

# Evaluation and Medical Management of Uncomplicated Diverticulitis

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## Abstract

### Keywords

- ▶ uncomplicated diverticulitis
- ▶ diverticulitis
- ▶ medical management
- ▶ mesalamine
- ▶ probiotics

Uncomplicated diverticulitis is common, and its evaluation and treatment have evolved over time. Most patients present in a nontoxic manner with localized pain, leukocytosis, and reliable findings on computed tomography (CT). Healthy and stable patients are typically treated in the outpatient setting with very high rates of success. Recently, the necessity of antibiotic therapy has come into question, and several alternative agents have emerged, with the jury still out on their relative roles in diverticular disease. Currently, colonoscopy is still recommended after the resolution of an index episode of uncomplicated diverticulitis, and recurrence rates remain low. Several diet and lifestyle modifications have been shown to impact the rates of diverticulitis recurrence.

Diverticulosis is a common finding in the western world, affecting 40% of patients by the age of 60 years and up to 70% of patients over 80 years or older.<sup>1,2</sup> Roughly 20% of these patients will develop diverticulitis,<sup>3</sup> with significant variation in the severity of their symptoms and the associated disability. As a medical community, our understanding of diverticulitis continues to evolve, and treatment strategies have changed dramatically over time. This is partly due to a growing body of high-quality literature, which allows the surgeon to practice in a manner that is well aligned with the available evidence.

The most significant shifts in diverticulitis care are the increase in nonoperative management in the acute care setting<sup>4</sup> and the increased threshold for recurrent attacks prior to a recommendation for elective colectomy.<sup>3</sup> This study focuses on the evaluation and medical management of acute uncomplicated diverticulitis (UD). It includes a discussion of current standards as well as areas of ongoing research.

## Definitions: Complicated versus Uncomplicated Disease

A meaningful discussion of diverticulitis must start with clear definitions of commonly used terminology. Complicated diverticulitis refers to acute episodes that are associated

with (1) free perforation and associated peritonitis, (2) pelvic abscess requiring surgery or percutaneous drainage, (3) fistula to adjacent organs including the small bowel, bladder, vagina, or skin, and (4) large bowel obstruction (LBO) and/or colonic stricture.<sup>2,5</sup>

UD is more common and typically refers to episodes of localized abdominal pain associated with leukocytosis and inflammation of the sigmoid colon on computed tomography (CT).<sup>2</sup> Patients with microperforations and small paracolic abscesses on CT scan are typically considered to be uncomplicated as well.

Perhaps more difficult to define are episodes that occur in immunocompromised patients and moderately sized paracolic abscesses. A discussion of these special situations is reserved for another study.

## Clinical Manifestations

Patients with acute UD can seek treatment in several locations, including the office and the emergency room. Many patients with a known history of diverticulitis will seek treatment over the phone as well. Signs and symptoms of diverticulitis can vary based on the severity of illness. Patients with uncomplicated disease frequently report localized abdominal pain, which usually occurs in the left

lower quadrant but can occasionally be present on the contralateral side in patients with mobile and floppy sigmoid colons. Patients may also report fevers, chills, and anorexia, although nausea and emesis are less common.<sup>2,6</sup>

Urinary complaints including dysuria and urgency can also be present. Changes in bowel habits do occur, with stools being looser or thinner than normal, and patients occasionally reporting severe constipation. Of note, hematochezia is very uncommon in diverticulitis, and the presence of significant bleeding should warn the clinician that alternative diagnoses are likely.<sup>2</sup>

On physical examination, patients with uncomplicated disease will typically appear nontoxic, demonstrating localized abdominal tenderness. Left lower quadrant guarding may be present, but diffuse pain and other signs of peritonitis should be absent. Some abdominal distention can be present due to ileus or partial LBO. The astute clinician may be able to appreciate an abdominal mass on deep palpation related to the sigmoid phlegmon, but this finding is often limited to thin patients and is unreliable.

Laboratory values may vary, but most patients will have some degree of leukocytosis. Inflammatory markers such as C-reactive protein and procalcitonin may also be elevated but have little utility in the work-up of uncomplicated disease. Other laboratory values are typically normal but may still be warranted to assess for dehydration, electrolyte abnormalities, and pregnancy prior to CT.

## Diagnostic Evaluation

### Imaging

Several imaging modalities have been employed over the years, including plain X-rays, ultrasonography, and magnetic resonance imaging (MRI). However, these have little utility in the routine patient, and a CT abdomen/pelvis with oral and intravenous (IV) contrast should instead be employed. CT scan has a sensitivity and specificity of 98% and 99%, respectively, for diverticulitis,<sup>3</sup> and allows not only for an assessment of the severity of disease but also for the identification of alternative or concomitant intra-abdominal pathology.

