

## Update on the management of sigmoid diverticulitis

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### Abstract

Diverticular disease and diverticulitis are the most common non-cancerous pathology of the colon. It has traditionally been considered a disease of the elderly and associated with cultural and dietary habits. There has been a growing evolution in our understanding and the treatment guidelines for this disease. To provide an updated review of the epidemiology, pathogenesis, classification and highlight changes in the medical and surgical management of diverticulitis. Diverticulitis is increasingly being seen in young patients (< 50 years). Genetic contributions to diverticulitis may be larger than previously thought. Potential similarities and overlap with inflammatory bowel disease and irritable bowel syndrome exist. Computed tomography imaging represents the standard to classify the severity of diverticulitis. Modifications to the traditional Hinchey classification might serve to better delineate mild and intermediate forms as well as better classify chronic presentations of diverticulitis. Non-operative management is primarily based on antibiotics and supportive measures, but antibiotics may be omitted in mild cases. Interval colonoscopy remains advisable after an acute attack, particularly after a complicated form. Acute surgery is needed for the most severe as well as refractory cases, whereas elective resections are individualized and should be considered for chronic, smoldering, or recurrent forms and respective complications (stricture, fistula, etc.) and for patients with factors highly predictive of recurrent attacks. Diverticulitis is no longer a disease of the elderly. Our evolving understanding of diverticulitis as a clinical entity has led into a more nuanced approach in both the medical and surgical management of this common disease. Non-surgical management remains the appropriate treatment for greater than 70% of patients. In individuals with non-relenting, persistent, or recurrent symptoms and those with complicated disease and sequelae, a segmental colectomy remains the most effective surgical treatment in the acute, chronic, or elective-prophylactic setting.

**Key Words:** Diverticulitis; Epidemiology; Antibiotics; Surgical resection; Laparoscopic lavage; Classification

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**Core Tip:** Diverticular disease and diverticulitis—specifically sigmoid diverticulitis—represent the most common non-cancerous pathology of the colon. It has traditionally been considered a disease of the elderly and associated with cultural and dietary habits. There is a constant evolution in our understanding and the treatment guidelines. This review provides an update of the epidemiology, pathogenesis, and classification, and it highlights changes in the medical and surgical management of diverticulitis.

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## INTRODUCTION

Sigmoid diverticulitis is one of the leading gastrointestinal pathologies responsible for inpatient hospitalization in Western society<sup>[1,2]</sup>. With over 300000 hospital admissions resulting in 1.5 million days of inpatient care, diverticulitis places significant economic burden on the healthcare system at 2.4 billion dollars annually<sup>[3-5]</sup>. These numbers are expected to increase substantially with the increasing prevalence of this disease as the population ages and with a higher incidence in younger individuals. Concepts and management recommendations are in constant evolution. The aim of this article is to provide an update on epidemiology, pathogenesis, medical and surgical management of sigmoid diverticulitis.

## EPIDEMIOLOGY AND RISK FACTORS

It has been historically reported that 10%-25% of patients with diverticulosis will eventually develop diverticulitis. This claim largely stems from a benchmark review of the natural history of diverticular disease by Parks<sup>[6]</sup>. In a 1947 review of 47000 radiological images of the colon, the prevalence of diverticulosis was 8.5% amongst the entire cohort, 15% of which were diagnosed with diverticulitis<sup>[7]</sup>. In 1958, a double-contrast barium enema study in 300 patients with diverticulosis estimated the risk of developing diverticulitis at 10% over a 1-5 year period and up to 25% after a 6-10 years follow up period<sup>[8]</sup>.

More recent data suggest that the traditionally quoted lifetime risk of developing diverticulitis from diverticulosis is exaggerated<sup>[9-11]</sup>. In a study on veterans with diverticulosis with an 11 year follow up, there was a 1% risk of diverticulitis as confirmed by computed tomography (CT) or at time of surgery<sup>[9]</sup>. In a cohort of 2100 patients, there was a 4.3% risk of diverticulitis over a median follow up period of 7 years<sup>[12]</sup>.

On the other hand, the overall incidence of diverticulitis has been trending upwards in recent years<sup>[13,14]</sup>. Furthermore, a substantial increase was observed in the prevalence of diverticulitis in younger patients<sup>[15]</sup>. When confining analysis to patients in their 40s, there was an 11% risk of diverticulitis—a 2.5 times higher risk than previously reported for the entire cohort of patients<sup>[12]</sup>. This is in stark contrast to older reports of 1%-2% incidence of diverticulitis in young patients<sup>[16,17]</sup>. In an analysis of the Nationwide Inpatient Sample of 267000 admissions for diverticulitis, the incidence of diverticulitis in patients between 18-44 years old nearly doubled over a 7 year period; of note, over the same time period, there was no change in patients older than 75 years of age and only a moderate increase in the age group in between<sup>[13]</sup>. Similarly, smaller single institution cohorts have also reported higher incidence rates of diverticulitis in young patients ranging from 20% to 26% in some studies<sup>[18,19]</sup>.

Recent reports also suggest potential gender differences among patients with diverticulitis. Nationwide and single institution reviews have noted a male predominance in young patients as opposed to a female predominance in older patients with diverticulitis<sup>[14,18,20,21]</sup>. Lahat *et al*<sup>[21]</sup> demonstrated a male:female ratio of 3:1

in patients with diverticulitis under the age of 45, compared to a 1:2 ratio in patients over 45<sup>[21]</sup>. Similarly in patients admitted for diverticulitis, Schauer *et al.*<sup>[18]</sup> noted a 2:1 male:female ratio in patients under 40 and a 1:1.5 ratio in older patients<sup>[18]</sup>. In reviewing hospital discharge data for diverticulitis in England from 1989 to 2000, the likelihood to be hospitalized under 50 years of age was higher for males, and over the age of 50 higher for females<sup>[20]</sup>. It should be noted that none of the authors offered a plausible explanation for these gender-related observations.

A diet low in fiber has long been regarded as the predominant exogenous or environmental factor leading to the development of diverticular disease. This hypothesis was initially put forth by Painter and Burkitt based on their observation of the extremely low rates of diverticular disease in rural Africa compared to developed Western countries<sup>[22,23]</sup>. Colonic transit studies by Burkitt demonstrated increased colonic transit times (80 h *vs* 34 h) and lower stool weights (110 g/d *vs* 450 g/d) in English individuals consuming a low fiber diet compared to individuals living in rural Uganda respectively<sup>[24]</sup>. It was speculated that the increased transit time would lead to elevated intraluminal pressure particularly on the left side of the colon, thereby promoting the development of diverticular disease. As countries become more developed and Westernized, an increase in the incidence of diverticulitis was commonly observed<sup>[25,26]</sup>. Analyzing a prospective cohort of 47888 United States men over a 4 year period, an inverse association between fiber intake and the development of diverticular disease (relative risks risk ratio 0.58, CI: 0.41-0.83,  $P = 0.01$ ) was found<sup>[27]</sup>. This finding was corroborated in a study looking at 47033 men and women in the United Kingdom, 15459 (33%) of whom self-declared as vegetarians<sup>[28]</sup>. This subgroup as a whole was noted to have a 30% risk reduction of developing diverticular disease (risk ratio 0.7, CI: 0.56-0.87,  $P = 0.001$ ), while the highest quintile of fiber intake was associated with a 41% risk reduction (risk ratio 0.59, CI: 0.46-0.78,  $P < 0.001$ ) compared to non-vegetarians and individuals in the lowest quintile of fiber intake, respectively. Most recently, a study on 50019 healthy women in the Nurses' Health Study showed that a higher intake of various sources of dietary fiber, except from vegetables, was associated with a lower risk of diverticulitis<sup>[29]</sup>.

