segment of inflammation on baseline CT (86 mm versus 65mm) is also associated with an increased risk of progression to complicated diverticulitis. 22 Therefore, patients with one of these factors should be considered high risk and treated with a course of antibiotics.

When antibiotic treatment is necessary, the regimen usually includes broad spectrum agents with gram-negative and anaerobic coverage. In the outpatient setting, treatment of mild uncomplicated diverticulitis most commonly includes either a combination of an oral fluoroquinolone and metronidazole or monotherapy with oral amoxicillin-clavulanate. 23 – 25 The duration of treatment is usually 4–7 days but can be longer. In our practice, duration of therapy is based on general health status, immune status, severity of presentation, CT findings, and patient expectations. Antibiotic regimens for diverticulitis in the inpatient setting are numerous and well described. 23 , 24

Immunocompromised patients are more likely to present with severe or complicated disease. For these patients there should be a low threshold for cross sectional imaging, antibiotic treatment, and consultation with a colorectal surgeon.

Corticosteroid use is a risk factor for diverticulitis and may contribute to complications including perforation and death. 26 – 29 This is also the case for other forms of immunosuppression such as chemotherapy and the regimens used for organ transplant although the risks are less well-defined. 28 Patients with an impaired immune system and diverticulitis can present with milder signs and symptoms compared to an immunocompetent patient. Therefore, computed tomography should be considered to make a diagnosis and to rule out complications. Patients with uncomplicated diverticulitis who are immunosuppressed are high risk for progression to complicated diverticulitis and/or sepsis and should be treated with antibiotics. The antibiotic regimen usually includes broad spectrum agents with gram-negative and anaerobic coverage with a longer duration of treatment (10–14 days). After recovery from an episode of diverticulitis successfully managed without surgery, a patient who is chronically immunosuppressed should consult with a colorectal surgeon to discuss elective resection. 17 – 19

To reduce the risk of recurrence, patients with a history of diverticulitis should consume a high-quality diet, achieve or maintain a normal body mass index, routinely be physically active, and not smoke. Additionally, patients with a history of diverticulitis should avoid regular use (≥ 2 times per week) of nonsteroidal anti-inflammatory drugs except aspirin prescribed for secondary prevention of cardiovascular disease.

Patients should understand that approximately 50% of the risk for diverticulitis is attributable to genetic factors.

Identified risk factors for incident diverticulitis fall into several broad categories – diet, lifestyle, medications and genetics (Figure 1). 30 A prudent dietary pattern (high in fiber from fruits, vegetables, whole grains and legumes and low in red meat and sweets) and a vegetarian diet are associated with decreased risk of incident diverticulitis. 31 A fiber supplement is not a replacement

for a high-quality diet. Nut, corn, and popcorn consumption is not associated with an increased risk of diverticulitis. 32 Similarly, consuming fruits with small seeds (strawberries and blueberries) is not associated with diverticulitis risk. 32 Physical activity, particularly when it is vigorous, decreases risk. 33 Obesity, particularly central obesity, weight gain and smoking are also risk factors. 34 , 35 Alcoholism, but not alcohol consumption by itself, increases risk as well. Regular use of nonsteroidal anti-inflammatory drugs (NSAIDs) increases the risk of diverticulitis; the risk is greater for non-aspirin NSAIDs than for aspirin. 36 Opiate analgesics, like corticosteroids, are associated with diverticulitis and perforation. 26 Menopausal hormone therapy is associated with increased risk, but the risk is not dependent on dose or duration. 37

Genetics also play a central role in determining the risk of diverticulitis. 38 Twin and sibling studies indicate that 40–50% of the risk for diverticulitis is attributed to genetic effects. 39 , 40 The risk is three times higher for siblings of cases versus the general population and higher in monozygotic twins than dizygotic twins. 40 Genome-wide association studies (GWAS) have identified over 30 susceptibility loci for diverticular disease. 41 – 43 Of these, four have stronger effects for diverticulitis than diverticulosis or non-specific diverticular disease including PHGR1, FAM155A, CALCB and S100A10 . Genes implicated in diverticular disease are important for immunity, cell adhesion, connective tissue integrity, membrane transport, and smooth muscle function.

Patients with a history of diverticulitis should not be treated with 5-aminosalicylic acid, probiotics, or rifaximin to prevent recurrent diverticulitis.

While patients understandably seek nonoperative therapy to prevent recurrent diverticulitis, there is nothing yet to offer these patients. In a meta-analysis of seven randomized controlled trials, there was no benefit when comparing 5-aminosalicylic acid compared to control for prevention of recurrent diverticulitis. 44 There is insufficient evidence to support the use of any probiotic or cyclic rifaximin to prevent diverticulitis. 45 , 46

Patients should be educated that complicated diverticulitis is most often the first presentation of diverticulitis. The risk of complicated diverticulitis decreases with recurrences.

