

Uma Mahadevan MD, Series Editor
guildconference.com

Evaluation, Management, and Prevention of Diverticular Disease



Jason D. Eckmann



Aasma Shaukat

Diverticular disorders are frequently encountered in the primary care setting. Diverticular bleeding is the most common cause of lower gastrointestinal bleeding. Low risk patients with uncomplicated diverticulitis can be managed in the outpatient setting, in some cases without the need for antibiotics. In patients with diverticulosis and persistent abdominal pain, chronic smoldering diverticulitis, segmental colitis associated with diverticulosis (SCAD), symptomatic uncomplicated diverticular disease (SUDD), and visceral hypersensitivity should all be considered. To avoid these complications, patients should be encouraged to lead an active lifestyle, consume a healthy diet, and avoid tobacco, alcohol, and certain medications. Contrary to conventional teaching, seeds and nuts do not need to be avoided.

INTRODUCTION

Colonic diverticulosis is a common syndrome involving protrusion of mucosa and submucosa through weak points in the muscular layer of the wall of the colon, resulting in sac-like pockets called diverticula. Diverticulosis can develop anywhere in the colon, but is more commonly encountered in Western populations in the left colon (distal to the splenic flexure), where sigmoid involvement occurs in >90% of patients with diverticulosis.¹ In comparison, while diverticulosis is overall less common in Asian populations, right-sided (proximal to the

splenic flexure) diverticulosis predominates.²⁻⁴ The likelihood of diverticulosis increases with age and has been estimated to be over 50-60% in patients >60 years.^{5,6} Rates are increasing worldwide, and are significant contributors to healthcare costs.⁷⁻⁹ Most patients are incidentally found to have diverticulosis on imaging or colonoscopy and remain asymptomatic. However, a small proportion develop complications including bleeding, inflammation, and chronic pain. In this article, we will review the common clinical syndromes seen in patients with diverticulosis (Table 1), and provide a practical approach to the evaluation, management, and prevention of these diseases for the primary care clinician.

Jason D. Eckmann, MD¹ Aasma Shaukat, MD MPH²
¹Division of Gastroenterology, Hepatology, and Nutrition, University of Minnesota, Minneapolis, MN ²Division of Gastroenterology NYU Langone, New York, NY

(continued on page 34)

(continued from page 32)

Diverticular Bleeding

Diverticular bleeding is the most common cause of overt lower gastrointestinal (GI) bleeding in the United States,^{10–12} and is seen in up to 15% of patients with diverticulosis with an incidence of ~0.5 per 1,000 person-years.^{13–15} Bleeding occurs when the vasa recta, blood vessels which penetrate the colonic wall at the site of diverticulum formation, hemorrhage into the gastrointestinal lumen. Diverticular bleeding most commonly arises from the right colon, where the colonic wall is thinner and diverticula tend to have larger openings.^{10,15–17}

Presentation

Patients with diverticular bleeding most commonly present with painless hematochezia.¹⁸ Some patients report cramping or bloating (likely related to the cathartic effect of blood in the GI tract), however predominant pain should prompt investigation into alternative etiologies such as ischemic colitis or inflammatory bowel disease (IBD). For most patients, bleeding is relatively minor and self-limited.^{16,19} However, in some cases, bleeding can

be brisk, and patients may present with signs of hemodynamic compromise including hypotension and tachycardia. The abdominal exam is typically benign, and rectal examination usually reveals bright red or maroon stool.

Diagnosis

The diagnosis of diverticular bleeding is generally suspected based on typical clinical signs and symptoms. Additional testing to support the diagnosis should include laboratory evaluation with a complete blood count and basic metabolic panel, with endoscopy or radiographic studies utilized for both diagnostic and therapeutic purposes (see Table 1 below).

Management

Patients with suspected diverticular bleeding should be managed in the inpatient setting, with initial care focusing on adequate intravenous (IV) access, telemetry monitoring, and fluid and blood product resuscitation when indicated. Patients with hemodynamically significant diverticular bleeding despite initial resuscitation should be cared for in an intensive care setting. In these patients, upper

Table 1. Summary of Diverticular Disorders

| | Diverticulitis | SCAD | SUDD |
|---------------------------|---|--|---|
| Frequency | 5% of patients with diverticulosis | 1% of patients with diverticular disease | 20% of patients with diverticular disease |
| Typical Symptoms | LLQ abdominal pain Fever | Abdominal pain Hematochezia | Chronic abdominal pain |
| Diagnosis | CT | CT Lower endoscopy | Clinical suspicion |
| Medical Management | Symptomatic care Antibiotics for complicated disease | Fiber, mesalamine, steroids, anti-TNF agents | Pain modulation |
| Prevention | Exercise, healthy BMI, smoking cessation | Unknown | Unknown |