In uncomplicated disease, CT will typically demonstrate sigmoid wall thickening as well as inflammation of the surrounding tissues with fat stranding. There may also be a small amount of pericolic air suggesting microperforation. These findings along with a benign abdominal examination usually suggest that the patient's disease will follow a straightforward clinical course.

Repeat CT scans may be employed acutely when patients have increased pain, worsening signs of sepsis or LBO, or a failure to progress, as the patient may have a more complicated disease than originally determined, including the presence of a developing pelvic abscess. Repeat CT scans may also be employed for subsequent attacks when the surgeon believes that the subsequent presentation is more severe, or if documentation of recurrent attacks will impact the long-term care plan.

### Endoscopy

Flexible endoscopy during an acute attack of diverticulitis is not necessary to make a diagnosis and is unlikely to impact the treatment plan. Additionally, the inflamed nature of the colon may predispose patients to endoscopy-induced perforations. Therefore, colonoscopy during an acute attack should be avoided if possible.

The traditional approach to diverticulitis includes a total colonoscopy six or more weeks after an acute attack. This has the purpose of confirming the diagnosis of diverticulitis while excluding other diseases that may have similar presentations and radiographic findings, such as ischemia, inflammatory colidites, and cancer. It also allows for the identification of ongoing inflammation or complications of diverticulitis such as colonic strictures.

However, this convention has been recently challenged. The classical teaching that cancer can clinically mimic diverticulitis was based on historical data that predated modern imaging. CT scans have become much more accurate in recent years, and therefore older concerns may be unfounded. For example, older studies evaluating 4- and 8-slice CT scans demonstrated 94% sensitivity and 99% specificity for diverticulitis.<sup>7</sup> Now that most hospitals use 16- and 32-slice CT scanners, misidentification of colonic malignancies may not be an ongoing concern.

The literature still supports follow-up colonoscopy for patients who had complicated disease, suspicious findings on CT including irregular wall thickening, and worrisome associated symptoms such as changes in bowel habits and hematochezia, and patients who would otherwise qualify for colon cancer screening based on age and risk factors. However, for patients with uncomplicated disease and the absence of other indications, several recent studies have focused on the utility of colonoscopy. Navigating through these numerous studies, big and small, is quite time-consuming, but, in general, they conclude that routine colonoscopy is unnecessary.<sup>8-12</sup>

One of the more comprehensive studies was a 2014 systematic review that evaluated 1,796 colonoscopies performed after UD.<sup>13</sup> They reported that 20.2% of patients had colonic polyps, with an adenoma detection rate of 14%. Overall, 3.6% of patients had an advanced adenoma (AA) and 1.6% had a colorectal cancer (CRC). This translates to a pooled prevalence of AA and CRC of 4.9%, with a range of 3.4 to 6% within the included studies. Since the general public has a pooled prevalence of 5 to 10%, the authors concluded that routine colonoscopy was not warranted after UD.

Among ongoing controversy, 2014 the American Society of Colon and Rectal Surgeons (ASCRS) practice parameters for diverticulitis still recommend colonoscopy after resolution of a patient's first episode of diverticulitis.<sup>3</sup> It is important to point out that colonoscopy is not used solely to distinguish diverticulitis from cancer, and, as previously mentioned, other pathologies such as ischemia, strictures, inflammatory bowel disease, and incidental right-sided lesions are still important to identify when present. It is unlikely that there will be a widespread change in practice

unless higher quality evidence from prospective studies becomes available.

## Treatment

The acute management of UD rarely involves surgery, and there is little debate about the efficacy of nonoperative management in the acute setting. Instead, ongoing discussions focus on (1) where to treat the patient (inpatient vs. outpatient), (2) how to treat the patient (observation vs. antibiotics vs. alternative agents), and (3) how long to treat the patient.

### Outpatient versus Inpatient

The traditional approach to acute UD involved inpatient admission, bowel rest, IV fluids, and IV antibiotics. Such an aggressive approach is not usually necessary in modern medicine, and outpatient management is currently three times more common than inpatient management.<sup>14</sup> While retrospective studies should be interpreted with caution due to variations in the work-up, definition, and severity of acute UD, there are several recent high-quality studies showing outpatient management of acute UD to be safe and effective. Outpatient therapy typically includes diet as tolerated, oral rehydration, and oral antibiotics, and has been shown to be successful in 94 to 97% of patients, with an associated cost savings of 35 to 83%.<sup>14–17</sup>

Despite the efficacy of outpatient management, there are still some patients who will require hospitalization. In general, inpatient management is appropriate for patients who have significant comorbidities and/or frailty or those who have an insufficient support structure at home. Additionally, patients who have nausea and oral intolerance may become significantly dehydrated and require admission for supportive care. There are also patients with an unclear clinical picture who will require serial abdominal examinations prior to determining that their disease will run a benign course.