Additional environmental factors implicated in diverticulitis include smoking<sup>[30,31]</sup>, use of steroids and non-steroidal anti-inflammatory medications<sup>[31-33]</sup>, and obesity<sup>[34]</sup>. A traditionally held belief was that patients with diverticulosis should avoid particulate foods such as nuts, popcorn, corn, or sunflower seeds for fear of particulate material obstructing diverticula and triggering diverticulitis<sup>[35]</sup>. This myth has since been solidly debunked *via* the benchmark study that analyzed 47288 men over a follow-up period of 18 years: The authors did not observe a negative effect, but surprisingly there was even a potential protective impact of nut, corn or popcorn consumption with regards to the development of diverticulitis<sup>[36]</sup>.

In contrast to associating extrinsic and environmental factors as the leading cause for the development of diverticular disease, the contribution of potential endogenous, *i.e.* genetic factors, has largely been underreported - until recently. A Swedish national database analysis of over 104000 twins reported nearly 2300 hospitalizations for diverticular disease. An odds ratio of 7.15 (CI: 4.82-10.61) was noted for monozygotic twins, compared to 3.2 (CI: 2.21-4.63) for dizygotic twins; the overall contribution of genetics to diverticular disease was calculated to be 40%<sup>[37]</sup>. A review of the Danish national registry data from 1977-2011 found 10400 index siblings and 920 twins with diverticular disease. The authors calculated the risk ratio for siblings to be 2.92 (CI: 2.5-3.39) compared to the general population. Similar to the Swedish study, the risk ratio for diverticular disease was substantially higher in twins with 14.5 (CI: 8.9-23) and 5.5 (CI: 3.3-8.6) for monozygotic and dizygotic twins, respectively. The calculated heritable contribution in this study was 53% (CI: 0.45-0.61)<sup>[38]</sup>. Last but not least, yet unpublished data from our own institution showed an incidental prevalence of diverticula in young patients undergoing abdominal CT scans for unrelated suspected appendicitis; 14% of patients less than 20 years of age and 40% of patients between 20-39 years of age had evidence of diverticulosis, suggesting that there could not yet have been sufficient lifetime to allow for extrinsic factors alone, such as fiber-deficiency related constipation, to take effect.

In summary, the development of diverticula may have both constitutional/genetic as well as extrinsic environmental and nutritional factors<sup>[10]</sup>. The risk of developing diverticulitis in individuals with diverticulosis is lower than previously estimated. However, the overall incidence of diverticulitis is on the rise with an increasing proportion of cases seen in younger patients. Lifestyle factors may not be solely responsible for diverticulosis but play a more crucial role in initiating an inflammatory cascade once diverticula are present.

## PATHOGENESIS AND PRESENTATION

The traditional concept of the pathogenesis of diverticulosis has been that the development of diverticula is associated with chronic constipation leading to increased intraluminal pressure, colonic muscular hypertrophy, and mucosal and submucosal herniation at the entry points of the penetrating blood vessels (vasa recta)<sup>[39,40]</sup>. While acquired diverticula may develop throughout the entire colon, the characteristic distribution predominates in the sigmoid and left-sided colon where the stool is most formed<sup>[23]</sup>. In contrast, isolated right-sided diverticula are comparably rare and likely represent a different entity (true diverticula, possibly congenital) that regardless of migration and dietary adjustments are more frequently seen in Asian patients<sup>[26,41,42]</sup>.

The pathogenesis of diverticular disease is still not completely understood and appears to have multiple facets. Diverticulosis, *i.e.* the presence of diverticula alone without any inflammatory signs, is typically not thought to cause any symptoms. However, there may be a substantial overlap/coexistence with constipation-predominant irritable bowel syndrome (IBS). Hence, for diverticulosis with non-specific symptoms of pain and constipation, the term symptomatic uncomplicated diverticular disease (SUDD) was coined. Such patients may show visceral hypersensitivity whereas the bowel compliance is normal<sup>[43,44]</sup>. Colonic dysmotility has also been described in SUDD patients, possibly related to a reduction in the interstitial cells of Cajal (GI pacemaker cells) and increased duration of low contractile activity<sup>[45,46]</sup>.

The two most common true complications of diverticulosis are (1) Bleeding (usually from non-inflamed diverticula); and (2) Diverticulitis. Bleeding or chronic anemia are not usually associated with diverticulitis, and the presence of either entity should raise the concern for an underlying malignancy.

Diverticular bleeding can be abrupt and range from severe to massive lower GI bleeding. Yet, it poses a common diagnostic and treatment challenge as the bleeding may be cyclic and difficult to localize, even if one might speculate the origin to likely be in the left-sided colon. However, the presence of diverticula alone may not be sufficient evidence for targeted treatment, particularly as the differential diagnosis of a bleeding arterio-venous malformation is more commonly found on the right side<sup>[47,48]</sup>.

The pathway to diverticulitis includes stasis or obstruction within a diverticulum, alteration in the gut microenvironment/microbiome, local tissue ischemia, and a microperforation<sup>[49,50]</sup>. Depending on the location and evolution of the inflammatory process *vs* the promptness and effectiveness of the host response, varying degrees of local mucosal and pericolic inflammation, abscess formation, or even macroperforation result. Clinically, acute diverticulitis usually presents with a basic triad of increased abdominal pain, fever and elevated inflammatory parameters (white blood cells, C-reactive protein) with varying degrees of aggravated symptoms<sup>[51,52]</sup>. More chronic forms of diverticulitis manifest as smoldering diverticulitis with or without formation of a fibrostenotic stricture (possibly causing a large bowel obstruction)<sup>[51]</sup>, or of fistulae to other organs (bladder, vagina, occasionally small bowel and skin). Even a classical constellation of symptoms is far from specific for diverticulitis, and a wide differential diagnosis should be considered (Table 1). In particular, it should be highlighted that in 1%-5% of patients, the suggestive clinical and even radiological features are in fact caused by a locally advanced malignancy on the verge of micro/macro-perforation (see later discussion on colonoscopy)<sup>[53,54]</sup>.

