Review

Sigmoid Diverticulitis
A Systematic Review

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IMPORTANCE Diverticulitis is a common disease. Recent changes in understanding its natural history have substantially modified treatment paradigms.

OBJECTIVE To review the etiology and natural history of diverticulitis and recent changes in treatment guidelines.

EVIDENCE REVIEW We searched the MEDLINE and Cochrane databases for English-language articles pertaining to diagnosis and management of diverticulitis published between January 1, 2000, and March 31, 2013. Search terms applied to 4 thematic topics: *pathophysiology*, *natural history*, *medical management*, and *indications for surgery*. We excluded small case series and articles based on data accrued prior to 2000. We hand searched the bibliographies of included studies, yielding a total of 186 articles for full review. We graded the level of evidence and classified recommendations by size of treatment effect, according to the guidelines from the American Heart Association Task Force on Practice Guidelines.

FINDINGS Eighty articles met criteria for analysis. The pathophysiology of diverticulitis is associated with altered gut motility, increased luminal pressure, and a disordered colonic microenvironment. Several studies examined histologic commonalities with inflammatory bowel disease and irritable bowel syndrome but were focused on associative rather than causal pathways. The natural history of uncomplicated diverticulitis is often benign. For example, in a cohort study of 2366 of 3165 patients hospitalized for acute diverticulitis and followed up for 8.9 years, only 13.3% of patients had a recurrence and 3.9%, a second recurrence. In contrast to what was previously thought, the risk of septic peritonitis is reduced and not increased with each recurrence. Patient-reported outcomes studies show 20% to 35% of patients managed nonoperatively progress to chronic abdominal pain compared with 5% to 25% of patients treated operatively. Randomized trials and cohort studies have shown that antibiotics and fiber were not as beneficial as previously thought and that mesalamine might be useful. Surgical therapy for chronic disease is not always warranted.

CONCLUSIONS AND RELEVANCE Recent studies demonstrate a lesser role for aggressive antibiotic or surgical intervention for chronic or recurrent diverticulitis than was previously thought necessary.

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Before effective broad-spectrum antibiotics were available, diverticulitis was a devastating disease associated with substantial morbidity and mortality. Now, most cases resolve with antibiotic therapy. Because of the fear of complications associated with perforation, if multiply recurrent disease occurs, surgical resection of the involved colon is performed.[1] However, recent advances in the understanding of the disease's pathophysiology and natural history have led to substantial changes in diverticulitis treatment guidelines.

Over the past decade, 4 key innovations have changed the thinking about and management of diverticulitis: complicated diverticulitis (ie, with perforation, abscess, or phlegmon) is now reliably distinguished from uncomplicated disease by computed tomography (CT)[2]; large clinical and administrative databases have facilitated more complete follow-up of large populations, resulting in changes in the understanding of the natural history of diverticulitis, clinical and behavioral risk factors for the disease, and what the indications and outcomes of its treatments are; similarities exist between the physiology and inflammatory processes for diverticulitis, irritable bowel syndrome, and inflammatory bowel disease. These insights led to new approaches to managing chronic disease and preventing recurrent diverticulitis.[3] Surgeons now pursue less invasive intervention, increasing the use of percutaneous drainage, intraperitoneal lavage, and minimally invasive surgical techniques.[4]

Diverticulitis treatments are rapidly evolving. This review summarizes recent medical literature describing the pathophysiology and natural history of chronic and recurrent sigmoid diverticulitis and reviews new recommendations for the medical management and indications for surgery. Four key questions are addressed: (1) What is known about the pathophysiology of diverticulitis? How do diverticula become inflamed, and what are associated risk factors? (2) How have large observational trials clarified the natural history of diverticulitis that is managed nonoperatively? (3) What are the proposed mechanisms, options, and outcomes of medical therapy for diverticulitis? and (4) What are the indications for surgical treatment of diverticulitis?

Methods

Data Sources

We performed a systematic review of the MEDLINE and Cochrane databases, using separate search terms for each of the 4 key questions (eAppendix in the Supplement), for articles published between January 1, 2000, and March 31, 2013. Broad search terms for question 1 included (*pathophysiology* or *etiology* or *pathogenesis*) and *diverticulitis*; for question 2, broad search terms were (*natural history* or *outcome*) and *diverticulitis*; for questions 3 and 4, broad search terms were (*chronic* or *acute* or *smoldering* or *recurrent*) and *diverticulitis* and (*management* or *treatment*). Searches were limited to English language articles published since 2000 that addressed diverticulitis in adult humans. All articles were then combined into a single list, and duplicates were excluded, resulting in 1383 abstracts and articles for review.

Study Selection

We reviewed abstracts and excluded commentary or opinion pieces, review articles that reported data present in other included references, articles based on data accrued before 2000, and articles containing primary data duplicated in another included article. In the case of duplicate presentation of data, we selected articles with the most recent analyses. We excluded small case series with fewer than 30 patients, except for the search of articles for question 1 regarding pathophysiology. We supplemented our automated search by manually searching additional references from the bibliographies of included studies, yielding a total of 186 articles for full review.