### Antibiotics

The conventional approach to acute UD includes oral or IV antibiotics aimed at the colonic flora. Common IV agents include piperacillin-tazobactam, carbapenems such as meropenem and ertapenem, and third-generation cephalosporins. Common oral agents include amoxicillin-clavulanate and dual therapy with fluoroquinolone (e.g., ciprofloxacin or levofloxacin) and metronidazole. All of these antibiotics have side effects but are generally well tolerated.

The necessary duration of antibiotics therapy is not well studied, and clear guidelines do not exist. As a result, the clinician's choice is often arbitrary, focusing on a number that is a multiple of 5 or 7. A 2010 randomized controlled trial (RCT) did conclude that 4 days of IV ertapenem was just as effective as 7 days,<sup>18</sup> but a few studies focus on outpatient oral therapy. In general, it is safe to stop antibiotics once the patient's symptoms have resolved.

When patients have unresolving or worsening symptoms despite antibiotics, it is appropriate to consider a change or

escalation in therapy, as well as repeat imaging to exclude disease progression and/or abscess.

### No Antibiotics

Microperforation and infection have long been thought to cause diverticulitis, and antibiotic therapy has been a surgical dogma. However, new theories have emerged regarding the pathophysiology of acute UD, which will be discussed in detail below, that have led experts to question the need for antibiotics in acute UD. Several small, heterogeneous studies emerged from Europe within the past 10 years, but perhaps the most influential work has come from the AVOD group ("Antibiotika Vid Okomplicerad Divertikulit," which is Swedish for "antibiotics in uncomplicated diverticulitis"<sup>19</sup>).

In 2012, the AVOD study group published a multicenter, RCT involving 623 patients with acute UD. In this study, the control arm involved inpatient admission with IV antibiotics for 7 days, whereas the intervention arm received inpatient admission, IV fluids, and no antibiotics. The authors found that there was no significant difference between the two groups for treatment failure, pain, progression to complicated disease, length of hospital stay, or diverticulitis recurrence at 1 year. They concluded that antibiotic therapy "neither accelerates recovery nor prevents complications or recurrence."<sup>19</sup>

This 2012 study included 10 centers and occurred over 7 years, suggesting issues with patient accrual and possible selection bias. It also involved inpatient admission for both groups, which is rarely done in the United States. However, the same authors went on to publish a 2015 prospective case series with improved patient accrual that focused on outpatient management of UD without antibiotics.<sup>20</sup> In this series of 155 patients, patients were diagnosed with acute UD based on examination and CT findings and then discharged home from the emergency room with instructions for oral rehydration and the use of oral acetaminophen, as needed, for pain. This approach was successful in 97.4% of patients, with the other 2.6% requiring eventual inpatient admission and antibiotics, but no patients requiring emergent surgery.

The most recent study on this topic was the DIABOLO trial, a 2017 multicenter RCT involved 22 clinical sites in the Netherlands, which focused on patients with an index episode of acute left-sided UD.<sup>21</sup> This study randomized 528 patients to observation versus 10 days of antibiotics. The majority of patients in both groups were admitted to the hospital, although 13% of the observation group were treated as outpatients. At 6 months of follow-up, there was no significant difference between the two groups in terms of success rate, time to recovery, abdominal pain, complications, disease recurrence, or need for sigmoid colectomy.

In summary, oral antibiotics in the outpatient management of acute UD are well tolerated but they may not be necessary. Well-designed European studies have shown that omission of antibiotics is safe in select patients, and, when successful, these patients will have similar rates of disease recurrence compared with those who receive antibiotics. However, the ASCRS still recommends antibiotics for patients with UD,<sup>3</sup> and the nonantibiotic approach has not gained widespread acceptance in the United States.

## Alternative Agents

As briefly mentioned previously, the pathophysiology of diverticulitis has conventionally focused on microperforation and infection, but recently this has been called into question, and research has demonstrated that diverticulitis may be a primary inflammatory process similar to ulcerative colitis and Crohn's disease.<sup>2,3,22,23</sup> While this question remains unanswered, there has been increased focus in recent years on alternative therapies, including probiotics and anti-inflammatory medications, to treat acute diverticulitis as well as maintain remission after an attack.