BMI: body mass index; CT: computed tomography; LLQ: left lower quadrant; TNF: tumor necrosis factor

endoscopy (EGD) is generally performed first to exclude a brisk upper GI bleed, which is the underlying etiology in 10-15% of patients with brisk hematochezia.²⁰ Once upper GI bleeding has been excluded, colonoscopy can be pursued after appropriate colonic preparation. While rare to identify a culprit bleeding diverticulum at the time of colonoscopy, a presumptive diagnosis of diverticular bleeding can be given in patients with diverticula who are found to have colonic blood with no alternative explanation.^{14,21} If active bleeding is found endoscopically, various tools can be utilized by the endoscopist to achieve hemostasis including epinephrine injection, cautery, and hemostatic clips.^{14,22} If colonoscopy fails to reveal a source, or if the patient cannot undergo colonoscopy, radiographic evaluation with computed tomography (CT) angiography or nuclear scintigraphy can be used to localize bleeding and guide angiographic intervention.

Acute Diverticulitis

Approximately 4-5% of patients with diverticulosis will develop diverticulitis, with an annual incidence in the United States of approximately 188/100,000 persons per year.^{23,24} Historically, diverticulitis was felt to develop from diverticular obstruction by fecaliths, seeds, or other solid material, leading to inflammation or perforation of the diverticulum.²⁵ However, this obstructive etiology is now felt to be uncommon. More likely, a combination of altered motility, gut microbiome changes, and underlying genetic and lifestyle factors over time cause breakdown of the colonic mucosal barrier and altered immunity, ultimately leading to a localized inflammatory response.²⁶

Subtypes

Diverticulitis can be divided into uncomplicated and complicated disease. Most cases of diverticulitis are uncomplicated, with inflammation isolated to the diverticulum and surrounding colonic mucosa. However, 12-15% of cases are complicated by phlegmon or abscess (70% of complications), perforation, obstruction, stricture, or fistula.²⁶⁻²⁸ In most cases patients recover fully after an episode of acute diverticulitis, but in 5-10% symptoms and ongoing inflammation persist, resulting in chronic or “smoldering” diverticulitis.^{29,30}

Presentation

Patients with acute diverticulitis typically present with cramping lower abdominal pain, most commonly in the left lower quadrant. Patients may also report low grade fevers, nausea, poor oral intake, or a change in bowel habits. Rectal bleeding is not commonly seen in acute diverticulitis. Abdominal guarding, rigidity, palpable mass, or the presence of hemodynamic instability should raise suspicion for complicated diverticulitis. Both inflammatory markers and white blood cell count are typically elevated. Given the nonspecific symptoms and laboratory findings in acute diverticulitis, a clinical diagnosis of diverticulitis is only accurate in 40-65% of patients.^{31,32} Therefore, in most cases CT of the abdomen with IV contrast should be obtained to confirm the diagnosis given its high sensitivity and specificity for the disease (94% and 99%, respectively).³³

Management

The key initial decision in patients presenting with acute diverticulitis is to determine the need for inpatient care. Otherwise young, healthy patients with mild uncomplicated diverticulitis can generally be managed as an outpatient, whereas patients with complicated diverticulitis generally require hospitalization.³⁴⁻³⁶ Additional populations requiring inpatient care include the elderly, immunosuppressed, patients with extensive medical comorbidities, and those with signs of sepsis, high fever, significant leukocytosis, severe pain, inability to tolerate oral intake, or who have failed outpatient management.^{34,37,38}

Role of Antibiotics

Antibiotics have historically been the cornerstone of medical therapy for acute diverticulitis, although recent data suggest that in certain populations antibiotic therapy may not be necessary.^{30,39-41} A meta-analysis including over 2,500 patients with mild uncomplicated diverticulitis showed no difference in relevant clinical outcomes between those treated with antibiotics and those who were not.⁴² Therefore, most major societies now endorse selective rather than routine use of antibiotics in immunocompetent patients with mild uncomplicated acute diverticulitis.^{27,36,38,43} In patients with complicated disease, hospitalized

patients, and those with uncomplicated disease at high risk for complications, a 7-10 day course of antibiotics with enteric coverage is recommended.²⁸ Surgical intervention is generally not necessary in most cases of acute diverticulitis.⁴⁴ However, in patients with overt perforation, fistula, obstruction, non-resolving or recurrent abscess, or those with uncomplicated disease who fail to improve despite medical management, surgical consultation should be obtained.³⁸

Role of Surgery

Surgery is no longer recommended routinely for patients with recurrent episodes of uncomplicated diverticulitis. While quality of life overall seems to be improved after resection, recent literature suggest that partial colectomy reduces (but does not eliminate) the risk for recurrent diverticulitis, and that a significant portion of patients have ongoing abdominal pain despite surgical resection.⁴⁵⁻⁴⁸ Therefore, the decision to perform segmental colectomy in patients with recurrent diverticulitis should be an individualized one. Prior to pursuing surgical intervention, patients and clinicians should consider the severity and frequency of diverticulitis episodes, presence of complications, medical comorbidities, effect on quality of life, and the patient's ability to tolerate surgical intervention.³⁸