Data Extraction

Studies selected for inclusion were reviewed according to guidelines from the Strengthening the Reporting of Observational Studies in Epidemiology.[5] We graded the level of evidence and classified recommendations by size of treatment effect, according to the guidelines from the American Heart Association Task Force on Practice Guidelines.[6] We compared the resulting recommendations with those of the most comprehensive recent clinical practice guidelines on management of diverticulitis.[4]

Results

Eighty articles were selected from the 186 reviewed. Articles were excluded if there was an absence of data regarding the topic of interest, if the majority of data accrued prior to 2000, and if it was a small case series. Articles were organized into 4 categories consistent with the study questions and summarized below.

Pathophysiology and Risk Factors

Twenty-five articles fulfilled criteria and were included in this review of the pathophysiology of diverticulitis. Although *colonic diverticulum* refers specifically to a thin-walled outpouching of the mucosa and serosa, absent the muscularis, and *diverticulosis* refers to the presence of many diverticula, *diverticulitis* is distinguished by the presence of inflammation. If untreated, diverticular inflammation may resolve, become chronic, or progress, leading to bacterial translocation or even perforation of the colon wall at the inflamed site.

The prevailing explanation for colonic diverticula formation posits that altered bowel motility leading to increased intraluminal pressure causes mucosal outpouching adjacent to the vasa recta. Whether diverticula, once formed, can spontaneously resolve is unknown. The mechanism by which asymptomatic diverticula become inflamed and perforate (diverticulitis) is still under investigation but is plausibly associated with altered gut motility and increased pressure combined with a deranged colonic microenvironment. In recent series, when ex vivo colonic tissue from patients with diverticulitis was exposed to chemicals that contract or relax smooth muscle, the response was significantly abnormal with increased hypercontractility and lower maximum relaxation responses.[7-9] These findings are consistent with neuropeptide abnormalities and the altered histologic appearance of muscle and nerves in the bowel wall of patients with diverticulitis compared with healthy patients. For example, reduced serotonin transporter expression and fewer interstitial cells of Cajal were found among patients with diverticulitis but not among those with normal colons or with noninflamed diverticula.[10-12] Moreover, patients who ingest calcium channel blockers, which reduce smooth muscle contractility, appear to have a re-

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duced risk of perforated diverticulitis compared with patients who do not take calcium blockers.[13]

Recurrent or chronic diverticulitis displays chemical and histological similarities to inflammatory bowel disease and irritable bowel syndrome.[14,15] These diagnoses may be concurrent, sequential, or entirely separate. Although the mechanisms of inflammation are unknown, higher levels of histamine, tumor necrosis factor α (TNF-α), and matrix metalloproteinases have been identified in colonic biopsies from patients with irritable bowel syndrome, inflammatory bowel disease, and diverticulitis.[16-18] Other common evidence of chronic inflammation includes the presence of granulomas and infiltrating lymphocytes. Ultimately, however, there were minimal mechanistic data to support or refute a common or related pathway and key distinguishing features of each persist. For example, a hallmark of *irritable bowel syndrome* is relief of crampy pain upon defecation; *inflammatory bowel disease* is characterized by mucosal injury frequently resulting in bloody diarrhea; *diverticulitis* is by definition associated with diverticula.

Lifestyle risk factors such as diet, smoking, and medication use have long been considered important in the etiology of diverticular disease. A prospective UK population-based cohort study found a relative risk of 0.69 (95% CI, 0.55-0.86) of diverticular disease among vegetarians compared with meat eaters.[19] The relationship between dietary fiber and diverticula is not clear, however. A large cohort study of patients undergoing colonoscopy found that those who reported the highest fiber intake were at highest risk of diverticulosis.[20] A longitudinal survey of 47 228 health professionals recently reported that incident diverticulitis was not associated with nut, corn, or popcorn ingestion and that increased nut intake was associated with lower risk of diverticulitis.[21] Smoking and obesity have been linked to diverticulitis and to complicated diverticulitis in several large cohort studies,[22-26] whereas increased physical activity is associated with decreased risk.[27,28] Nonsteroidal anti-inflammatory drugs, opioids, and corticosteroids have been convincingly associated with increased risk of perforated diverticulitis.[29-32] A unifying hypothesis to integrate these diverse lifestyle effects and their contribution to pathophysiology has not been advanced.

Natural History

We defined the *natural history of diverticulitis* as the longitudinal outcomes for patients whose disease was managed nonoperatively. Six articles fulfilled criteria and were reviewed. Most of the data regarding natural history were focused on nonoperative outcomes and specifically on risk of recurrence, that is, subsequent acute diverticulitis after an asymptomatic interval, rather than on chronic disease in which there is no asymptomatic interval.

