Diverticular Disease: Reconsidering Conventional Wisdom

ANNE F. PEERY and ROBERT S. SANDLER
Division of Gastroenterology and Hepatology, Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina

Colonic diverticula are common in developed countries and complications of colonic diverticulosis are responsible for a significant burden of disease. Several recent publications have called into question long-held beliefs about diverticular disease. Contrary to conventional wisdom, studies have not shown that a high-fiber diet protects against asymptomatic diverticulosis. The risk of developing diverticulitis among individuals with diverticulosis is lower than the 10% to 25% proportion that commonly is quoted, and may be as low as 1% over 11 years. Nuts and seeds do not increase the risk of diverticulitis or diverticular bleeding. It is unclear whether diverticulosis, absent diverticulitis, or overt colitis is responsible for chronic gastrointestinal symptoms or worse quality of life. The role of antibiotics in acute diverticulitis has been challenged by a large randomized trial that showed no benefit in selected patients. The decision to perform elective surgery should be made on a case-by-case basis and not routinely after a second episode of diverticulitis, when there has been a complication, or in young people. A colonoscopy should be performed to exclude colon cancer after an attack of acute diverticulitis but may not alter outcomes among individuals who have had a colonoscopy before the attack. Given these surprising findings, it is time to reconsider conventional wisdom about diverticular disease.

Keywords: Colonic Diverticula; Diverticular Disease.

Diverticula of the large bowel are out-pouchings in the wall of the colon at weak points in the circular muscle where blood vessels penetrate to supply the mucosa. Diverticula may be found throughout the colon, but are most common in the sigmoid colon where abnormalities include thickening and elastosis of the teniae, shortening of the bowel, and thickening and folding of the circular muscle. Diverticulosis most often is uncomplicated and asymptomatic. Complications may occur, including bleeding, abscess, perforation, fistula, stricture, or colitis. The term diverticular disease generally is used to denote diverticulosis with a complication.

Recent reports have challenged long-accepted dogma. The hypothesis that diverticulosis is a deficiency disease of Western civilization was made popular by Painter and Burkitt based on their observation that diverticulosis was rare in rural Africa, but increasingly common in economically developed countries. They attributed the difference in disease prevalence to differences in dietary fiber. They presumed that the rural African diet was high in dietary fiber and that economically developed countries consumed a low-fiber diet. They proposed that this deficiency of fiber predisposed the population to diverticulosis. Neither diet nor diverticulosis was actually measured in their studies and they did not account for important potentially confounding variables such as age and sex.

Fiber

The hypothesis that diverticulosis is a deficiency disease of Western civilization was made popular by Painter and Burkitt based on their observation that diverticulosis was rare in rural Africa, but increasingly common in economically developed countries. They attributed the difference in disease prevalence to differences in dietary fiber. They presumed that the rural African diet was high in dietary fiber and that economically developed countries consumed a low-fiber diet. They proposed that this deficiency of fiber predisposed the population to diverticulosis. Neither diet nor diverticulosis was actually measured in their studies and they did not account for important potentially confounding variables such as age and sex.
Painter\textsuperscript{13} proposed that the deficiency of fiber led to constipation and high-pressure segmentation of the colon that resulted in mucosal herniation through weak sections of the colon wall. To support their hypothesis they conducted motility studies that compared intracolonic pressures in patients with diverticulosis with intracolonic pressures in controls. Although they reported that patients with diverticulosis had higher colonic pressures, the investigators only reported pressure measurements for select cases and there were no statistical analyses. Motility studies of the colon have not consistently shown that patients with diverticulosis have increased colonic pressures.\textsuperscript{14–19} Along the same lines, Burkitt et al\textsuperscript{20} conducted colonic transit studies and found that a population consuming a Western diet had longer mean colonic transit times and lower colonic transit studies and found that a population consuming a Western diet had longer mean colonic transit times and lower mean stool weights compared with an African population. Studies in populations with colonic diverticula, on the other hand, have shown shorter colonic transit times compared with controls.\textsuperscript{21,22}

The fiber hypothesis is extremely popular. The concept of forceful contractions of the colon leading to herniation makes sense. However, the hypothesis has persisted for 4 decades largely without proof. Historically it has been a challenge to refute the hypothesis because a proper study would require a structural examination (eg, barium enema) in asymptomatic individuals to document the presence of diverticula. With the widespread use of screening colonoscopy we now have the opportunity to study large numbers of people who are undergoing a structural examination of their colon in the absence of symptoms.