Role of Colonoscopy

Anecdotal evidence and conventional wisdom suggest colonoscopy should not be obtained during an acute episode of diverticulitis due to increased procedural difficulty, patient discomfort, and the theoretical potential for perforation.²⁸ However, data reveal an increased risk of colorectal cancer (CRC) in patients with diverticulitis, particularly in those with complicated diverticulitis (6-8%).^{49,50} Therefore, follow-up colonoscopy is recommended 6-8 weeks after presentation in patients with complicated diverticulitis and those with a first episode of uncomplicated diverticulitis to exclude concomitant CRC.^{28,51} This can be deferred in patients in whom a high-quality colonoscopy has been performed within the last 12 months. Patients with recurrent episodes of uncomplicated diverticulitis do not require a colonoscopy following every episode; rather, they should follow conventional screening or surveillance intervals.^{28,51}

Other Diverticular Disorders

Segmental Colitis Associated with Diverticulosis (SCAD)

In approximately 1% of patients with diverticulosis, inflammation of the mucosa between diverticula can develop, termed segmental colitis associated with diverticulosis (SCAD, also known as diverticular-associated colitis).^{52,53} Unlike in diverticulitis, the inflammation in SCAD typically spares the diverticula themselves. The exact pathogenesis of SCAD is not fully understood, but likely results at least in part from localized ischemia, mucosal prolapse, and stasis of fecal matter leading to chronic inflammatory changes.⁵⁴ Rather than distinct, acute episodes as in diverticulitis, patients with SCAD typically present with chronic symptoms of diarrhea, abdominal pain, and sometimes mild hematochezia. These symptoms may mimic other diseases such as irritable bowel syndrome (IBS) or IBD; in fact, it is likely that SCAD lies on the spectrum of IBD, with debate surrounding whether SCAD is a distinct entity or merely represents the coexistence of IBD and diverticulosis.⁵⁵ CT imaging and colonoscopic evaluation reveals mucosal inflammation in an area of diverticulosis, typically sparing the rectum.⁵⁵⁻⁵⁷ Data for management are limited, but first line therapy typically involves a course of antibiotics and high fiber diet, similar to diverticulitis. With refractory symptoms, therapies traditionally used in IBD including mesalamine, oral steroids, and anti-tumor necrosis factor-alpha (TNF- α) agents can be considered.^{57,58}

Symptomatic Uncomplicated Diverticular Disease (SUDD)

SUDD should be suspected in patients with diverticulosis and persistent unexplained abdominal pain, in the absence of radiologic or endoscopic evidence of active inflammation that would suggest an alternative etiology such as diverticulitis or SCAD. SUDD has been reported in 15-25% of patients with diverticulosis,⁵⁹ however, there is controversy surrounding this diagnosis, and there is likely a significant overlap with disorders of gut-brain interaction (DGBIs, previously referred to as functional gastrointestinal disorders) such as IBS.

(continued on page 38)

(continued from page 36)

Proposed underlying mechanisms are similar to those for IBS, including visceral hypersensitivity, microbial dysbiosis, altered GI motility, and low-level inflammation.^{60–64} Given the similarities to DGBIs, neuromodulators such as tricyclic antidepressants may be beneficial to patients with SUDD.⁶⁵ Numerous other treatments including fiber, probiotics, antibiotics, and aminosaliclates have been investigated with inconclusive results, and cannot be recommended at this time.^{66–72}

Prevention of Diverticular Disease

Given diverticular disease's prevalence and effect on quality of life, many patients inquire as to what can be done to prevent future or recurrent episodes. Importantly, the development of diverticular disease can be attributed both to genetic influences as well as lifestyle factors. Various genetic loci have been implicated, with estimates of up to 50% of the risk for diverticulitis attributable to genetic effect.^{73–77} While of primarily academic interest at this time, these genetic associations may allow for targeted therapies in the future.

There are numerous lifestyle interventions patients can follow to decrease risk of diverticulitis and other diverticular disorders. For years, patients with diverticulosis were counseled to avoid ingestion of seeds, nuts, popcorn, and related foods, due to the concern for obstructing diverticula and precipitating diverticulitis. As mentioned previously, this is now felt to be a rare inciting factor for diverticulitis. In fact, a large-scale observational study of nearly 50,000 patients showed an inverse correlation between ingestion of these foods and development of diverticular disease.⁷⁸ Rather, studies have associated diets that are low in fiber and high in red meat and refined sugars as leading to increased risk for the development of diverticular disease.⁷⁹ Additional risk factors include obesity, sedentary lifestyle, as well as tobacco, opioid, alcohol, and non-steroidal anti-inflammatory drug (NSAID) use.^{80–86} Therefore, patients with diverticulosis should be encouraged to follow a high fiber diet which is low in red meat and refined sugars, and counseled to maintain an active lifestyle with the goal of achieving a normal body mass index. Additionally, depending on each patient's individual habits, they

should be advised to quit smoking, and minimize use of opioids, alcohol, and NSAIDs whenever possible.