Risk of Recurrence

Two large multicenter studies[33,34] confirmed that recurrence is rare and is a relatively benign process for the substantial majority of patients. Broderick-Villa et al[34] reported on 2366 of 3165 patients (75%) hospitalized with acute diverticulitis and treated nonoperatively in the Kaiser Permanente system. Eighty-six percent of those patients required no further inpatient care for diverticulitis over the 8.9 years of follow-up. Recurrence occurred in only 13.3% of patients and only 3.9% had a second recurrence. No patient with a second recurrence required an operation, and repeat recurrences plateaued after 4 episodes. Although the risk for a second recurrence increased to 29% among those with a first recurrence, the authors concluded that recurrence overall is rare and therefore does not warrant elective colectomy.

Binda et al[33] obtained complete follow-up for 320 patients treated with antibiotics in 17 Italian hospitals after admission for acute diverticulitis. Over a mean period of 10.7 years, 61% of patients required no further inpatient care. Twenty-two percent of patients had persistent or recurrent symptoms requiring hospitalization, and 17% had a recurrent episode resulting in an emergency operation. In adjusted analyses, the risk of recurrence was greatest among patients younger than 50 years and among those with at least 3 previous episodes. The authors noted that unlike other studies of recurrence, episodes were not clustered into the first 2 years or even the first 5 years following the index diagnosis.

Complications of Diverticulitis

A large population-based study linked primary care and hospital-based data to examine patterns of morbidity associated with complicated diverticulitis among 2950 patients hospitalized in the United Kingdom.[35] Seventy-two percent of patients had no antecedent episodes of diverticulitis, and 2 or more prior episodes were not associated with abscess or stricture formation, although they were associated with increased risk of fistula. Although most serious complications of diverticulitis were linked to the first episode, not to recurrence, they were consequential. Compared with age- and sex-matched cases in the general population, patients with perforation or abscess had 4.5-fold increased risk of death in the ensuing year.

Shifting Morphology

Morphologic characteristics of recurrent diverticulitis may differ considerably from the first episode. A single institution study[36] of 60 patients with recurrent disease after initial medical management of uncomplicated diverticulitis compared CT scans from the index and second admission. At the time of recurrence, 6 patients (10%) had complicated diverticulitis and 3 underwent an urgent Hartmann procedure. Among the 54 patients with a CT-defined recurrence that was uncomplicated, 19 (35%) had a morphologically distinct recurrence of diverticulitis at an average of 8 cm from the previous site.

Chronic Pain

Nelson et al[37] analyzed a cohort of 99 patients with complicated diverticulitis whose care was managed nonoperatively with follow-up over 76 months. Forty-six patients had recurrent disease and 20 underwent an elective resection more than 6 months after the initial episode. Unlike Binda et al, the authors found no difference between recurrence or need for emergency operation based on age. Although about half of the patients had recurrent or chronic disease, none died of complications of diverticulitis. Similarly, a longitudinal survey of 124 patients with diverticular disease who were managed medically over 7 years reported that 34% continued to experience abdominal pain for 3.5 days per month. Odds of chronic pain were increased 4-fold among those who had been previously diagnosed with diverticulitis.[38]

Until recently, recommendations for management and prevention of diverticulitis were well-established. Patients with perforation, abscess, fistula, or stricture were managed definitively with an

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Table 1. Medical Management of Chronic and Recurrent Diverticulitis

Source	Evidence Level[a]	Evidence Class[b]	Sample Size[c]	Study Design	Intervention	Primary Outcome(s)	Main Finding(s)	*P* Value
Alonso et al,[39] 2010	B	IIb	70	Cohort	7-d Oral antibiotics	Symptom relief	97% Outpatient symptom relief	
Bianchi et al,[40] 2011	C	IIb	1660	Meta-analysis	Rifaximin + fiber vs fiber	1-y Symptom relief	29% Rifaximin + fiber relief	.001
Brandimarte et al,[41] 2004	C	IIa	86	Cohort	Mesalamine and rifaximin, then 8-wk mesalamine	Symptom relief	78% Asymptomatic	
Chabok et al,[42] 2012	A	III	623	RCT	Antibiotics vs none	Recurrence prevention	16 % Recurrence in both groups	.88
Comparato et al,[43] 2007	B	IIa	244	RCT	High- vs low-dose rifaximin vs high- vs low-dose mesalamine	Symptom relief	Mesalamine > rifaximin high dose > low dose	
De Korte et al,[44] 2011	B	III	3 Studies	Retrospective cohort study + RCTs	Antibiotics vs none	Symptom relief	No significant difference	
Dughera et al,[45] 2004	B	IIa	76	RCT	Oral probiotics vs placebo	Symptom relief, recurrence prevention	Reduced symptoms with treatment, but recurrence no difference	.28
Hjern et al,[46] 2007	B	III	311	Retrospective cohort	Antibiotics vs none	Symptom relief	29% Recurrence in treated vs 28% in not treated	
Mizuki et al,[47] 2005	B	IIa	65	Cohort	10-d oral antibiotics and gradual diet resumption	Recurrence prevention	25% Recurrence	
Moya et al,[48] 2012	C	III	76	Cohort	IV vs oral antibiotics	Symptom relief, cost	No significant difference	
Ribas et al,[49] 2010	B	IIb	50	RCT	Short vs long course	Symptom relief	No significant difference	
Ridgeway et al,[50] 2009	B	IIa	79	RCT	Oral vs IV antibiotics	Symptom relief	No significant difference	
Shabanzadeh et al,[51] 2012	B	III	3 Studies	Review	Antibiotics vs none	Recurrence prevention	No significant difference	
Tursi et al,[52] 2002	B	IIb	193	RCT	Cyclic combined rifaximin and mesalamine vs cyclic rifaximin only	Recurrence prevention	3% Recurrence combined therapy vs 12% rifaximin only	.005