More recently, it has been recognized that a small subset of patients with chronic diverticulitis show signs of segmental colitis associated with diverticulosis (SCAD)<sup>[55]</sup>. The macroscopic colitis occurs as an epiphenomenon around an area of diverticulitis, but generally does not involve the diverticula themselves<sup>[56]</sup>. Histopathological analysis of SCAD demonstrates similarities to inflammatory bowel disease (IBD) in the form of crypt abscesses, granulomas and significant architectural disruption<sup>[57,58]</sup>. Non-corroborated case series have even suggested a progression to either Crohn's or ulcerative colitis in small subset of SCAD patients<sup>[56,59]</sup>.

## EVALUATION AND CLASSIFICATION OF DIVERTICULITIS

Initial evaluation of diverticulitis aims at defining the acuteness and severity of symptoms and patterns of complications or chronicity (Table 2). Amongst symptom analysis, it includes obtaining information about previous surgeries, colon evaluations, as well as comorbidities. The focus of the initial physical examination is to distinguish a localized disease process from diffuse peritonitis with systemic manifestations

**Table 1 Differential diagnosis for acute and chronic presentations of diverticulitis**

Acute presentation	Chronic presentation
Appendicitis	Malignancy
Anastomotic leak (post-surgical)	IBS/SUDD
Perforating malignancy	IBD
Constipation	Constipation
IBS	Post-surgical
IBD	
Ischemic colitis	
Post-radiation enteritis	
Urogynecological pathology (tubo-ovarian abscess, endometriosis, pyelonephritis, cystitis etc.)	
Non-malignant viscus perforation (peptic ulcer)	

IBD: Inflammatory bowel disease; IBS: Irritable bowel disease; SUDD: Symptomatic uncomplicated diverticular disease.

**Table 2 Workup for acute and chronic presentations of diverticulitis**

	Acute	Chronic
History	Onset, progression, severity, location. Previous colon evaluation (< 2 yr). Previous episodes. Bowel habits	Recurrent attacks. Previous hospitalizations. Previous imaging. Previous colon evaluation (< 2 yr). Change in bowel habits
Physical examination	Localized <i>vs</i> diffuse peritonitis?	Abdominal distension. Fistula
Lab tests	WBC, CRP	Anemia? UTI?
Imaging	CT with oral/rectal and intravenous contrast: (1) Phlegmon; (2) Abscess/contrast extravasation; (3) Free air; and (4) Findings suggestive of other diagnosis	CT with oral/rectal and intravenous contrast: (1) Wall thickening; (2) Extraluminal contrast/air; (3) Fistulization; (4) Proximal colon distention; and (5) Rule out cancer features
Endoscopy	Avoid in acute phase, plan after 6 wk to rule out malignancy/IBD and/or synchronous pathology	Always to assess for mucosal pathology at target site and for synchronous pathology in the rest of the colon
Additional	(1) Possible CT-guided abscess drainage; and (2) Possible water-soluble contrast enema	(1) If colon evaluation incomplete to CT colonography or barium double contrast enema; and (2) Potentially cystoscopy, colposcopy

WBC: White blood cell; CRP: C-reactive protein; UTI: Urinary tract infection; CT: Computed tomography; IBD: Inflammatory bowel disease.

(sepsis) which typically warrants an urgent surgical exploration. More than 90% of patients, however, have a less advanced disease and undergo further evaluation<sup>[60]</sup>. Apart from the clinical parameters and blood work, cross-sectional imaging with CT scans has universally become the radiological tool of choice with extremely high sensitivity (93%-97%) and specificity (near 100%) at evaluating the severity of the disease<sup>[33,60-62]</sup>. Analysis of 16 of the 528 patients included in the DIABOLO trial<sup>[63]</sup>, who unexpectedly progressed from mild to complicated disease suggested that fluid collections and to a lesser extent the length of the inflamed colon segment might represent predictive factors<sup>[64]</sup>. In situations where there is a concern for an underlying malignancy, a limited water-soluble contrast enema may have a role in discerning diverticular from malignant morphologies (apple core lesion), but modern cross-sectional imaging has largely eliminated that need. Endoscopic evaluation of the colon is increasingly debated but overall still considered a crucial safety measure to assess the target area and rule out synchronous pathology. However, it should be avoided in the acute setting and deferred to about 6 wk later (see below)<sup>[13,65]</sup>.

Optimizing treatment strategies and the ability to compare different cohorts of patients depends on defining the disease severity for each individual patient. Traditionally, the Hinchey classification (1978) was used to define the severity of acute diverticulitis based on clinical and operative findings<sup>[66]</sup>. However, this system lacks details on intermediate severities which are recognized by modern imaging<sup>[60]</sup>. A number of different classification systems have since been suggested<sup>[67-71]</sup>. The CT-based classification by Ambrosetti *et al*<sup>[72]</sup> distinguishes between mild and severe

(complicated) acute diverticulitis<sup>[72]</sup>, but the system insufficiently distinguishes the different grades of complicated diverticulitis, thus limiting its usefulness in decision-making and tracking disease progression for outcome analysis. The modified (1999) and further adapted (2005) Hinchey classification system (Table 3) added subgroups for milder and complicated forms of acute diverticulitis as well as categories for chronic complications (obstruction, fistula) with the goal to define criteria for management decisions<sup>[69,71]</sup>. In an era of the near ubiquitous use of CT for diagnosis and evaluation of diverticulitis, the 2005 modification of the Hinchey classification appears well suited to correlate clinical and radiographic findings to serve as the basis for treatment strategies<sup>[71]</sup>.

Work-up for chronic presentations of diverticulitis tends to focus more on defining the anatomy and disease configuration than its severity (Table 2). Endoscopic evaluation is relevant to rule out underlying or coexisting neoplastic conditions, but imaging modalities (CT, CT colonography, contrast enemas) are crucial to obtain “anatomical road maps” and information about fistulizing and stricturing segments. Characteristic features seen on imaging include thickening of bowel/bladder wall, adjacency of the inflamed colon to other structures as well as air in the bladder<sup>[73]</sup>. In addition, obtaining a CT colonography or contrast is superior in identifying the overall distribution of diverticula and presence of fistulas or a strictured segment.

## DIVERTICULITIS, COLORECTAL CANCER, AND THE ROLE OF ENDOSCOPY

From epidemiological data, there is no indication to believe that diverticulitis could cause colorectal cancer. In that sense, cancer and diverticulitis are two completely independent entities that happen to have a parallel age-dependent increase in incidence. Occasionally, the two entities may present a similar symptomatology which typically points to a locally advanced cancer that penetrates the colon wall. It is therefore important that any patient with “characteristic” symptoms could potentially have an underlying cancer that mimics the diverticulitis or coexists in a different part of the colon. That concern is reflected in the call for colonoscopy after cooling off the acute episode. The probability to detect a cancerous nature responsible for the symptoms is certainly higher for complicated presentations than it is for mild forms which has led some authors question whether a colonoscopy is needed in all.