We recently published a colonoscopy-based, cross-sectional study of dietary risk factors for diverticulosis.\textsuperscript{23} Each of the 2104 subjects had a colonoscopy to the cecum between 1998 and 2010. Participants completed a telephone interview that included a comprehensive semiquantitative food frequency questionnaire as well as questions about bowel frequency and physical activity. Contrary to expectation, we found that a high-fiber diet was associated with a higher (not lower) prevalence of diverticula.\textsuperscript{23} The association with dietary fiber intake was dose-dependent and stronger when limited to cases with multiple diverticula. We also found that constipation was not a risk factor for diverticulosis. Instead, we found that participants who had regular bowel movements (<7 bowel movements/wk) had a 34\% higher risk of diverticulosis compared with participants who had less frequent bowel movements (7 bowel movements/wk).

Study participants were interviewed after their colonoscopy and were aware, in most cases, that diverticulosis had been found. In response to the concern that the study might have been susceptible to response bias and reverse causality from the subjects’ knowledge of their diagnoses,\textsuperscript{24} we performed a second cross-sectional study in a different population in which we limited the analysis to participants with no knowledge of their diverticulosis status. The second study confirmed the results of the initial work (unpublished data). Similar results with respect to fiber were found in 2 colonoscopy-based studies in non-Western populations, although diverticula in Asia are found predominantly in the right colon and may have a different etiology.\textsuperscript{25,26}

Although recent studies have suggested that a high-fiber diet does not protect against the development of diverticulosis\textsuperscript{25} there is some evidence that a high-fiber diet may protect against diverticular disease. Crowe et al\textsuperscript{27} studied 47,033 men and women in England and Scotland. Individuals who reported consuming a vegetarian diet had a lower risk of admission to the hospital or death from diverticular disease. There was also an inverse association for fiber intake. Those in the highest quintile of fiber consumption were 41\% less likely to have a complication from diverticular disease. Similar results were seen in a prospective study of US male health professionals.\textsuperscript{28}

It is important to recognize that the research to date was designed to improve our understanding of risk factors for diverticulosis and its complications and not to make dietary recommendations. There are advantages to eating a high-fiber, plant-based diet with respect to constipation, heart disease, and cancer.\textsuperscript{29,30}

### Risk of Diverticulitis

It is generally reported that 10\% to 25\% of patients with diverticulosis will develop diverticulitis during their lifetime.\textsuperscript{31} This estimate is based on a widely cited review of the natural history of diverticular disease published by Parks\textsuperscript{32} in 1975. The largest case series, published almost 3 decades earlier in 1947, included 47,000 roentgenologic examinations of the colon.\textsuperscript{33} Diverticulosis was diagnosed in 8.5\% of the examinations. Of the patients with diverticulosis, 15\% were diagnosed with diverticulitis. Because the study did not include any formal description of the methods, the indication for the original roentgenologic examination and the criteria for a diagnosis of diverticulitis are unknown. A 1958 case series described the natural history of diverticulosis in 300 patients diagnosed with diverticulosis by double-contrast barium enema.\textsuperscript{34} A diagnosis of diverticulitis was made for patients who subsequently presented with acute constipation or diarrhea, abdominal cramping, localized tenderness, fever, and leukocytosis. In that study, 10\% of patients with diverticulosis developed diverticulitis over a follow-up period of 1 to 5 years. Among those followed up for 6 to 10 years, 25\% developed diverticulitis. Smaller case series also have reported estimates of the risk of developing diverticular disease in those with diverticulosis.\textsuperscript{35}

To accurately calculate the cumulative incidence of diverticulitis it would be necessary to enroll a population of patients with diverticulosis and no history of diverticulitis. These individuals then would be observed over time for the development of diverticulitis. The widely quoted estimates are based on studies that were performed more than 50 years ago and potentially were biased. The studies began with patients who sought medical care and subsequently received a diagnosis of diverticulitis. This approach selects a population more likely to have diverticular disease and thus likely overestimates the risk of diverticulitis. Furthermore, these studies only included patients who were followed up in subsequent visits. Patients with diverticulitis without any symptoms were less likely to attend a follow-up visit.

Recent data suggest that the lifetime risk of diverticulitis is lower than commonly cited. Shahedi et al\textsuperscript{36} estimated the incidence of acute diverticulitis in a retrospective cohort of veterans with diverticulosis incidentally found on colonoscopy. The risk of diverticulitis confirmed by computerized tomography (CT) scan or surgery was 1\% over 11 years of follow-up evaluation.