Abbreviations: IV, intravenous; RCT, randomized clinical trial.

[a] Level of evidence indicates the precision of the estimate of treatment effect.

[b] Class of recommendation indicates the size of the treatment effect. Level A indicates the strongest weight of evidence; Level B is intermediate; Level C indicates the lowest rank of evidence, for example, when evidence is based on expert consensus.

[c] Sample size indicates the number of study patients for whom complete data were available.

urgent or elective sigmoid colon resection. Those with uncomplicated disease were managed with antibiotics and bowel rest. In the event of a recurrence or failure to resolve, patients were scheduled for an elective sigmoid colectomy. The rationale for elective surgery was largely preventive, based on concerns that recurrence would result in progressively increased risk of sepsis or the need for a colostomy. More recently, emerging medical therapies are under investigation as a potentially lower-risk means of prevention.

Emerging Medical Therapies

The goals of medical therapy for diverticulitis are to decrease inflammation acutely, to prevent recurrence, and to manage chronic symptoms. With the advantage of more current pathophysiologic data and large database-derived studies of natural history, new medical approaches toward these goals have been proposed. A total of 14 articles on existent or emerging medical therapies met criteria for review (**Table 1**); however, the quality of most available evidence was poor (level B or C) and only 1 article met level A criteria.

Fiber

The traditional approach to prevention of recurrence of diverticulitis has been to increase dietary or supplemental fiber. Ünlü et al[53] recently published a systematic review of the evidence supporting this longstanding recommendation. The authors found 4 studies on treatment and no studies on prevention of recurrence that met inclusion criteria. One randomized trial showed no treatment effect of fiber ingestion on resolution of symptoms, whereas the other 3 studies did show a significant treatment advantage with fiber ingestion. The authors concluded that recommendations for ingestion for dietary fiber are based on inconsistent level 2 and level 3 evidence. None of the studies examined met criteria for inclusion in our study because the data were collected prior to 2000. A systematic review[40] of 4 trials of fiber vs rifaximin plus fiber found that the combined therapy was slightly but significantly more effective in obtaining symptom relief and preventing complications at 1 year. Two of the 4 studies were based on data from prior to 2000, the third was not explicitly about diverticulitis, and the fourth did not state what years data were collected.

Antibiotic Therapy

A major change in the approach to the management of acute uncomplicated diverticulitis is the progressively reduced use of antibiotics. Specifically, prospective randomized and open trials have shown no advantage of intravenous over oral antibiotics, and there-

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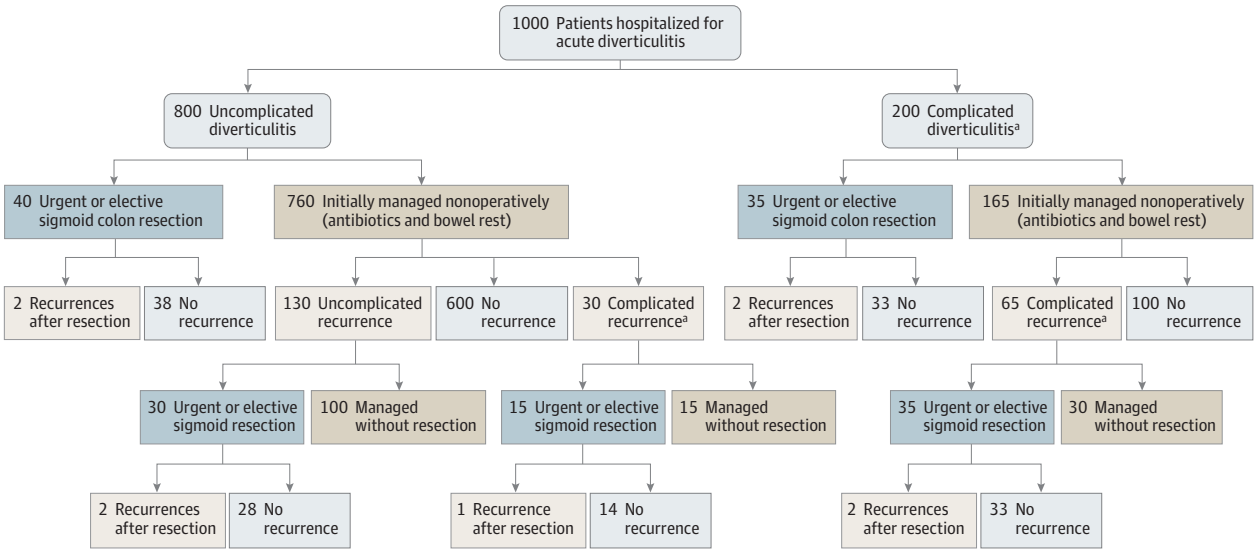
Figure. Clinical Outcomes Based on Current Treatment Standards for a Hypothetical Cohort of 1000 Patients Presenting With Acute Diverticulitis