Current practice guidelines, including those from the American Society of Colon and Rectal Surgeons (ASCRS), continue to recommend an interval colonoscopy after an episode of diverticulitis<sup>[52,65,74]</sup>. The goal of endoscopic evaluation is to rule out underlying or coexisting conditions (neoplasm, IBD) that could mimic the index presentation or be independent entities. To avoid disease aggravation with avoidable associated healthcare cost, *i.e.* in converting the inflamed segment’s micro- into a macro-perforation, the instrumentation and insufflation are typically postponed for 4-6 wk from the immediate time of an acute attack<sup>[75]</sup>. In recent years, the utility of routine colonoscopy after an attack of uncomplicated diverticulitis has come under scrutiny, predominantly in the European literature<sup>[76,77]</sup>.

The incidence for cancer and adenomas was reported in the range of 1.6%-5.5% and 8%-30.9%, respectively<sup>[78]</sup>. A large population-based cohort study from Denmark with a total of nearly 41000 patients admitted with acute diverticulitis reported a two-fold higher incidence of colon cancer compared to individuals without diverticulitis (4.3% *vs* 2.3% respectively)<sup>[79]</sup>. A systemic review analyzing 9 studies with 2490 diverticulitis patients found that of the 1468 patients (59%) that underwent colonoscopy after a bout of uncomplicated diverticulitis, the prevalence of an underlying malignancy, advanced adenoma, or low grade adenoma was 1.2%, 2.2% and 6.1%, respectively<sup>[53]</sup>. Another metaanalysis pooled 1970 patients from 11 studies in 7 countries and revealed a proportional estimate of malignancy of 1.6% (95%CI: 0.9-2.8); but in the subgroup of complicated diverticulitis, the pooled proportional estimate of malignancy increased to 10.8% (95%CI: 5.2-21.0)<sup>[80]</sup>. Lastly, a systematic review of 30 studies with a total of 29348 subjects with CT-diagnosed diverticulitis reported the overall rate of malignancy as 1.67% (95%CI: 1.24-2.14); compared to 1.22% (95%CI: 0.63-1.97) in uncomplicated diverticulitis, the rate was 6.14% (95%CI: 3.20-9.82) for complicated diverticulitis, representing a relative risk of 5.033 (95%CI: 3.194-7.930; *P* < 0.001)<sup>[81]</sup>. The rates of malignancy and advanced adenoma were across the literature significantly higher (5%-11% and 19%, respectively) in patients with complicated diverticulitis<sup>[54,80]</sup>.

One might argue that the percentages of colon cancer in uncomplicated diverticulitis are relatively low but are higher than those seen in a general screening

**Table 3 Hinchey classification and modified Hinchey classification of acute diverticulitis**

Hinchey classification <sup>[66]</sup>		Modified Hinchey classification <sup>[60,69,91]</sup> (imaging- or surgery-defined)		Comment
I	Pericolic abscess or phlegmon	0	Mild clinical diverticulitis	LLQ pain, elevated WBC, fever, no confirmation by imaging or surgery
		I	Confined pericolic inflammation: Phlegmon	
		I	Confined pericolic abscess	
II	Pelvic, intra-abdominal or retroperitoneal abscess	II	Pelvic, distant intra-abdominal, or retroperitoneal abscess	
III	Generalized purulent peritonitis	III	Generalized purulent peritonitis	No open communication with bowel lumen (ruptured abscess)
IV	Generalized fecal peritonitis	IV	Fecal peritonitis	Free perforation, open communication with bowel lumen
		SMOL <sup>1</sup>	Smoldering diverticulitis/peridiverticulitis	Recurrent/intermittent or chronic
		FIST <sup>2</sup>	Colovesical/vaginal/enteric/cutaneous fistula	Chronic or acute
		OBST <sup>3</sup>	Large and/or small bowel obstruction	Chronic or acute

<sup>1</sup>Smoldering.

<sup>2</sup>Fistula formation.

<sup>3</sup>Obstruction. LLQ: Left lower quadrant; WBC: White blood cell.

population<sup>[82,83]</sup>. Furthermore, the yield is higher than the one obtained for evaluation of occult rectal bleeding.

Reconciling the current evidence suggests that interval endoscopy remains essential after complicated diverticulitis due to the higher risk of underlying malignancy even if the value and cost effectiveness remain to be determined.

## NON-OPERATIVE MANAGEMENT OF DIVERTICULITIS

Antibiotics have been the cornerstone of treatment for acute diverticulitis with the goal to resolve the underlying bacterial inflammation and alleviate related symptoms. Whether the treatment is delivered in an outpatient or an inpatient setting depends on the healthcare setup, the presentation, and the severity of symptoms. With increasing severity, cases may require hospitalization with intravenous measures, potential temporary bowel rest and interventions. In many instances, the opposite strategy, *i.e.* gentle bowel stimulation and cleansing with small aliquots of magnesium citrate, might help reduce the stool load to promote resolution of symptoms and—if surgery should be needed—increase the chances for a primary anastomosis<sup>[84]</sup>. The duration of treatment is not universally defined but will primarily be related by the time to normalization of clinical and inflammatory parameters.

Due to the increased antibiotic stewardship in clinical practice, there has been a recent push against the standard antibiotic treatment of acute diverticulitis. A 2012 Cochrane Review of 3 studies showed insufficient evidence to confirm the safety of avoiding antibiotic therapy in diverticulitis<sup>[85]</sup>. Subsequently, a pivotal randomized controlled trial (RCT), the “Antibiotika Vid Okomplicerad Divertikulit” (AVOD, Antibiotics For Uncomplicated Diverticulitis) study, randomized 623 patients with CT-evidence of phlegmonous diverticulitis to at least 10 d of antibiotic therapy *vs* supportive IV fluids only<sup>[86]</sup>. There was no significant difference in the length of stay (3 d in both groups) and no difference in the incidence of abscess formation, recurrent diverticulitis or readmission at 1 year of follow-up (16% in both groups, *P* > 0.05)<sup>[86]</sup>.

Furthermore, there was no differences in long-term recurrences (both 31.3%;  $P = 0.986$ ), complications (4.4% *vs* 5.0%;  $P = 0.737$ ), surgery for diverticulitis (6.2% *vs* 7.1%;  $P = 0.719$ ) or colorectal cancer (0.4% *vs* 2.1%;  $P = 0.061$ ). Quality of life was also not significantly different between the two groups<sup>[67]</sup>.

The previously mentioned DIABOLO trial was another RCT with 528 patients with CT-proven uncomplicated acute diverticulitis randomized to a 10 d course of antibiotics *vs* observation as outpatient if patients met criteria<sup>[63]</sup>. The primary outcome was time to recovery during 6 mo of follow-up. Median time to recovery was 14 d for the observational and 12 d for the antibiotic treatment strategy ( $P = 0.151$ , hazard ratio for recovery of 0.91). Hospital stay was significantly shorter in the observation group (2 *vs* 3 d;  $P = 0.006$ ), but there was no significant differences in secondary endpoints, such as complicated diverticulitis, ongoing diverticulitis, recurrent diverticulitis, readmission, adverse events and mortality (Table 4)<sup>[63,88]</sup>. However, more than one third of patients experienced persistent symptoms even though the long-term quality of life was comparable after initial antibiotic or observational treatment<sup>[89]</sup>.