Aminosalicylates (also known as 5-ASA, mesalamine, mesalazine) have been extensively studied in the treatment of inflammatory bowel disease, and recent studies have expanded to include the treatment of diverticulitis. Unfortunately, many of these studies had a seemingly loose definition of UD, basing it mostly on symptoms rather than endoscopy or CT findings.<sup>24,25</sup> Additionally, authors frequently mixed UD with the clinical condition of symptomatic uncomplicated diverticular disease, which is a term used mostly by the gastroenterology community to describe a milder and more indolent disease.

Currently, there are no meaningful data regarding the efficacy of mesalamine as a monotherapy for acute UD, but there are studies that evaluated mesalamine in combination with oral antibiotics for UD and found improved resolution of symptoms compared with antibiotics alone.<sup>24,25</sup> Daily scheduled mesalamine has also been shown to help prevent recurrent diverticular symptoms. Because of study heterogeneity, the role of aminosalicylates in the treatment of acute UD and the prevention of recurrent UD remains undefined.

Recent years have seen increased research on the human microbiome, and some believe that an altered fecal microbiota may be associated with diverticulitis, although it is unclear if this phenomenon is cause or effect.<sup>2</sup> With this in mind, probiotics have been studied for the prevention of recurrent diverticulitis after resolution of acute symptoms. A 2004 randomized trial focused on patients with recurrent diverticulitis (two or more previous episodes) and found that probiotic therapy was associated with decreased symptoms such as bloating and pain but no difference in rates of recurrent diverticulitis.<sup>26</sup>

## Diverticulitis Recurrence

### Recurrence Rates

Rates and severity of diverticulitis recurrence will be discussed in greater detail in another study of this volume. However, it should be briefly mentioned that rates were likely overestimated in the past due to loose definitions of diverticulitis and lack of confirmatory CT scans. Most modern series report that 13 to 34% of patients with UD will experience a second episode of diverticulitis in the future and 5 to 12% will develop more than one recurrence.<sup>5,27-29</sup>

As one looks further into the natural history of diverticulitis recurrence, it becomes evident that diverticulitis is not a progressive disease, and the first attack is usually the worst attack, with the severity of subsequent attacks mimicking

the initial episode, with only 4 to 5% of patients progressing to a complicated recurrence.<sup>5</sup>

### Prevention of Recurrence

Several lifestyle modifications have been studied to determine if they impact the rates of diverticulitis recurrence. In particular, diet modification has been a focus. High-residue foods such as nuts, seeds, and popcorn were traditionally avoided by patients at the instruction of their primary care doctor, as these small kernels were thought to cause mucosal trauma and become impacted in diverticuli, predisposing the patient to inflammation and perforation. However, there has never been any evidence to support this theory, and a landmark 2008 population study challenged conventional teachings by looking at almost 50,000 men with 18 years of follow-up.<sup>30</sup> The authors determined that nut, seed, and popcorn consumption did not increase the risk of diverticulosis or diverticulitis, and intake was instead found to be inversely correlated.

While popcorn is now known to be safe, other diet factors do seem to impact diverticular disease, and vegetarians have been shown to have lower rates of diverticulitis than meat-eaters (relative risk = 0.69).<sup>31</sup> Fiber intake has been extensively studied with conflicting results, but most population studies show lower rates of diverticulitis in patients with a high-fiber diet.<sup>2,32</sup> However, it is unclear if a transition to a high-fiber diet after an episode of diverticulitis will help to prevent recurrence.

Cigarette smoking is associated with an increased incidence of diverticulitis, as well as an increased risk of complicated disease,<sup>33,34</sup> but smoking cessation does not necessarily prevent diverticulitis recurrence. Obesity has also been linked with diverticulitis,<sup>2,22,35-38</sup> and exercise has been associated with a decreased risk<sup>22,39,40</sup>; therefore, physical activity certainly plays a partial role in diverticular disease.

## Conclusion

The evaluation of UD has become more linear and evidence-based over time. Additionally, it is now known that nonoperative management, typically in the outpatient setting, is safe and effective. In the future, antibiotics may play a smaller role in the treatment of UD, whereas alternative agents become more prominent.

Dr. Mark Ravitch (1910–1989) is credited with first saying that “textbooks of a previous generation were as large as the textbooks of today, but contained a different body of misinformation.”<sup>41</sup> This quote certainly applies to the evolving treatment of diverticular disease. It is likely that treatment will continue to change over time as higher levels of evidence become available, and it is the surgeon's obligation to remain open to these changes to ensure the best possible patient outcomes.

### Disclosures

The author has no relevant financial disclosures.

### Conflict of Interest

None declared.

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