With the widespread use of colonoscopy for screening for colorectal cancer, many patients are being given a diagnosis of diverticulosis and then warned that their risk of a complication is 1 in 4. This prediction appears to be exaggerated.
Nuts and Seeds

For more than 50 years, patients with diverticulosis were advised to avoid foods that may leave coarse particulate in the stool (ie, nuts, corn, and seeds). This recommendation was based on the hypothesis that these particles might obstruct a narrow-necked diverticulum or physically abrade a diverticulum, thereby initiating a cascade of events resulting in diverticulitis or diverticular hemorrhage. In a landmark study, Strate et al found that dietary nuts, corn, and seeds were not associated with an increased risk of diverticulitis or diverticular bleeding in a prospective cohort of male health professionals.

Chronic Symptoms

A recent taxonomy of diverticular disease terms distinguishes several types of symptomatic disease. The taxonomy includes 2 types of chronic diverticulitis: chronic recurrent diverticulitis and segmental colitis associated with diverticulosis. Chronic recurrent diverticulitis may begin early after the initial episode, and may be consistent with failure of the index episode to “settle.” Segmental colitis associated with diverticulosis is defined as peridiverticular colitis that spares the rectum. It is not surprising that patients with chronic recurrent diverticulitis and segmental colitis associated with diverticulosis have symptoms, given their measurable colonic inflammation. Another category of chronic disease has been termed symptomatic uncomplicated diverticular disease and is defined as diverticulosis associated with chronic gastrointestinal symptoms in the absence of diverticulitis or overt colitis. The criteria for a diagnosis of symptomatic uncomplicated diverticular disease do not include a history of acute diverticulitis. The literature on symptomatic uncomplicated diverticular disease is limited and confusing. For example, a small Italian study administered a general quality-of-life survey (Short-Form 36) to 58 outpatients who met the criteria for symptomatic uncomplicated diverticulitis and had symptoms of abdominal pain/discomfort, bloating, tenesmus, diarrhea, abdominal tenderness, fever, or dysuria. Not surprisingly, the quality-of-life scores were lower than a normative Italian population at baseline. It is not possible to conclude that either the symptoms or the decrement in quality of life were the result of diverticulosis. At 6 months, quality-of-life scores had improved, suggesting that the initial low scores were caused by diverticulitis or other acute illness at baseline. In another study, 12 patients with symptomatic uncomplicated diverticular disease were compared with 13 controls. The diverticular disease patients were found to have visceral hypersensitivity based on rectal barostat studies, perhaps mediated by ongoing inflammation and up-regulation of tachykinins based on colonic histology.

In contrast, a study of 784 subjects who had a structural examination of their colon found that the frequency of abdominal pain, diarrhea, constipation, and irritable bowel was similar in patients with and without diverticulosis. The study used Rome criteria for irritable bowel syndrome (IBS) to classify patients and the response rates were high. Subjects completed questionnaires before structural examinations. This study casts doubt on whether diverticulosis is associated with chronic symptoms.

Symptomatic uncomplicated diverticulitis disease simply may be irritable bowel syndrome in patients who are found to have diverticulosis because they undergo colonoscopy. A population-based, cross-sectional study found an increased risk for colonic diverticulosis among patients with irritable bowel syndrome compared with those without. Whether IBS and diverticular disease share an underlying pathophysiology or whether patients with IBS symptoms are simply more likely to undergo structural examinations that reveal diverticulosis is uncertain.

Some patients appear to have chronic abdominal pain after a bout of diverticulitis. This postdiverticulitis IBS may be akin to the IBS that develops after an acute bowel infection (postinfectious IBS), and would seem more appropriately considered a form of IBS rather than a type of chronic diverticular disease.

In summary, it is unclear whether diverticulosis, in the absence of diverticulitis or overt inflammation, is responsible for chronic gastrointestinal symptoms or decreased quality of life. The prevalence of diverticulosis approaches 80% in 80 year olds. The vast majority of those individuals do not have symptoms. We need more research to identify the subset that has symptoms and to determine why.

The Role of Antibiotics in Diverticulitis

A 2007 New England Journal of Medicine review on diverticulitis recommended that mild attacks of acute diverticulitis should be treated with 7 to 10 days of oral broad-spectrum antibiotics. The review noted that the pathogenesis of diverticulitis is unknown but restated the common hypothesis that diverticulitis is the result of an obstruction at the neck of the diverticulum, mucosal abrasion, low-grade inflammation, and bacterial translocation. Mild diverticulitis is thought to be associated with microperforation and more severe disease, gross perforation. In short, all manifestations of diverticulitis have been presumed to be caused by infection that should be treated with antibiotics.