Data derived from the following studies of diverticulitis outcomes: Ambrosetti et al,[59] Broderick-Villa et al,[34] Nelson et al,[37] Kaiser et al,[60] Dharmarajan et al,[57] Anaya et al,[71] and Hall et al.[70]

[a]Complicated diverticulitus refers to the presence of perforation, abscess, or phlegmon.

fore have recommended outpatient management.[39,47-50] In addition, more recent data indicate equivalent efficacy of a 4-day vs 7-day course of an appropriately broad-spectrum antibiotic.[54] This study recommended short-course therapy with ertapenem but rifaximin has also been favored for chronic or recurrent diverticulitis due to limited gut absorption and low cost.[52] A Cochrane review[51] of antibiotic use in acute uncomplicated diverticulitis found that, in spite of published guidelines, the best available data[42] do not support use of antibiotics. A more inclusive systematic review[44] and a retrospective cohort study[46] have also found that antibiotic use has no effect on complications, need for surgery, or recurrence rate. Thus, newer data support a noninterventional policy for treatment of uncomplicated diverticulitis.

Probiotics

The rationale for use of probiotics in diverticular disease is based on the theory that a deranged colonic microenvironment, including abnormal gut flora, precipitates chronic inflammation and recurrent disease. One study of probiotics met inclusion criteria.[45] The authors randomized 83 consecutive patients, whose index episode was resolved after treatment with rifaximin or ciprofloxacin, to receive an oral polybacterial lysate suspension or placebo twice daily for 2 weeks every month within 3 months after an acute attack. Complete follow-up data were available for 76 patients. The probiotic group reported significantly less abdominal pain, bloating, and fever, but there was no significant difference in recurrence rates (2 of 41 vs 5 of 35).

Anti-inflammatory Medication

A recent appreciation of chronic mucosal inflammation has sparked interest in alterations of the colonic microenvironment and the potential for use of anti-inflammatory medication. A head-to-head comparison of anti-inflammatory treatment using mesalamine vs antibiotic therapy with rifaximin demonstrated significantly reduced symptoms after 6 to 12 months of high-dose cyclic mesalamine.[43] A nonrandomized comparison[52] of rifaximin and mesalazine vs rifaximin alone showed 3% recurrence in the combined medication group and 13% recurrence in the rifaximin alone group over 1 year. A cohort study from the same authors[41] showed that combined mesalamine and rifaximin followed by mesalamine alone led to resolution of symptoms for nearly all patients but recurrent disease among 2% at 8 weeks. The duration of follow-up for this study was notably short; most studies of recurrence require a minimum asymptomatic period of 3 to 6 months from the time of the index diagnosis before the next symptom onset.

Current Indications for Surgical Treatment

Surgery for acute diverticulitis is indicated for patients who present with sepsis and diffuse peritonitis and for patients whose condition did not improve with medical therapy, percutaneous drainage, or both.[4,55] Surgical options include simple colostomy formation in the setting of profound inflammation, traditional sigmoid resection with colostomy (Hartmann procedure), and sigmoid resection with a primary colocolonic or colorectal anastomosis with or without a diverting loop ileostomy. Based on selection criteria, we identified 35 relevant articles describing indications for surgical therapy (in the Supplement). Most articles met only level B or C criteria and none met level A criteria, thereby limiting the conclusions that can be drawn.

Urgent Setting

In 2 cohort studies, the presence of complicated diverticulitis, abscess, free intraperitoneal air on computed tomography alone, or all 3 did not mandate an urgent operation among hemodynamically stable patients.[56,57] Still, up to 25% of patients with evidence of abscess, perforation, or both underwent surgery during the acute in-

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Table 2. Level of Recommendation for Systematic Review of Recent Literature Compared to Current Practice Guidelines for Prevention of Recurrent Sigmoid Diverticulitis