CONCLUSION

Diverticular disorders are commonly encountered conditions whose evaluation, management, and prevention can prove challenging for patients and clinicians alike. Patients with suspected diverticular bleeding should be carefully monitored in the inpatient setting, and usually require colonoscopy for diagnosis and potentially therapeutic intervention. When diverticulitis is suspected clinically, CT should generally be obtained to confirm the diagnosis. Healthy patients with uncomplicated diverticulitis can be treated in the outpatient setting, some without antibiotic therapy. Surgical resection is generally only pursued in certain patients with complicated diverticulitis, but can be considered in those with recurrent uncomplicated diverticulitis after weighing risks and benefits. Colonoscopy should follow first episodes of complicated diverticulitis in those without recent high-quality colonoscopy. In patients with diverticulosis and chronic abdominal symptoms, SCAD and SUDD should be considered. While genetics are a significant factor in the development of diverticular disorders, patients should be counseled that lifestyle modifications including physical activity, healthy diet, and smoking cessation play important roles in decreasing risk for diverticular disease. ■

References

1. Parks TG. Natural history of diverticular disease of the colon. *Clin Gastroenterol.* 1975;4(1):53-69.
2. Delvaux M. Diverticular disease of the colon in Europe: epidemiology, impact on citizen health and prevention. *Aliment Pharmacol Ther.* 2003;18 Suppl 3:71-74. doi:10.1046/j.0953-0673.2003.01720.x
3. Chan CC, Lo KK, Chung EC, Lo SS, Hon TY. Colonic diverticulosis in Hong Kong: distribution pattern and clinical significance. *Clin Radiol.* 1998;53(11):842-844. doi:10.1016/s0009-9260(98)80197-9
4. Markham NI, Li AK. Diverticulitis of the right colon—experience from Hong Kong. *Gut.* 1992;33(4):547-549. doi:10.1136/gut.33.4.547
5. Peery AF, Barrett PR, Park D, et al. A high-fiber diet does not protect against asymptomatic diverticulosis. *Gastroenterology.* 2012;142(2):266-272.e1. doi:10.1053/j.gastro.2011.10.035
6. Painter NS, Burkitt DP. Diverticular disease of the colon, a 20th century problem. *Clin Gastroenterol.* 1975;4(1):3-21.
7. Everhart JE, Ruhl CE. Burden of digestive diseases in the United States part II: lower gastrointestinal diseases.