There is a growing body of high-level evidence to suggest that a more nuanced selective patient-centric approach is warranted as opposed to routine use of antibiotics in uncomplicated acute diverticulitis, but there remain significant obstacles to more widespread acceptance of the omission of antibiotics in the management of acute diverticulitis<sup>[90]</sup>.

## SECONDARY PROPHYLAXIS

With regards to secondary prevention of recurrent diverticulitis<sup>[91]</sup>, it is hard to identify one specific effective strategy since the pathogenesis of diverticulitis is—as previously mentioned—multifactorial and encompasses both lifestyle and genetic factors<sup>[90]</sup>. Smoking cessation, decreased intake of red meat, increased physical activity and loss of excess body weight seem to be intuitively smart health improvement choices and may potentially reduce the risk of diverticulitis. High fiber diet has been associated with a risk reduction of the first episode of acute diverticulitis but has an unclear efficacy in secondary prevention of recurrent attacks<sup>[90]</sup>.

Rifaximin has recently been advocated as candidate for secondary prevention of recurrent acute diverticulitis. A retrospective study of 142 patients with symptomatic disease who were treated with rifaximin noted a significant decrease in their symptoms including abdominal pain and tenderness<sup>[92]</sup>. A prospective randomized study of 165 patients, assigned to high fiber diet either with and without rifaximin, observed a 9% lower rate of recurrent diverticulitis on follow-up with addition of rifaximin<sup>[93]</sup>. Finally, a metaanalysis of a total of 1660 patients found the combination of rifaximin and high fiber diet to be effective in secondary prevention with patients continuing to be symptom free at 1 year<sup>[50]</sup>.

Probiotics have also been investigated with the goal to decrease the incidence of diverticulitis by adjusting the microbiome of the colon. A RCT of 210 patients found that patients who were randomized to mesalamine and *Lactobacillus* for 10 d *per* month had decreased recurrence of symptoms with a follow up of 12 mo<sup>[94]</sup>.

Unfortunately, most studies investigating secondary prophylaxis were heterogeneous in nature and lacked a gold standard for comparison. As the evidence remains weak, most guidelines still refrain from recommending routine use of these medications to reduce the risk of diverticulitis recurrence. However, there is an increasing enthusiasm to use such measures for their benefit in reducing symptoms in patients with chronic ongoing disease<sup>[90]</sup>.

## PRACTICAL STAGE-BASED MANAGEMENT APPROACH TO AN ACUTE DIVERTICULITIS EPISODE (INDEX EPISODE)

When it comes to defining the role of medical *vs* surgical management for diverticulitis, it is important to distinguish between the single acute episode (index hospitalization) as opposed to subsequent disease, be it in form of recurrent events, smoldering disease, formation of complications (stricture, fistula). In this section, the focus is on getting control of the acute episode, regardless of the future risks.

### ***Uncomplicated diverticulitis, modified Hinchey 0 and IA (phlegmon, SUDD)***

The vast majority (> 70%) of acute presentations of diverticulitis are uncomplicated



**Table 4 Randomized controlled trials of antibiotics vs omission of antibiotics in the treatment of uncomplicated diverticulitis**

Ref.	Number of patients	Antibiotics group	Control group	Primary outcome	Conclusions
AVOD <sup>[86]</sup>	623	At least 10 d of Abx, IV initially, then PO after admission or upon discharge	IV fluids	Complications, length of stay, need for surgery	Complications: 1% in Abx arm, 1.9% in control group ( $P = 0.302$ ). LOS: 3 d in both groups. Recurrent diverticulitis/readmission in 1 year: 16% in both groups ( $P = 0.881$ )
DIABOLO <sup>[63]</sup>	528	10 d course of Abx, IV for 2 d, then PO	Observation as outpatient if clinical criteria satisfied	Time to recovery	Median time (d) to recovery: Observation 14 (IQR 6-35); antibiotic 12 (7-30; HR 0.91; $P = 0.151$ )

Abx: Antibiotics; LOS: Length of stay; IQR: Interquartile range; HR: Hazard ratio; AVOD: Antibiotika Vid Okomplicerad Divertikulit.

(modified Hinchey 0 and IA), for which the success rates of conservative management are high (> 90%)<sup>[38]</sup>. Antibiotics remain the mainstay treatment for the initial non-operative management, be it as outpatient or in hospitalized patients<sup>[36,95]</sup>. It is important and advisable to set a time frame for benchmarks expected to be reached. For example, within 72 h after initiation of appropriate treatment, symptoms, and objective parameters [pain, fever, leukocytosis, systemic inflammatory response syndrome (SIRS), *etc.*] must improve without exception or completely resolve/normalize. Failure to achieve this goal should prompt either (1) Repeat imaging to discern whether a drainable abscess has formed; or (2) A surgical intervention. It remains poorly understood at the present time why a small 5%-10% fraction of patients with seemingly mild diverticulitis on initial imaging do not respond to standard conservative management and ultimately require a surgical intervention<sup>[60]</sup>.

With the potential for a superimposed IBS component in SUDD, the use of probiotics in treatment of diverticular disease has been suggested and studied by various groups. A review included 4 studies with a total of 134 patients (104 SUDD, 30 uncomplicated diverticulitis) who were treated with probiotics over short term average follow-up of 12 mo<sup>[96]</sup>. For SUDD patients, probiotic administration was successful in rendering 70% of patients' symptom free in one study and maintained remission for 14.1 mo in another. Overall, the authors concluded that use of probiotics in SUDD is safe and has demonstrable efficacy in the short term. The fact however that most studies lacked a control arm and any randomized comparison significantly limits the strength of the recommendation; at best it paves the way for future studies of the role of probiotics for SUDD.

Use of rifaximin has been tested in recent years with the goal to restore the altered colon microflora that was attributed by some to the pathogenesis of diverticular disease. A meta-analysis of 4 randomized studies with a total of 1660 patients (970 rifaximin, 690 control) found significant symptom relief (rate difference 29%, CI: 24.5-33.6) in the rifaximin-treated group compared to controls<sup>[97]</sup>. The number needed to treat in order to attain symptom relief was 3 in SUDD patients; however, when patients with diverticulitis were included, the number needed to treat substantially increased to 50.

Utilization of anti-inflammatory medication (mesalamine) has been studied in the treatment of SUDD, SCAD, and prevention of recurrent diverticulitis. In a randomized study of 40 SUDD patients, daily doses of mesalamine compared to a cyclical regimen (10 d/mo dosing) resulted in 20% more patients remaining symptom-free at 24 mo<sup>[98]</sup>. Compared to rifaximin, mesalamine demonstrated improved efficacy at 3 mo in the treatment of 170 SUDD patients<sup>[99]</sup>. However, data on treatment of SCAD with mesalamine is limited to small case series. Of 24 patients with SCAD, 21 were treated with mesalamine, of which 17 (81%) demonstrated resolution within 6 mo; the remaining 4 patients took 2-7 years of therapy before symptom resolution<sup>[100]</sup>. Recurrence rates were high (30%) with a large variability in the time to recurrence. In the phase 3 controlled PREVENT trial on the use of mesalamine for the prevention of recurrence of diverticulitis, daily mesalamine compared to placebo achieved no significant difference in disease recurrence (53%-63% vs 65%, respectively)<sup>[101]</sup>.