Intervention	Current Evidence Review and Guidelines[a]	Recommendation[b] Level	Recommendation[b] Class
Recovered From 1 or More Uncomplicated Episode			
Fiber supplementation		C	IIa
Evidence review	Not addressed.		
Practice guidelines[c]	Long-term fiber supplementation may prevent recurrence (ASCRS)		
Antibiotic use		A	III
Evidence review	For acute uncomplicated diverticulitis, a Cochrane review,[42,51] a systematic review,[44] and a retrospective cohort study[46] do not support use of antibiotics for prevention of recurrence		
Practice guidelines[c]	Not addressed		
Probiotics		C	IIb
Evidence review	A trial of 83 patients randomized to receive oral polybacterial lysate vs placebo reported no significant difference in recurrence rates (P = .2 using χ^2 comparison of proportions)[45]		
Practice guidelines[c]	Not addressed		
Mesalamine		B	IIa
Evidence review	Small uncontrolled trials indicate approximately 3% recurrence rate over 1 y with use of combined mesalamine and rifaximin[52]		
Practice guidelines[c]	Not addressed		
Avoiding nuts and seeds		A	III
Evidence review	A survey of 47 228 health professionals reported that incident diverticulitis was not associated with nut, corn, or popcorn ingestion and that increased nut intake was associated with lower risk of diverticulitis[21]		
Practice guidelines[c]	Not addressed		
Surgical resection		B	IIb
Evidence review	Several cohort studies compared recurrence among patients who treated operatively vs nonoperatively. They noted that a complicated recurrence occurred in fewer than 5% of patients treated nonoperatively[62,69-73]; the occurrence of multiple subsequent episodes did not increase the risk of major complications of diverticulitis[74]; and complicated diverticulitis most commonly occurred during the first episode rather than during recurrent episodes.[75-78] Taken together, these data support a real but limited role for surgery in preventing recurrence of diverticulitis		
Practice guidelines[c]	The decision to recommend elective sigmoid colectomy after recovery from acute diverticulitis should be made on a case-by-case basis (ASCRS)	B	I
	Indications for surgery most frequently reported include: ≥2 episodes of diverticulitis severe enough to cause hospitalization and any episode of diverticulitis associated with contrast leakage, obstructive symptoms, or an inability to differentiate between diverticulitis and cancer (WGO)	C	IIb
	Elective sigmoid resection may not be necessary after any specific number of episodes of uncomplicated diverticulitis or with any definite age thresholds (SSAT)	C	IIb
	Recurrent diverticulitis is rare after surgery (1%-10%) (WGO)	C	IIb
	Extraluminal air, contrast or abscess is a predictor of an adverse natural history and may be helpful in determining the need for surgery (ASCRS)		

(continued)

dex hospitalization.[58-60] Elective surgery after successful nonoperative management of an episode of complicated diverticulitis was often recommended due to rates of recurrence, hospital readmission, and need for elective resection as high as 50 to 70,[34,58-61] especially among those with a pelvic or paracolic abscess that required percutaneous drainage.[59] However, few of these patients needed an emergency operation.[37,62]

Preoperative Colonoscopy

Elective evaluation of patients who recovered from an episode of acute diverticulitis was controversial. Some authors advocated colonoscopy to confirm the diagnosis and exclude malignancy.[63,64] Others reported no increased detection of advanced neoplasia in patients with a typical presentation of acute diverticulitis.[65-68]

Recurrent Diverticulitis

Among studies comparing surgical with nonsurgical management, several important considerations challenged routine elective surgical therapy for recurrent or chronic diverticulitis. First, complicated recurrence after recovery from an uncomplicated episode of diverticulitis occurred in fewer than 5% of patients whose care was managed nonoperatively.[62,69-73] Second, the occurrence of multiple sub-

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Table 2. Level of Recommendation for Systematic Review of Recent Literature Compared to Current Practice Guidelines for Prevention of Recurrent Sigmoid Diverticulitis (continued)

Intervention	Current Evidence Review and Guidelines[a]	Recommendation[b] Level	Recommendation[b] Class
Young Patients (≤50 y)			
Surgical resection		C	IIb
Evidence review	Several cohort studies found modestly higher rates of recurrence among patients younger than 40 y than among those older than 40 y[71,72,85,86]; however, these data were countered by other cohort studies that did not document a more aggressive disease course based on age[87-93]		
Practice guidelines[c]	The decision to recommend elective sigmoid colectomy after recovery from acute diverticulitis should be made on a case-by-case basis (ASCRS)	B	I
	There is no clear consensus regarding whether younger patients (<50 y) are at increased risk of complications; however, they are probably at increased risk of recurrent diverticulitis (ASCRS)	C	IIa
	In young patients with no comorbid conditions, elective surgery after a single episode of diverticulitis is still a reasonable recommendation (WGO)	C	IIa
	Elective sigmoid resection may not be necessary after any specific number of episodes of uncomplicated diverticulitis or with any definite age thresholds (SSAT)		
Immunocompromised Patients			
Surgical resection			
Evidence review	Cohort studies indicate that immunocompromised patients have higher risk of complicated recurrence, perforation, and emergency surgery, resulting in a low threshold for operation[97,98]; however, risk of postoperative morbidity and mortality is also higher among these patients[94]	C	IIb
Practice guidelines[c]	Immunocompromised patients are more likely to present with perforation and to fail medical management, so a lower threshold for urgent and for elective surgery should be applied to them (ASCRS)	C	IIa
	Immunocompromised patients (including using steroids and immunosuppressive agents or having diabetes, renal failure, malignancy, cirrhosis) have increased risk of freed perforation, increased need for surgery (WGO)		

Abbreviations: ASCRS, American Society of Colon and Rectal Surgeons; SSAT, Society for Surgery of the Alimentary Tract; WGO, World Gastroenterology Organization.