- Gastroenterology. 2009;136(3):741-754. doi:10.1053/j.gastro.2009.01.015
8. Yamamichi N, Shimamoto T, Takahashi Y, et al. Trend and risk factors of diverticulosis in Japan: age, gender, and lifestyle/metabolic-related factors may cooperatively affect on the colorectal diverticula formation. *PLoS One*. 2015;10(4):e0123688. doi:10.1371/journal.pone.0123688
 9. Shaheen NJ, Hansen RA, Morgan DR, et al. The burden of gastrointestinal and liver diseases, 2006. *Am J Gastroenterol*. 2006;101(9):2128-2138. doi:10.1111/j.1572-0241.2006.00723.x
 10. Gostout CJ, Wang KK, Ahlquist DA, et al. Acute gastrointestinal bleeding. Experience of a specialized management team. *J Clin Gastroenterol*. 1992;14(3):260-267. doi:10.1097/00004836-199204000-00014
 11. Browder W, Cerise EJ, Litwin MS. Impact of emergency angiography in massive lower gastrointestinal bleeding. *Ann Surg*. 1986;204(5):530-536. doi:10.1097/00000658-198611000-00004
 12. Gayer C, Chino A, Lucas C, et al. Acute lower gastrointestinal bleeding in 1,112 patients admitted to an urban emergency medical center. *Surgery*. 2009;146(4):600-606; discussion 606-607. doi:10.1016/j.surg.2009.06.055
 13. Niikura R, Nagata N, Shimbo T, et al. Natural history of bleeding risk in colonic diverticulosis patients: a long-term colonoscopy-based cohort study. *Aliment Pharmacol Ther*. 2015;41(9):888-894. doi:10.1111/apt.13148
 14. Jensen DM, Machicado GA, Jutabha R, Kovacs TO. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. *N Engl J Med*. 2000;342(2):78-82. doi:10.1056/NEJM200001133420202
 15. McGuire HH, Haynes BW. Massive hemorrhage for diverticulosis of the colon: guidelines for therapy based on bleeding patterns observed in fifty cases. *Ann Surg*. 1972;175(6):847-855. doi:10.1097/00000658-197206010-00004
 16. Casarella WJ, Kanter IE, Seaman WB. Right-sided colonic diverticula as a cause of acute rectal hemorrhage. *N Engl J Med*. 1972;286(9):450-453. doi:10.1056/NEJM197203022860902
 17. Wong SK, Ho YH, Leong AP, Seow-Choen F. Clinical behavior of complicated right-sided and left-sided diverticulosis. *Dis Colon Rectum*. 1997;40(3):344-348. doi:10.1007/BF02050427
 18. Wilkins T, Baird C, Pearson AN, Schade RR. Diverticular bleeding. *Am Fam Physician*. 2009;80(9):977-983.
 19. McGuire HH. Bleeding colonic diverticula. A reappraisal of natural history and management. *Ann Surg*. 1994;220(5):653-656. doi:10.1097/00000658-199411000-00008
 20. Farrell JJ, Friedman LS. Review article: the management of lower gastrointestinal bleeding. *Aliment Pharmacol Ther*. 2005;21(11):1281-1298. doi:10.1111/j.1365-2036.2005.02485.x
 21. Smoot RL, Gostout CJ, Rajan E, et al. Is early colonoscopy after admission for acute diverticular bleeding needed? *Am J Gastroenterol*. 2003;98(9):1996-1999. doi:10.1111/j.1572-0241.2003.07635.x
 22. Fouch PG, Zimmerman K. Diverticular bleeding and the pigmented protuberance (sentinel clot): clinical implications, histopathological correlation, and results of endoscopic intervention. *Am J Gastroenterol*. 1996;91(12):2589-2593.
 23. Shahedi K, Fuller G, Bolus R, et al. Long-term risk of acute diverticulitis among patients with incidental diverticulosis found during colonoscopy. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc*. 2013;11(12):1609-1613. doi:10.1016/j.cgh.2013.06.020