In summary, these limited data sets on various supportive measures currently provide only weak evidence for their use in the management of symptomatic diverticular disease or mild diverticulitis. It cannot be stressed enough that proper diagnostic elements should be used to distinguish true diverticulitis from SUDD or IBS. Finally, surgery is typically discouraged for IBS and SUDD, but a recent

retrospective study with 52 patients suggested an improvement in quality of life at 12 mo after laparoscopic sigmoid resection<sup>[102]</sup>.

### **Complicated diverticulitis with abscess formation, modified Hinchey IB and II**

Acute diverticulitis associated with an abscess (modified Hinchey IB, II) represents complicated diverticulitis and has been reported in up to 15%-25% of acute presentations<sup>[60,103,104]</sup>. Increased resolution and universal use of CT scanners unquestionably improved our ability to diagnose these abscesses and if amenable percutaneously drain them. Management invariably starts with broad-spectrum antibiotics<sup>[65,74,84]</sup>. Small abscesses (< 4 cm) may have a chance to resolve with antibiotic therapy alone. Larger abscesses, particularly if > 5 cm, warrant an attempt at an image-guided percutaneous drainage placement. Immediate success rates—defined as the ability to safely access and drain the abscess and achieve resolution of associated signs of sepsis—show a wide range between 49%-94%<sup>[60,104]</sup>. Treatment goals remain similar to conservative management: resolution of symptoms and normalization of objective clinical and inflammatory parameters within a defined time frame (*e.g.*, 72 h). Short-term failure during the index hospitalization of medical management including percutaneous abscess drainage occurs in 12%-30% and should prompt a surgical intervention<sup>[84,104]</sup>. Unfortunately, even after clinical resolution, there is a substantially higher risk of recurrent disease. In our systematic review, only 28% of patients with an abscess neither had surgery nor a recurrent attack<sup>[105]</sup>. Analysis of our own institutional data, one of the largest series, the recurrence rate after an episode of diverticulitis with an abscess was 61% overall and 71% in the subset of patients treated with CT-guided drainage. 42% experienced more than one recurrent episodes, 46% of the recurrences were more severe than during the index episode, and 63% of recurrences were complicated by abscess, fistula, stricture, or peritonitis<sup>[104]</sup>. This observation should trigger a much broader discussion about whether or not an elective surgery should be recommended (see below).

### **Complicated diverticulitis with free perforation and diffuse peritonitis, modified Hinchey III (purulent, non-feculent) and IV (feculent)**

Historically, there was little debate about the immediate indication for surgery in patients with evidence of free perforation as evidenced by intraperitoneal gas distant from the originating bowel segment. More recently, however, the approach has become a bit more tailored and the optimal treatment for perforated diverticulitis with peritonitis continues to evolve, both in regards to the indication for surgery as well as the type of surgery required<sup>[74]</sup>.

Perhaps the most crucial first step is to distinguish patients with clinical evidence of diffuse peritonitis from the subset of patients who on imaging show distant free air but display no clinical signs of sepsis or diffuse peritonitis. A combination of clinical judgment and analysis of the CT findings is quintessential for sound decision-making. A grading system was proposed that characterized CT findings of perforation based on the amount and location of air and peritoneal fluid and allowed the authors to defer acute interventions in 91% of grade III diverticulitis cases<sup>[106]</sup>. Other authors, however, found less utility in the CT scan and stressed the importance of clinical judgement when avoiding emergency surgery in 64% of patients<sup>[107]</sup>.

Regarding the surgical strategy, the best source control is unquestionably achieved by resecting the inflamed and perforated bowel segment. Diversion alone and drainage alone have been associated with prolonged recovery and higher morbidity. In the past, a discontinuous resection (Hartmann resection) was most commonly performed and still to the present date represents an overall safe approach, particularly if the patient is unstable, frail, or if the tissue quality is poor. However, the chance of never having the stoma reversed is remarkably high, and an immediate reconstructive effort (primary anastomosis with or without proximal diversion) has been shown to be a safe approach in appropriately selected patients. Several mostly retrospective studies and systematic reviews attempted to define the outcome and concluded that the mortality was comparable at 14% for both, Hartmann resection *vs* primary anastomosis<sup>[108,109]</sup>. A modeling *via* decision-analysis suggested that a primary anastomosis with proximal diversion has the highest probability of a favorable short- and long-term outcome<sup>[110]</sup>. The utility of a non-resective surgery (lavage) has been extensively scrutinized for even localized abscesses and appears to be an inferior tool for diffuse peritonitis (see below).

## RECURRENCES AFTER INITIAL CONSERVATIVE MANAGEMENT

Recurrence rates after a bout of acute diverticulitis depend on several intrinsic and extrinsic factors, but a key parameter is the severity of the initial index episode<sup>[91]</sup>. One Italian study on over 1000 patients with a mean follow-up period of 10.7 years reported a 17% recurrence rate with only a 6.9% need for eventual surgery<sup>[111]</sup>. In an even larger study of 3165 patients, a subset of 2551 patients (80.6%) who were treated conservatively over a mean of 8.9 years revealed that 2366 (92.7%) did not require a colectomy<sup>[71]</sup>. Recurrence of diverticulitis was reported only in 314 patients (13.3%), 71% of which had only a single recurrence<sup>[71]</sup>. Based on these data, both authors concluded that elective colectomy after acute diverticulitis is not warranted. While this conclusion may be true for a single uncomplicated episode of acute diverticulitis, the decision is a lot more nuanced when complicated or recurrent diverticulitis is considered.

For diverticulitis associated with an abscess (modified Hinchey IB, II), the literature has reported significantly higher recurrence rates (up to 40%-61%), particularly in patients with a pelvic abscess (modified Hinchey II)<sup>[60,104,105,112]</sup>. While some retrospective studies suggested even long-term success with expectant management after percutaneous abscess drainage<sup>[71,103]</sup>, our systematic review including 1051 patients revealed a substantial bias in the data sets and reported that of all patients with abscesses, only 28% had neither any surgery nor a recurrence<sup>[105]</sup>. 30% underwent urgent surgery during the same hospitalization, 36% were scheduled for elective surgery (whereby two fifth of these had to undergo an urgent intervention before their scheduled elective surgery), and 6% were not planned for surgery but urgently needed one<sup>[105]</sup>. However, given the substantially high rates of recurrences, regardless of whether a CT guided drainage was successful or not, the ASCRS practice guidelines recommend consideration of an elective colectomy in these patients<sup>[65,74]</sup>.