A recent multicenter randomized controlled trial in Sweden and Iceland recruited 623 patients who had typical symptoms, uncomplicated left-sided diverticulitis documented by CT scan, and a temperature higher than 38°C. Subjects were excluded if they had an abscess, fistula, or free air on CT, or if they had high fever, peritonitis, or sepsis. Subjects were randomized to broad-spectrum antibiotics or intravenous fluids without antibiotics. Despite randomization, the groups were not completely balanced, with more episodes of prior diverticulitis in the antibiotic group (44.8%) compared with the nonantibiotic group (35.6%) (P = .02). During the first 5 days after admission there were no differences in abdominal pain, temperature, or abdominal tenderness. There was no difference in mean hospital stay, complications (perforation or abscess), or recurrent diverticulitis necessitating re-admission to the hospital during the first year. In the group randomized to no antibiotics, only 3 (1%) patients developed an abscess compared with no cases in the antibiotic group (P = .8) The investigators concluded that antibiotics should be used only in cases of complicated diverticulitis. Danish national guidelines for the treatment of diverticulitis do not recommend antibiotics for the treatment of uncomplicated diverticulitis (grade A). The guidelines support the use of antibiotics for the treatment of uncomplicated diverticulitis if the patient is septic, pregnant, or immunosuppressed based on limited data (grade C).

The strong evidence from a large randomized controlled trial showing no benefit of antibiotics in uncomplicated diverticulitis
raises important questions about etiology and management of diverticulitis. Acute diverticulitis may be an inflammatory rather than an infectious condition. Recently, a form of segmental colitis associated with diverticular disease that mimics chronic idiopathic inflammatory bowel disease histologically has been recognized. Although this entity is not common, it might explain some cases of diverticulitis that improve without antibiotics.

**Elective Surgery**

Guidelines for the diagnosis and management of diverticular disease of the colon in adults published in 1999 state that elective (prophylactic) surgery may be reasonable in patients with recurrent attacks of diverticulitis. The recommendation was based on the fact that the risk of recurrent symptoms after an attack of acute diverticulitis ranged from 7% to 62%, and because recurrent attacks were less likely to respond to medical therapy and have a higher mortality rate. The guidelines suggested that the approach should be individualized based on the severity and responsiveness of the attack, general health of the patient, and the risk of surgery compared with the risk of a future attack.

More recent studies of the natural history of acute diverticulitis, on the other hand, suggest that medically managed acute diverticulitis has a low recurrence rate and rarely progresses to complications. In one retrospective cohort study, the risk of recurrent acute diverticulitis after an initial episode of medically managed acute diverticulitis was 13% over 9 years. A second retrospective cohort found that the risk of recurrent acute diverticulitis was 19% over 16 years. A study published in 2010 found that 23% of patients had a recurrence. Most had a single recurrence, with only 4.7% having more than 2 episodes of diverticulitis. After an initial episode of uncomplicated acute diverticulitis, the risk of complicated disease was 5% over 8 years. The risk of recurrence was no greater in complicated future attack of diverticulitis. The examination typically is postponed for at least 6 weeks.

Janes et al calculated that the risk of an individual requiring urgent surgery was 1 in 2000 patient-years of follow-up evaluation. They further noted that there was a high complication rate in surgery for diverticular disease and that 27% to 33% of patients had ongoing symptoms after bowel resection, not necessarily attributed to recurrent acute diverticulitis.

The more widespread use of laparoscopic resection might be expected to decrease the surgical risk for elective colectomy. We still must balance the risk of surgery with the risk of a complicated future attack of diverticulitis. The American Society of Colon and Rectal Surgeons has appropriately recommended consideration of elective sigmoid colectomy after recovery from acute diverticulitis on a case-by-case basis, with the decision based on the age, comorbid disease, the frequency and severity of the attacks, and whether symptoms persist after the acute episode.

Diverticulitis in Younger Patients

Diverticulitis is thought to be more virulent in younger patients, with 25% to 80% reportedly requiring urgent surgery during their initial attack. The recurrence rate also has been reported to be higher in younger patients in older studies. American College of Gastroenterology practice guidelines for diverticular disease state that elective (prophylactic) surgery after one episode of uncomplicated diverticulitis may be reasonably considered in younger patients based on both the low surgical risk of an elective procedure in a healthy young person and the many years of future risk of recurrence.