[a] Level of recommendations are based on Gibbons et al.[6]The current practice guidelines are based on Rafferty et al,[4] SSAT practice guidelines,[101] and the WGO practice guidelines.[102]

[b] For the definition of the levels of evidence and class, see the Table 1 footnotes. .

[c] ASCRS represents 2006[4,101,102]; SSAT, 2007[101]; and WGO, 2007 practice guidelines.[102]

sequent episodes did not increase the risk of major complications of diverticulitis.[74] Third, complicated diverticulitis most commonly occurred during the first episode, rather than during recurrent episodes.[75-78] Fourth, 5% to 25% of postoperative patients had recurrent or unresolved abdominal symptoms.[33,79-84]

Patient Characteristics

Although several articles found modestly higher rates of recurrence and need for resection among patients younger than 50 years,[71,72,85,86] most did not document a greater likelihood of perforation or worse outcomes among this cohort.[87-93] Young patients do have a longer life expectancy (thus, increased potential for future episodes and more to gain from prevention) and lower operative risk.[94-96] In general, however, the data supported decision making for operative therapy based on the severity of symptoms and complexity of the disease rather than the age of the patient.[72,85] Exceptions to the current rule are immunosuppressed patients, such as those with solid organ transplants, collagen vascular diseases, steroid use, malnutrition, and chronic renal failure, who had 5-fold greater risk of complicated recurrence and perforation compared with nonimmunosuppressed patients (36% vs 7%).[97,98] Thus, the threshold for immunosuppressed patients to proceed with elective resection after 1 or more episodes is lower, provided that the surgical risk due to these same comorbidities is not prohibitive.[94]

Discussion

Sigmoid diverticulitis is an increasingly common and costly disease endemic in industrialized nations. Between 1998 and 2005, US hospital admissions for diverticulitis increased by 26% and elective operations by 29%.[99] As incidence rates are increasing, the understanding and management of sigmoid diverticulitis is evolving. Collectively, several recent studies indicate a pathogenetic role for inflammation in diverticulitis that may be similar to that of irritable bowel syndrome, inflammatory bowel disease, or both, based on common histologic findings such as granulomas, infiltrating lymphocytes, TNF-α, histamine, and matrix metalloproteinases. However, studies of the etiology and pathophysiology of diverticulitis were limited by a focus on associative rather than causal pathways. Similarly, while lifestyle alterations were often recommended in response to the first incidence of diverticulitis, we found no studies testing the effect of lifestyle modifications on the disease course.

The risk of recurrence among patients with uncomplicated diverticulitis was approximately 13% to 36% and the risk of future emergency surgery was approximately 4% to 7%. Therefore, the available data do not support a routine policy of prophylactic sigmoidectomy on clinical grounds alone (**Figure**). In addition, given the possibility of shifting morphology,[36] a prophylactic resection may

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Table 3. Level of Recommendation for Systematic Review of Recent Literature vs Current Practice Guidelines for Management of Chronic Sigmoid Diverticulitis

Intervention	Current Evidence Review and Guidelines[a]	Recommendation[b] Level	Recommendation[b] Class
Fiber supplementation			
Evidence review	A systematic review of fiber vs rifaximin + fiber found that the combined therapy was significantly more effective in obtaining symptom relief at 1 y; Use of fiber was not compared with nonuse[40]	C	IIb
Practice guidelines	Not addressed		
Antibiotic use			
Evidence review	One study found 90% resolution of symptoms among patients using rifaximin over 1 y; Use of rifaximin alone was not compared with nonuse[52]	C	IIb
Practice guidelines	Not addressed		
Probiotics			
Evidence review	A trial of 83 patients randomized to receive oral polybacterial lysate vs placebo reported significantly less abdominal pain, bloating, and fever[45]	B	IIa
Practice guidelines	Not addressed		
Mesalamine			
Evidence review	A randomized comparison of mesalamine vs rifaximin demonstrated significantly reduced symptoms after 6-12 mo of high-dose cyclic mesalamine.[43]	B	IIa
Practice guidelines	Not addressed		
Confirmation of diagnosis			
Evidence review	Most cohort studies reported no benefit of colonoscopy among patients following acute diverticulitis[65-68]; however, several large cohort studies reported a 2%-3% incidence of cancer and up to 26% incidence of adenoma[34,63,64]	C	IIa
Practice guidelines[c]	Colonoscopy (or contrast enema + sigmoidoscopy) should be uniformly recommended after recovery from acute diverticulitis (ASCRS)	C	I
	Care must be taken to exclude other diagnoses (IBS, ischemic colitis) (WGO)	C	IIa
	Colonoscopy or barium enema is indicated 6-8 wk following hospital discharge to document the extent of diverticula and exclude cancer (SSAT)	C	I
Elective Surgical Resection			
Evidence review	No study prospectively compared resection to nonresection for chronic diverticulitis. However, several cohort studies examined aspects of chronic disease. Specifically, 5%-25% of postoperative patients had recurrent or unresolved abdominal symptoms[33,79-84]	C	IIb
Practice guidelines[c]	The decision to recommend surgery should be influenced by whether there are persistent symptoms after the acute episode (ASCRS)	C	I
	Sigmoid resection provides complete resolution of smoldering diverticulitis in 70% of cases (WGO)	C	IIa