## SURGICAL INDICATION FOR DIVERTICULITIS

The indication for surgery needs to distinguish between the acute, *i.e.* urgent or emergency setting, as opposed to the elective prophylactic setting that occurs after the acute symptoms have resolved.

With up to 20% of patients with acute diverticulitis failing non-operative management<sup>[71,109,113]</sup>, it is important to understand the criteria that warrant surgical intervention. In general, patients who require emergency or urgent surgery for diverticulitis in the acute setting fall into 3 main categories: (1) Signs of diffuse peritonitis and/or free perforation; (2) Suspicion of underlying malignancy; and (3) inadequate response to non-operative measures (antibiotics, bowel rest, percutaneous abscess drainage) after 72 h as demonstrated by persistent symptoms and lack of normalization of objective findings (fever, tachycardia, leukocytosis). The presence of complicated diverticulitis (abscess, fistulae, stricture) by itself generally does not mandate emergency/urgent surgical intervention (70%-92%) as demonstrated in numerous prospective and retrospective studies<sup>[60,61,103-106,114-116]</sup>.

A major paradigm shift in the elective surgical management of uncomplicated diverticulitis occurring in the 2000s was that strict criteria such as age and number of attacks were no longer considered absolute indications for prophylactic elective colectomy<sup>[74]</sup>. Large cohort studies demonstrated that the long-term recurrence rates for uncomplicated diverticulitis (13%-20%) and subsequent need for emergent surgery (6%-7%) was low<sup>[117-120]</sup>. Younger patients (< 50 years) were historically thought to have a more virulent form of the disease and hence elective surgery was meant of stave off worsening and increased attacks. A whole body of evidence, however, showed that this is not the case with younger patients having similar rates of recurrence and subsequent need for colectomy as older patients<sup>[119,121,122]</sup>.

Instead of applying rigid criteria, the decision process for elective colectomy in uncomplicated diverticulitis should be individualized to each patient and take into account the severity of attacks, comorbidities, and the effect on quality of life. The prospective randomized DIRECT trial in patients with ongoing symptoms or at least 2 attacks suggested that offering surgery was associated with improved cost and quality of life in patients undergoing surgery<sup>[123,124]</sup>. Immunocompromised patients tend to have more masked symptoms, more complications and worse outcomes with recurrent attacks<sup>[125-127]</sup>. An analysis on 166 immunocompromised patients found that in severe diverticulitis, the risk of recurrence was significantly increased compared to controls (46% *vs* 20%), whereas it was not elevated in mild diverticulitis<sup>[128]</sup>.

There is general consensus for elective surgery as the definitive treatment of complicated diverticulitis with fistulae, symptomatic colonic stricture and persistent inflammatory mass or chronic smoldering disease given that these conditions are unlikely to resolve without surgical intervention<sup>[129,130]</sup>. As mentioned earlier, there is observational data demonstrating successful long-term non-operative management of diverticular abscess. However, given the high recurrence rates of up to 61% with often more complicated than the index presentation<sup>[104]</sup>, ASCRS guidelines adopted recommendations for elective colectomy in this scenario<sup>[74]</sup>.

## OPERATIVE APPROACH AND SURGICAL OUTCOMES

### **Resection**

Resection of the inflamed colonic segment remains the goal of surgical intervention. While it is not necessary to resect all diverticula-bearing bowel segments, the appropriate extent of the resection begins in the healthy bowel wall proximal to the target area and distally must include the high-pressure zone of the rectosigmoid junction as identified by the coalescence of the teniae. In general, oncological principals should be employed unless a malignant cause of the inflammation has definitively been ruled out. Placement of ureteral stents has not been shown to lower ureteral injury rate in elective colectomy, but should be considered in the setting of significant retroperitoneal inflammation or evidence of a preexisting hydro-ureter on imaging<sup>[131,132]</sup>.

### **Reconstruction vs diversion**

After resection of the inflamed colon segment, there are essentially three reconstructive/divertive options to consider: (1) A primary anastomosis; (2) A primary anastomosis with upstream diversion; and (3) Creation of an end colostomy (Hartmann procedure).

Factors associated with the creation of an end colostomy include non-elective surgery, particularly for modified Hinchey class 3 or 4, poor performance index, immunosuppression, and obesity (Body mass index > 30)<sup>[110,133]</sup>. 30%-45% of patients with an end colostomy never have their stoma reversed. In addition, reversal of an end colostomy has been associated with some morbidity<sup>[134-136]</sup>. A small randomized study comparing rates of ostomy closure in patients with an end colostomy *vs* a diverting ileostomy demonstrated significantly higher reversal rates the latter group (58% *vs* 90%, respectively), and the post-operative morbidity was higher in the former (20% *vs* 0%)<sup>[136]</sup>.

A decision analysis model suggested that the preferred strategy in the non-elective setting is to perform a primary colorectal anastomosis and an upstream diverting stoma<sup>[110]</sup>. A reality check, however, confirms that in the United States, more than 90% of surgeons performed a Hartmann resection in the acute setting, and only 7.6% of patients had a primary anastomosis with diverting loop ileostomy performed<sup>[137]</sup>. A systematic review revealed a 62% rate of restored intestinal continuity during damage-control surgery<sup>[138]</sup>. From a practical standpoint and as a rule of thumb, (1) 2 healthy bowel ends in healthy and stable patients merit a primary anastomosis without diversion; (2) 1 healthy and one suboptimal bowel end may allow for a primary anastomosis with an upstream diversion; and (3) 2 unhealthy bowel ends or an unstable/unfit patient warrant an end colostomy<sup>[84]</sup>. Under elective conditions, a primary anastomosis should always be the goal, even if the surgery is carried out for disease complications such as colo-vaginal/-vesical fistula formation<sup>[84]</sup>.

### **Morbidity and mortality**

Overall, outcomes data after damage-control surgery for diverticulitis demonstrate a 9.2% risk of mortality and high morbidity of close to 50% including a 7.4% leak rate<sup>[137,138]</sup>. Wound infection reported at 10%-20% was the most common morbidity with mortality rates being < 5%. Patient comorbidities and need for emergent surgery were the two main contributing factors to patient mortality<sup>[139-142]</sup>. Long term follow up data demonstrate low recurrence rates (6%-8%) and a long median time to recurrence at 29 mo<sup>[111,143,144]</sup>.

### **Open surgery vs minimally invasive surgery (laparoscopic/robotic)**

Of 3 randomized trials have demonstrated that minimally invasive surgery (laparoscopic, robotic) for diverticular disease is associated with lower short term

morbidity in terms of lower blood loss, decreased post-operative pain and shorter hospital stay compared to open surgery<sup>[145-147]</sup>. It would be important to draw a clear distinction between emergency damage-control surgery *vs* elective interventions for persistent or recurrent disease. Unfortunately, many studies in the literature either refer to the latter only or do not provide the necessary transparency of data. Long-term outcomes are comparable with an overall improvement in satisfaction scores with the minimally invasive approach<sup>[148,149]</sup>.