 24. Bharucha AE, Parthasarathy G, Ditah I, et al. Temporal Trends in the Incidence and Natural History of Diverticulitis: A Population-Based Study. *Am J Gastroenterol*. 2015;110(11):1589-1596. doi:10.1038/ajg.2015.302
 25. Rege RV, Nahrwold DL. Diverticular disease. *Curr Probl Surg*. 1989;26(3):133-189. doi:10.1016/0011-3840(89)90031-2
 26. Strate LL, Morris AM. Epidemiology, Pathophysiology, and Treatment of Diverticulitis. *Gastroenterology*. 2019;156(5):1282-1298.e1. doi:10.1053/j.gastro.2018.12.033
 27. Stollman N, Smalley W, Hirano I, AGA Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on the Management of Acute Diverticulitis. *Gastroenterology*. 2015;149(7):1944-1949. doi:10.1053/j.gastro.2015.10.003
 28. Peery AF, Shaukat A, Strate LL. AGA Clinical Practice Update on Medical Management of Colonic Diverticulitis: Expert Review. *Gastroenterology*. 2021;160(3):906-911.e1. doi:10.1053/j.gastro.2020.09.059
 29. Boostrom SY, Wolff BG, Cima RR, Merchea A, Dozois EJ, Larson DW. Uncomplicated diverticulitis, more complicated than we thought. *J Gastrointest Surg Off J Soc Surg Aliment Tract*. 2012;16(9):1744-1749. doi:10.1007/s11605-012-1924-4
 30. Daniels L, Ünlü Ç, de Korte N, et al. Randomized clinical trial of observational versus antibiotic treatment for a first episode of CT-proven uncomplicated acute diverticulitis. *Br J Surg*. 2017;104(1):52-61. doi:10.1002/bjs.10309
 31. Laméris W, van Randen A, van Gulik TM, et al. A clinical decision rule to establish the diagnosis of acute diverticulitis at the emergency department. *Dis Colon Rectum*. 2010;53(6):896-904. doi:10.1007/DCR.0b013e3181d98d86
 32. Andeweg CS, Knobben L, Hendriks JCM, Bleichrodt RP, van Goor H. How to diagnose acute left-sided colonic diverticulitis: proposal for a clinical scoring system. *Ann Surg*. 2011;253(5):940-946. doi:10.1097/SLA.0b013e3182113614
 33. Laméris W, van Randen A, Bipat S, Bossuyt PMM, Boermeester MA, Stoker J. Graded compression ultrasonography and computed tomography in acute colonic diverticulitis: meta-analysis of test accuracy. *Eur Radiol*. 2008;18(11):2498-2511. doi:10.1007/s00330-008-1018-6
 34. Etzioni DA, Chiu VY, Cannom RR, Burchette RJ, Haigh PI, Abbas MA. Outpatient treatment of acute diverticulitis: rates and predictors of failure. *Dis Colon Rectum*. 2010;53(6):861-865. doi:10.1007/DCR.0b013e3181cdeb243
 35. Sirany AME, Gaertner WB, Madoff RD, Kwaan MR. Diverticulitis Diagnosed in the Emergency Room: Is It Safe to Discharge Home? *J Am Coll Surg*. 2017;225(1):21-25. doi:10.1016/j.jamcollsurg.2017.02.016
 36. Qaseem A, Etzeandia-Ikobaltzeta I, Lin JS, et al. Diagnosis and Management of Acute Left-Sided Colonic Diverticulitis: A Clinical Guideline From the American College of Physicians. *Ann Intern Med*. Published online January 18, 2022. doi:10.7326/M21-2710
 37. Alonso S, Pera M, Parés D, et al. Outpatient treatment of patients with uncomplicated acute diverticulitis. *Colorectal Dis Off J Assoc Coloproctology G B Irel*. 2010;12(10 Online):e278-282. doi:10.1111/j.1463-1318.2009.02122.x
 38. Hall J, Hardiman K, Lee S, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Treatment of Left-Sided Colonic Diverticulitis. *Dis Colon Rectum*. 2020;63(6):728-747. doi:10.1097/DCR.0000000000001679
 39. Brochmann ND, Schultz JK, Jakobsen GS, Øresland T. Management of acute uncomplicated diverticulitis without