More recent studies have challenged the view that diverticulitis is more virulent in younger patients and the recommendation for surgical intervention after an initial event. Anaya and Flum found that although there was an increased relative risk for emergency colectomy or colostomy in younger patients, the absolute risk was low. These investigators found that 73% of younger patients had no recurrence and most resolved without surgery. Their work showed that a policy of routine elective colectomy in a younger population would require 13 elective surgeries to prevent 1 emergency colectomy.

Colonoscopy

The American College of Gastroenterology guidelines recommend colonic evaluation after resolution of clinically diagnosed diverticulitis to exclude other diagnostic considerations, particularly cancer. Because of the potential for perforation as a result of the microabscesses that presumably caused acute diverticulitis, the examination typically is postponed for at least 6 weeks.

There is an increased risk of colon cancer in the first year after a diagnosis of diverticular disease. A population-based, case-control study of 41,037 patients with colon cancer found an increased odds ratio of 25 (95% confidence interval, 17–38) of a colon cancer diagnosis within 6 months of an admission for diverticular disease. There was no association with a colon cancer diagnosis 12 months after the admission for diverticular disease. The increased risk of colon cancer within 12 months of an admission for diverticular disease was attributed to surveillance bias and misclassification.

If a patient has had a recent colonoscopy before developing acute diverticulitis, whether there is any use in a repeat endoscopic examination is unknown. Lau et al found a number of cancers and other significant lesions when they performed a colonoscopy after an acute attack of diverticulitis. However, they excluded patients who had a colonoscopy within a year, and therefore recommended only performing colonoscopic examinations for individuals who had not had a recent radiologic or endoscopic colonic examination.

A colonoscopy should be performed to exclude colon cancer after an initial episode of suspected diverticulitis. If a patient has had a recent colonoscopy before developing acute diverticulitis, the value of a repeat colonoscopy to exclude cancer is unknown.

Conclusions

Recent work in diverticulosis has created uncertainty among both researchers and clinicians. The theories of prior generations have been proven to be questionable and in some cases unsupportable. A high-fiber diet may not protect against asymptomatic diverticulosis. The risk of developing
diverticulitis is likely a fraction of the 10% to 25% commonly quoted. Nuts and seeds do not increase the risk of diverticulitis or diverticular bleeding. The decision to perform elective surgery after surgical management of acute diverticulitis should be made on a case-by-case basis. A colonoscopy should be performed to exclude colon cancer after an attack of acute diverticulitis but may not alter outcomes among individuals who have had a colonoscopy before the attack.

A number of important questions remain. What is the mechanism of diverticular disease? Is there an important component of infection, or is diverticulitis something else entirely? Are there high-risk patients who should undergo early elective surgery? Are there diets that truly prevent diverticular disease? We know so little, but at least we are starting to ask the right questions.

References

Reprint requests
Address requests for reprints to: Robert S. Sandler, MD, MPH, Division of Gastroenterology and Hepatology, University of North Carolina School of Medicine, CB#7555, Chapel Hill, North Carolina 27599-7555. e-mail: rsandler@med.unc.edu; fax: (919) 966-9185.

Conflicts of interest
The authors disclose no conflicts.

Funding
Supported by grants from the National Institutes of Health (R01 DK094738 and T32 DK07634).

1. Which of the following conditions are clearly recognized as causing symptoms
   a. acute diverticulitis
   b. uncomplicated diverticular disease
   c. segmental colitis associated with diverticulosis
   d. Chronic recurrent diverticulitis

**True or False**

2. An episode of diverticulitis may trigger new onset IBS

3. Patients with diverticulosis can eat nuts, corn and seeds without fear of precipitating diverticulitis

4. A patient who suffers acute diverticulitis after having had a good quality colonoscopy exam in the recent past does not need a repeat colonoscopy after resolution of the acute episode

5. Recurrence of diverticulitis after the first episode is <25%, more than 2 episodes of diverticulitis is <5%

6. The association of a low fiber diet and diverticulosis is based on rigorous scientific basis

7. Patients with constipation are more likely to develop diverticulosis

8. Risk of diverticulitis after finding asymptomatic diverticulosis on colonoscopy is about 1% over 11 years.

9. Young individuals with acute diverticulitis do not necessarily have more “virulent” disease, prophylactic surgery not recommended

10. A clinical and radiographic diagnosis of uncomplicated diverticulitis requires treatment with antibiotics to prevent progression to complicated diverticulitis.

11. After a second episode of diverticulitis, surgery should be recommended