The complications from diverticulitis, with the exception of fistula formation, occur more commonly with the first episode of diverticulitis than with subsequent episodes (Figure 1). Fistulizing disease from diverticulitis is relatively rare. 47 In a population-based cohort study, patients with a history of recurrent diverticulitis had a reduced risk of complicated diverticulitis (OR 0.78, 95% CI 0.62–0.98) compared to patients with no history of diverticulitis. 47 In another population-based cohort study, among 386 patients with complicated diverticulitis, 286 (74%) had no history of prior diverticulitis. 2

Individuals with diverticulitis are at risk of recurrence, with approximately 20% having one or more recurrent episodes within 10 years. 2 Approximately 8% of patients with incident disease have recurrences within the first year after complete recovery from the incident episode, and 20% have recurrences within 10 years. The risk of recurrence increases with subsequent episodes. After a second episode, the risk is 18% at 1 year and 55% at 10 years, and after a third episode it is 40% at 3 years. 2 The risk of recurrence is higher in patients with a history of complicated diverticulitis successfully treated without surgery compared to patients with a history of uncomplicated diverticulitis. In a large retrospective cohort study, the risk of diverticulitis recurrence was 25% within 5 years following an episode with an abscess successfully managed without surgery. 48

An elective segmental resection should not be advised based on the number of diverticulitis episodes.

A discussion of elective segmental resection for patients with a history of diverticulitis should be personalized to consider severity of disease, patient preferences and values, as well as risks and benefits including quality of life. Patients should understand that surgery reduces, but does not eliminate, diverticulitis risk and that chronic gastrointestinal symptoms do not always improve with

surgery.

An elective segmental resection should not be advised based on the number of diverticulitis episodes (Figure 1). With a few exceptions, new surgical guidelines recommend a more case-by-case approach. 17 – 19 Despite a more conservative approach, rates of elective surgery have continued to increase in the US. 49 The decision to recommend elective resection should include a discussion of the patient's comorbidities (i.e. immune status), severity of diverticulitis (i.e. abscess or not), patient preferences and values, as well as operative risks and benefits. 17 – 19

Colectomy should not be advised to an immunocompetent patient with a history of recurrent uncomplicated diverticulitis to prevent complicated diverticulitis. In this population, complicated diverticulitis is most often the first presentation of diverticulitis and is less likely with recurrences. The benefit of an elective segmental colectomy is a reduced risk of recurrent diverticulitis. Surgery may also improve a patient's quality of life. 50 , 51 In patients with recurrent diverticulitis or ongoing symptoms, elective resection resulted in improved quality of life at 5-year follow-up compared to conservative management. 51

Elective segmental colectomy reduces, but does not eliminate, diverticulitis risk. At 5-year follow up, the rate of recurrent diverticulitis was 15% in patients who had elective surgery compared to 61% in patients managed non-operatively. 52 While ongoing symptoms after recovery from acute diverticulitis are common, colectomy often does not improve these symptoms. 53 , 54 In two studies, 22–25% of patients continued to have ongoing abdominal pain after surgery. 53 , 54

Patients with a history of complicated diverticulitis successfully managed without surgery are at increased risk of recurrence and complicated recurrence. While some guidelines recommended interval elective resection, there is a growing literature suggesting a more conservative and personalized approach to these patients. 17 – 19 In an observational study, long-term rates of emergency surgery and/or death were low (5%) among patients after an episode of complicated diverticulitis successfully managed without surgery. 55 Elective resection was not associated with reduced rates of emergency surgery or death.

After recovery from an episode of acute diverticulitis successfully managed without surgery, a patient who is chronically immunosuppressed should consult with a colorectal surgeon. 17 – 19 This population is high risk for complicated recurrence and the goal of surgery is to prevent complicated diverticulitis.

Colonic diverticulitis is a painful disease that occurs unpredictably. While the majority of patients never experience a perforation or abscess, uncomplicated recurrences are a burden to patients. Patients often blame themselves for episodes and worry about recurrence, perforation, and need for surgery. Gastroenterologists can alleviate many of these concerns by making an accurate diagnosis, addressing chronic sequelae, and educating patients on risk factors, prognosis, and indications for surgery. While the advice in this document is based on low to moderate quality evidence, research is ongoing and has the potential to eventually identify better options for diverticulitis treatment and prevention.

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1642 . 30354951 10.1056/NEJMcp1800468 Figure 1. A step-wise approach to the diagnosis and management of acute uncomplicated diverticulitis.