- antibiotics: a single-centre cohort study. *Colorectal Dis Off J Assoc Coloproctology G B Irel.* 2016;18(11):1101-1107. doi:10.1111/codi.13355
40. Chabok A, Pählman L, Hjern F, Haapaniemi S, Smedh K, AVOD Study Group. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. *Br J Surg.* 2012;99(4):532-539. doi:10.1002/bjs.8688
 41. Isacson D, Thorisson A, Andreasson K, Nikberg M, Smedh K, Chabok A. Outpatient, non-antibiotic management in acute uncomplicated diverticulitis: a prospective study. *Int J Colorectal Dis.* 2015;30(9):1229-1234. doi:10.1007/s00384-015-2258-y
 42. Au S, Aly EH. Treatment of Uncomplicated Acute Diverticulitis Without Antibiotics: A Systematic Review and Meta-analysis. *Dis Colon Rectum.* 2019;62(12):1533-1547. doi:10.1097/DCR.0000000000001330
 43. Francis NK, Sylla P, Abou-Khalil M, et al. EAES and SAGES 2018 consensus conference on acute diverticulitis management: evidence-based recommendations for clinical practice. *Surg Endosc.* 2019;33(9):2726-2741. doi:10.1007/s00464-019-06882-z
 44. Morris AM, Regenbogen SE, Hardiman KM, Hendren S. Sigmoid diverticulitis: a systematic review. *JAMA.* 2014;311(3):287-297. doi:10.1001/jama.2013.282025
 45. Thornblade LW, Simianu VV, Davidson GH, Flum DR. Elective Surgery for Diverticulitis and the Risk of Recurrence and Ostomy. *Ann Surg.* 2021;273(6):1157-1164. doi:10.1097/SLA.0000000000003639
 46. van de Wall BJM, Stam MAW, Draaisma WA, et al. Surgery versus conservative management for recurrent and ongoing left-sided diverticulitis (DIRECT trial): an open-label, multicentre, randomised controlled trial. *Lancet Gastroenterol Hepatol.* 2017;2(1):13-22. doi:10.1016/S2468-1253(16)30109-1
 47. Bolkenstein HE, Consten ECJ, van der Palen J, et al. Long-term Outcome of Surgery Versus Conservative Management for Recurrent and Ongoing Complaints After an Episode of Diverticulitis: 5-year Follow-up Results of a Multicenter Randomized Controlled Trial (DIRECT-Trial). *Ann Surg.* 2019;269(4):612-620. doi:10.1097/SLA.0000000000003033
 48. Egger B, Peter MK, Candinas D. Persistent symptoms after elective sigmoid resection for diverticulitis. *Dis Colon Rectum.* 2008;51(7):1044-1048. doi:10.1007/s10350-008-9234-3
 49. Meyer J, Orci LA, Combesure C, et al. Risk of Colorectal Cancer in Patients with Acute Diverticulitis: A Systematic Review and Meta-analysis of Observational Studies. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc.* 2019;17(8):1448-1456.e17. doi:10.1016/j.cgh.2018.07.031
 50. Koo CH, Chang JHE, Syn NL, Wee IJY, Mathew R. Systematic Review and Meta-analysis on Colorectal Cancer Findings on Colonic Evaluation After CT-Confirmed Acute Diverticulitis. *Dis Colon Rectum.* 2020;63(5):701-709. doi:10.1097/DCR.0000000000001664
 51. Qaseem A, Etzeandia-Ikobaltzeta I, Lin JS, et al. Colonoscopy for Diagnostic Evaluation and Interventions to Prevent Recurrence After Acute Left-Sided Colonic Diverticulitis: A Clinical Guideline from the American College of Physicians. *Ann Intern Med.* Published online January 18, 2022. doi:10.7326/M21-2711
 52. Mann NS, Hoda KK. Segmental colitis associated with diverticulosis: systematic evaluation of 486 cases with meta-analysis. *Hepatogastroenterology.* 2012;59(119):2119-2121. doi:10.5754/hgel11043
 53. Tursi A, Elisei W, Brandimarte G, et al. The endoscopic spectrum of segmental colitis associated with diverticulosis. *Colorectal Dis Off J Assoc Coloproctology G B Irel.* 2010;12(5):464-470. doi:10.1111/j.1463-1318.2009.01969.x
 54. Ludeman L, Shepherd NA. What is diverticular colitis? *Pathology (Phila).* 2002;34(6):568-572. doi:10.1080/0031302021000035974
 55. Tursi A. Segmental colitis associated with diverticulosis: complication of diverticular disease or autonomous entity? *Dig Dis Sci.* 2011;56(1):27-34. doi:10.1007/s10620-010-1230-5
 56. Cassieri C, Brandimarte G, Elisei W, et al. How to Differentiate Segmental Colitis Associated With Diverticulosis and Inflammatory Bowel Diseases. *J Clin Gastroenterol.* 2016;50 Suppl 1:S36-38. doi:10.1097/MCG.0000000000000630
 57. Schembri J, Bonello J, Christodoulou DK, Katsanos KH, Ellul P. Segmental colitis associated with diverticulosis: is it the coexistence of colonic diverticulosis and inflammatory bowel disease? *Ann Gastroenterol.* 2017;30(3):257-261. doi:10.20524/aog.2017.0126
 58. Rampton DS. Diverticular colitis: diagnosis and management. *Colorectal Dis Off J Assoc Coloproctology G B Irel.* 2001;3(3):149-153. doi:10.1046/j.1463-1318.2001.00242.x
 59. Tursi A, Elisei W, Franceschi M, Picchio M, Di Mario F, Brandimarte G. The prevalence of symptomatic uncomplicated diverticular disease could be lower than expected: a single-center colonoscopy-based cohort study. *Eur J Gastroenterol Hepatol.* Published online April 16, 2021. doi:10.1097/MEG.0000000000002142
 60. Bassotti G, Sietchiping-Nzepa F, De Roberto G, Chistolini F, Morelli A. Colonic regular contractile frequency patterns in irritable bowel syndrome: the “spastic colon” revisited. *Eur J Gastroenterol Hepatol.* 2004;16(6):613-617. doi:10.1097/00042737-200406000-00016
 61. Bassotti G, Battaglia E, Bellone G, et al. Interstitial cells of Cajal, enteric nerves, and glial cells in colonic diverticular disease. *J Clin Pathol.* 2005;58(9):973-977. doi:10.1136/jcp.2005.026112
 62. Simpson J, Sundler F, Humes DJ, Jenkins D, Scholefield JH, Spiller RC. Post inflammatory damage to the enteric nervous system in diverticular disease and its relationship to symptoms. *Neurogastroenterol Motil Off J Eur Gastrointest Motil Soc.* 2009;21(8):847-e58. doi:10.1111/j.1365-2982.2009.01308.x
 63. Barbaro MR, Cremon C, Fuschi D, et al. Nerve fiber overgrowth in patients with symptomatic diverticular disease. *Neurogastroenterol Motil Off J Eur Gastrointest Motil Soc.* 2019;31(9):e13575. doi:10.1111/nmo.13575
 64. Kvasnovsky CL, Leong LEX, Choo JM, et al. Clinical and symptom scores are significantly correlated with fecal microbiota features in patients with symptomatic uncomplicated diverticular disease: a pilot study. *Eur J Gastroenterol Hepatol.* 2018;30(1):107-112. doi:10.1097/MEG.0000000000000995
 65. Drossman DA, Tack J, Ford AC, Szigethy E, Törnblom H, Van Oudenhove L. Neuromodulators for Functional Gastrointestinal Disorders (Disorders of Gut-Brain Interaction): A Rome Foundation Working Team Report. *Gastroenterology.* 2018;154(4):1140-1171.e1. doi:10.1053/j.gastro.2017.11.279
 66. Carabotti M, Annibale B, Severi C, Lahner E. Role of Fiber in Symptomatic Uncomplicated Diverticular Disease: A Systematic Review. *Nutrients.* 2017;9(2):E161. doi:10.3390/nu9020161