Even though diverticular disease represents a benign process, it can at times pose significant technical challenges in surgery secondary to the chronic inflammatory process leading to distortion of anatomy. In such a setting, the application of hand-assisted laparoscopic surgery (HALS) with tactile sensation might have some benefit. Two small, randomized trials comparing laparoscopic to HALS for diverticular disease reported lower overall operative times but slightly increased length of stay (1 d longer in HALS). No significant difference in short term post-operative morbidity was noted<sup>[150,151]</sup>.

### **Role of resection vs lavage**

When patients require an emergent intervention for non-relenting diverticulitis with abscess formation or with diffuse peritonitis, laparoscopic lavage and drainage has emerged as a potential alternative to resection and for a while gained some popularity, primarily in European centers<sup>[152,153]</sup>. Early studies were all small retrospective series subject to inherent selection biases. A systematic review of 11 studies with 871 patients noted that some series included up to 25% Hinchey I patients that by all means should have been managed with standard non-operative measures rather than an operation in the first place; the reported 30 d postoperative mortality rate was 4.8%, the conversion rate in Hinchey IV patients was 45%; but most importantly the overall success rate was only 24.3% defined as the patients being alive without surgical treatment for recurrent symptoms, and notably 6.9% of rehospitalized patients were found to have a cancer<sup>[42]</sup>.

Three prospective randomized controlled multicenter trials on laparoscopic peritoneal lavage were launched and resulted in high-quality evidence (Table 5).

The LADIES trial was conducted from 2010 to 2013 in Belgium, Italy and the Netherlands and consisted of the two sub-arms difficult intravenous access (comparing Hartmann *vs* primary anastomosis) and L-Ornithine L-Aspartate (lap lavage *vs* sigmoidectomy)<sup>[154]</sup>. The laparoscopic lavage arm of the trial, however, was terminated early upon governmental oversight pressure due to a significantly increased rate of perioperative morbidity, mortality, and need for surgical reintervention compared to the resection groups. Furthermore, an alarming and unexpected finding in the laparoscopic lavage group of 45 patients were 4 with cancer that were missed and thus required resection later.

The Scandinavian diverticulitis (SCANDIV) trial encompassed 101 laparoscopic lavage *vs* 98 resection patients in 21 centers in Norway and Sweden from 2010 to 2014<sup>[155]</sup>. In contrast to the LADIES trial, SCANDIV was continued to completion. The 90 d morbidity and mortality were not significantly different between the two groups. However, when compared to resection, the use of laparoscopic lavage did not reduce severe postoperative complications and rather led to worse outcomes in secondary end points<sup>[155]</sup>. The laparoscopic lavage group had a 14.6% significantly higher rate of reoperation within 90 d (20.3% *vs* 5.7%, *P* value 0.01). As with other trials, there were cases of missed cancer (4%) in the laparoscopic lavage group that required delayed resection<sup>[155]</sup>.

Finally, the Scandinavian DILALA trial offered the most favorable spin of the three. From 2010 to 2014, patients with intraoperatively confirmed Hinchey III generalized purulent peritonitis were randomized to either lavage (39 patients) *vs* open Hartmann's procedure (36 patients)<sup>[156]</sup>. Patients in the lavage group had a 45% reduced risk of undergoing subsequent operations within 24 mo (relative risk 0.55, 95%CI: 0.36-0.84; *P* = 0.012) and had fewer operations (ratio 0.51, 95%CI: 0.31-0.87; *P* = 0.024) compared with those in the Hartmann's group. There was no difference in the mean number of readmissions (1.37 *vs* 1.50%; *P* = 0.221) or mortality between the two groups. Three patients in the lavage group and nine in the Hartmann's group had a colostomy at 24 mo<sup>[157]</sup>.

Reconciling the currently available higher quality evidence, a systematic review concluded that the preservation of diseased bowel by laparoscopic lavage was associated with an approximately 3 times greater risk of persistent peritonitis, intraabdominal abscesses and the need for emergency surgery compared to a resection<sup>[158]</sup>.

**Table 5 Randomized controlled trials comparing laparoscopic peritoneal lavage for perforated diverticulitis**

Ref.	Number of patients	Morbidity (%)	Mortality (%)	Nonresolution (%)	Recurrence (%)	Elective resection (%)	No resection needed (%)
LADIES/LOLA <sup>[154]</sup>							
-Laparoscopic lavage	47	44	2	20	13	2	52
-Sigmoidectomy	43	29	1	N/A	N/A	71	N/A
SCANDIV <sup>[155]</sup>							
-Laparoscopic lavage	101	26	8	Not recorded	Not recorded	Not recorded	Not recorded
-Sigmoidectomy	98	14	7	N/A	N/A	Not recorded	N/A
DILALA <sup>[156]</sup>							
-Laparoscopic lavage	43	21	8	Not recorded	0	0	Not recorded
-Open Hartmann's	40	17	11	N/A	N/A	Not recorded	N/A

N/A: Not applicable; LOLA: L-ornithine L-aspartate; SCANDIV: Scandinavian diverticulitis.

## CONCLUSION

The prevalence of diverticulitis is expected to increase substantially in the future as the population ages and the disease becomes more prevalent in younger patient populations. The development of diverticula/diverticulosis may have both intrinsic and extrinsic factors. The pathogenesis from diverticulosis to diverticulitis has several components, many of which are extrinsic and related to lifestyle. Different sub-entities of diverticular disease have been recognized but are yet poorly understood; they may cause blurring and overlap of symptoms. CT imaging is essential in the diagnosis of diverticulitis and classification of diverticular disease severity as it carries prognostic and potentially therapeutic significance. Interval colonoscopy remains advisable after an acute attack, particularly after complicated diverticulitis to rule out malignancy or advanced adenomata at the target site and the rest of the colon. Non-operative management of diverticulitis remains primarily based on antibiotics, but those may be omitted in mild cases. Supportive measures may include probiotics or anti-inflammatories, as dietary changes. Secondary prophylaxis focuses broad health improvement goals whereas the evidence for targeted interventions remains weak. Failure of non-operative management is typically defined as persistent or worsening symptoms and objective findings (SIRS, leukocytosis) after 72 h of best treatment. This should prompt further intervention, either in the form of imaging-guided drainage of an abscess or surgery. Resection offers the best source control in the acute, chronic, or elective setting. Laparoscopic lavage is currently not considered non-inferior to a surgical resection and should not be used outside of specific circumstances or protocols. A primary colorectal anastomosis should be considered at time of a resection unless the patient is unstable or there is poor tissue quality on each bowel end. A protective diverting ostomy can allow for an anastomosis when not all parameters are optimal. The indication for an elective surgical resection should be individualized and not be based on rigid criteria such as young age or a specific number of attacks. Instead, high-risk constellations such as complicated diverticulitis or immunosuppression should lead the considerations for elective colectomy when there is no obvious objective disease pathology (stricture, fistula, inflammation) after resolution of acute symptoms. Minimally invasive surgery (robotic, laparoscopic) is the primary approach for all elective cases and may be used in select emergency cases.

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