Abbreviations: ASCRS, American Society of Colon and Rectal Surgeons; IBS, irritable bowel syndrome; SSAT, Society for Surgery of the Alimentary Tract; WGO, World Gastroenterology Organization.

[a] Level of recommendations are based on Gibbons et al.[6] The current practice guidelines are based on Rafferty et al,[4] SSAT practice guidelines,[101] and the WGO practice guidelines.[102]

[b] For the definition of the levels of evidence and class, see the Table 1 footnotes.

[c] ASCRS represents 2006[4,101,102]; SSAT, 2007[101]; and WGO, 2007 practice guidelines.[102]

actually miss the site of future inflammation, although these data should be confirmed in a larger cohort. Recent data also suggest that combination medical therapy, particularly rifaximin and mesalamine, may contribute to reduced symptoms in chronic disease. Further investigation into commonalities with irritable bowel syndrome and inflammatory bowel disease may provide insight and more opportunities for crossover of medical therapies.

Whether and when to perform elective surgery for chronic or recurrent episodes of uncomplicated diverticulitis remain controversial topics. The traditional recommendation for surgical resection after 2 such episodes was based on outdated evidence suggesting that the success of nonoperative treatment diminished with each subsequent recurrence.[100] Patients were told that an elective operation would permit primary anastomosis, whereas a potential emergency would necessitate fecal diversion with a colostomy. This recommendation has been challenged by more recent natural history information and recent studies of operative vs nonoperative management.

The current clinical practice guidelines[4,101,102] were largely written for a surgical audience and may be oriented toward the patient population seen by surgeons (**Table 2** and **Table 3**). However, no corresponding clinical practice guideline specifically targets primary care clinicians who encounter a different spectrum of disease in the primary care setting. Despite current clinical guidelines, we found minimal data to support the prevention of recurrence with fiber ingestion. We found that immunocompromised patients did not have a higher risk of mortality with recurrence. Nor did elective surgery always prevent recurrence or treat chronic disease. Up to 25% of pa-

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tients who underwent an operation for chronic diverticulitis had no sustained postoperative symptom relief. Finally, we found mixed data regarding the utility of routine postinflammation colonoscopy. In spite of these data, practice parameters from surgical societies[4,103] stipulate flexible endoscopy to distinguish diverticulitis from other causes of segmental colitis (eg, cancer, Crohn disease, and ischemic colitis).

Our review is subject to a number of limitations which should be noted. Throughout the review, the level of evidence was lower grade, thereby limiting our interpretation and conclusions. Most importantly, studies of diverticulitis were limited by the lack of a standard terminology for aspects of the disease, which resulted in some difficulty commenting across studies. For example, some articles clearly distinguished between complicated and uncomplicated diverticulitis while others did not. Some referred only to diverticular disease and did not discuss diverticulitis per se. Very few studies included outpatient data, and therefore we were unable to draw conclusions about resolution or recurrence of symptoms in this population.

In spite of these limitations, population-based data indicate that peritonitis and sepsis are rare complications of incident diverticulitis and are even more rare complications of recurrent disease. Therefore, although septic peritonitis remains a clear indication for urgent operation, there are few other indications for an urgent colectomy with or without colostomy formation. Moreover, several recommendations meant to reduce the risk of recurrence were based on associations with an index episode and have not been tested longitudinally. Future studies of causality and interventions to reduce recurrence are needed, especially given the increasing incidence of diverticulitis.

Conclusions

In summary, although decision making should be based on individual clinical characteristics and patient preferences, the current data support a substantially reduced role for aggressive antibiotic and surgical intervention in recurrent and chronic diverticulitis.

ARTICLE INFORMATION

Author Contributions: Dr Morris had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Morris, Regenbogen, Hardiman.
Acquisition of data: Morris, Regenbogen, Hardiman.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.
Administrative, technical, or material support: All authors.

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Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Mary McGrae McDermott, MD, at mdm608@northwestern.edu.

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