(continued on page 42)

(continued from page 40)

67. Bianchi M, Festa V, Moretti A, et al. Meta-analysis: long-term therapy with rifaximin in the management of uncomplicated diverticular disease. *Aliment Pharmacol Ther.* 2011;33(8):902-910. doi:10.1111/j.1365-2036.2011.04606.x
68. Di Mario F, Miraglia C, Cambiè G, et al. Long-term efficacy of rifaximin to manage the symptomatic uncomplicated diverticular disease of the colon. *J Investig Med Off Publ Am Fed Clin Res.* 2019;67(4):767-770. doi:10.1136/jim-2018-000901
69. Tursi A, Brandimarte G, Giorgetti GM, Elisei W. Mesalazine and/or *Lactobacillus casei* in preventing recurrence of symptomatic uncomplicated diverticular disease of the colon: a prospective, randomized, open-label study. *J Clin Gastroenterol.* 2006;40(4):312-316. doi:10.1097/01.mcg.0000210092.77296.6d
70. Tursi A, Brandimarte G, Elisei W, et al. Randomised clinical trial: mesalazine and/or probiotics in maintaining remission of symptomatic uncomplicated diverticular disease--a double-blind, randomised, placebo-controlled study. *Aliment Pharmacol Ther.* 2013;38(7):741-751. doi:10.1111/apt.12463
71. Kruis W, Meier E, Schumacher M, et al. Randomised clinical trial: mesalazine (Salofalk granules) for uncomplicated diverticular disease of the colon--a placebo-controlled study. *Aliment Pharmacol Ther.* 2013;37(7):680-690. doi:10.1111/apt.12248
72. Picchio M, Elisei W, Tursi A. Mesalazine to treat symptomatic uncomplicated diverticular disease and to prevent acute diverticulitis occurrence. A systematic review with meta-analysis of randomized, placebo-controlled trials. *J Gastrointest Liver Dis JGLD.* 2018;27(3):291-297. doi:10.15403/jgld.2014.1121.273.pic
73. Camilleri M, Sandler RS, Peery AF. Etiopathogenetic Mechanisms in Diverticular Disease of the Colon. *Cell Mol Gastroenterol Hepatol.* 2020;9(1):15-32. doi:10.1016/j.jcmgh.2019.07.007
74. Granlund J, Svensson T, Olén O, et al. The genetic influence on diverticular disease--a twin study. *Aliment Pharmacol Ther.* 2012;35(9):1103-1107. doi:10.1111/j.1365-2036.2012.05069.x
75. Strate LL, Erichsen R, Baron JA, et al. Heritability and familial aggregation of diverticular disease: a population-based study of twins and siblings. *Gastroenterology.* 2013;144(4):736-742.e1; quiz e14. doi:10.1053/j.gastro.2012.12.030
76. Sigurdsson S, Alexandersson KF, Sulem P, et al. Sequence variants in ARHGAP15, COLQ and FAM155A associate with diverticular disease and diverticulitis. *Nat Commun.* 2017;8:15789. doi:10.1038/ncomms15789
77. Maguire LH, Handelman SK, Du X, Chen Y, Pers TH, Speliotes EK. Genome-wide association analyses identify 39 new susceptibility loci for diverticular disease. *Nat Genet.* 2018;50(10):1359-1365. doi:10.1038/s41588-018-0203-z
78. Strate LL, Liu YL, Syngal S, Aldoori WH, Giovannucci EL. Nut, corn, and popcorn consumption and the incidence of diverticular disease. *JAMA.* 2008;300(8):907-914. doi:10.1001/jama.300.8.907
79. Liu PH, Cao Y, Keeley BR, et al. Adherence to a Healthy Lifestyle is Associated With a Lower Risk of Diverticulitis among Men. *Am J Gastroenterol.* 2017;112(12):1868-1876. doi:10.1038/ajg.2017.398
80. Strate LL, Liu YL, Aldoori WH, Giovannucci EL. Physical activity decreases diverticular complications. *Am J Gastroenterol.* 2009;104(5):1221-1230. doi:10.1038/ajg.2009.121
81. Hjern F, Wolk A, Håkansson N. Smoking and the risk of diverticular disease in women. *Br J Surg.* 2011;98(7):997-1002. doi:10.1002/bjs.7477
82. Ma W, Jovani M, Liu PH, et al. Association Between Obesity and Weight Change and Risk of Diverticulitis in Women. *Gastroenterology.* 2018;155(1):58-66.e4. doi:10.1053/j.gastro.2018.03.057
83. Thomas GAO, Rhodes J, Ingram JR. Mechanisms of disease: nicotine--a review of its actions in the context of gastrointestinal disease. *Nat Clin Pract Gastroenterol Hepatol.* 2005;2(11):536-544. doi:10.1038/ncpgasthep0316
84. Strate LL, Liu YL, Huang ES, Giovannucci EL, Chan AT. Use of aspirin or nonsteroidal anti-inflammatory drugs increases risk for diverticulitis and diverticular bleeding. *Gastroenterology.* 2011;140(5):1427-1433. doi:10.1053/j.gastro.2011.02.004
85. Aldoori WH, Giovannucci EL, Rimm EB, Wing AL, Willett WC. Use of acetaminophen and nonsteroidal anti-inflammatory drugs: a prospective study and the risk of symptomatic diverticular disease in men. *Arch Fam Med.* 1998;7(3):255-260. doi:10.1001/archfami.7.3.255
86. Humes DJ, Fleming KM, Spiller RC, West J. Concurrent drug use and the risk of perforated colonic diverticular disease: a population-based case-control study. *Gut.* 2011;60(2):219-224. doi:10.1136/gut.2010.217281

PRACTICAL GASTROENTEROLOGY

Visit our Website:

practicalgastro.com

*Celebrating
Six Decades
of Service*