Modern Concepts in Diverticular Disease

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Abstract: Over the last decade there has been a striking shift in our understanding of the epidemiology, pathology, and management of diverticular disease. Indeed, many of the guidelines published in the late nineties and early 2000s are now redundant. High-fiber diets, avoidance of nuts and seeds, antibiotic treatment for mild diverticulitis, elective resection after 2 attacks of diverticulitis, Hartmann's procedure (HP), and aggressive management of young patients are all open to question. The more we challenge our understanding of diverticulitis it becomes apparent how little we know about this disease entity. This review aims update the reader on current hypotheses and evidencebased modern management strategies in diverticular disease.

Key Words: diverticular disease, diverticulitis, diverticulosis

(*J Clin Gastroenterol* 2015;49:358–369)

SEARCH STRATEGY AND SELECTION CRITERIA

Data for this review were identified by searches of MEDLINE and PubMed and references from relevant articles using the search terms "diverticulosis," "diverticular disease," and "diverticulitis." Abstracts and reports from meetings were included only when they related directly to previously published work. Only articles published in English were included.

CHANGING EPIDEMIOLOGY

Until recently, much of the work on the epidemiology of diverticular disease is derived from studies performed almost half a century ago. Postmortem and barium enema data have shown a prevalence of diverticulosis of 0.6% to 57%. In his seminal studies on the prevalence of diverticulosis in postmortem and barium enema data, Parks suggested that between 10% and 25% of patients with diverticulosis will develop diverticulitis. However, in light of recent large-scale population-based studies, Parks's conclusions are probably an overestimate.

In the United Kingdom, diverticulosis is found in approximately 35% of patients over the age of 60 years.[1,2] Barium enema studies from 12,335 cases in Edinburgh, Scotland demonstrated an annual incidence of diverticulosis of 1.55/1000 with this figure increasing to 5.74/1000 in those over 75 years.[3] In a recent retrospective study of over 2000 patients with a colonoscopic diagnosis of diverticulosis, only 4% of patients developed diverticulitis over an 11-year follow-up period.[4]

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The authors declare that they have nothing to disclose.

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In Asian populations, the prevalence of diverticulosis is increasing. Korean data[5] from colonoscopy studies demonstrate a prevalence of 12.1% in 2008 which is a significant increase from 5% in the 1980s[6] and 10% in the 1990s.[7] In Singapore (one of the most westernized Asian nations), the prevalence of diverticulosis is increasing. Reports from the 1990s show a prevalence of 20% (mostly right sided), whereas more modern data suggest this figure could be higher.[8] Similar trends have been found in Japan[9] and Hong Kong.[10] Interestingly, in Africa and the Indian subcontinent, the presence of diverticulosis is relatively low.[11–14] In the middle east, diverticulosis has a prevalence of 1% to 19%.[15–17]

In the United States, diverticulitis accounts for a substantial number of hospital admissions with a crude incidence of 0.71/1000[18,19] (based on national inpatient sample data). Nguyen and Steinhart[20] also report an increase in diverticulitis-related hospital admissions from 61.8 per 100,000 in 1998 to 75.5 per 100,000 hospitalizations in 2005. In the health care professionals' follow-up study,[21] 1.7% of male health care professionals aged 40 to 75 developed diverticulitis giving a crude annual incidence of 1/1000 (801 events in 47,228 persons over 18 y). Data from northern Europe yield similar figures (in the region of 1.6%).[22] Diverticular disease admission rates in the United Kingdom are in the order of 1.20 per 1000 population.[23]

More relevant perhaps is the fact that diverticular disease is the third most common gastrointestinal (GI) disorder requiring hospitalization[24] costing 2.6 billion dollars per year in the United States (more than appendicitis, inflammatory bowel disease, and colorectal cancer) as well as commanding a substantial burden on outpatient resources.

CHANGING ETIOLOGY—A DISEASE OF WESTERN CIVILIZATION?

On the basis of the influential works of Painter and Burkitt[25] in the latter half of the 20th century, diverticulosis was termed "a disease of western civilization." Based on their findings that diverticulosis was virtually absent in rural Africa and extremely rare in Asia, they postulated that the changes in dietary habits that occurred during the industrial revolution contributed to the development of diverticulosis. In the late 1800s with the introduction of ground flour, refined carbohydrates, red meat, and decreased maize consumption, there was a dietary shift in Europe and the United States with a trend toward low-residue foods and a gradual depletion of dietary fiber intake. This hypothesis was readily accepted as, instinctively, a low-residue diet could contribute to slower transit times and increased colonic intraluminal pressure with the sequelae of propulsion diverticula. Motility and manometric studies investigating intraluminal pressure changes in patients with diverticular disease have yielded inconsistent results. Some studies demonstrate increased colonic transit times in

diverticular segments with increased intraluminal pressure readings; however, findings are variable and often difficult to analyze as readings may have been taken in the rectum (a "diverticulum-free" zone).[26–29] In addition, similar motility abnormalities can be found in irritable bowel syndrome (IBS).[30,31]

Fiber Asymptomatic Diverticulosis

Evidence for high-fiber intake in the prevention of diverticulosis is limited to small case-control or cross-sectional studies[5,32–34] and results are conflicting. In a study of 264 nonvegetarians and 56 long-time vegetarians, diverticulosis was significantly more prevalent in the nonvegetarian group who on average consumed significantly less fiber.[32] However, in the small group of vegetarians in this study, those with diverticulosis had a higher fiber intake. Most recently, Peery and colleagues analyzed dietary habits of 2104 patients undergoing colonoscopy for colorectal cancer screening. They found a positive correlation between dietary fiber and diverticulosis on colonoscopy[33] suggesting that high-fiber consumption does not prevent diverticulosis. Furthermore, there was no association with constipation and diverticulosis in this study. Instead, patients with diverticulosis were more likely to have diarrhea compared with normal controls. These findings were confirmed in a second cross-sectional study by the same authors investigating the effect of constipation and low-fiber intake on asymptomatic diverticulosis.[35] Based on a colonoscopic diagnosis of diverticulosis (539 patients) versus control (1569 patients), there was no significant association between constipation or fiber intake and the development of asymptomatic diverticulosis.

Some data suggest fiber supplementation may improve symptomatic diverticular disease (decreased bowel transit time, increased stool weight, and normalized muscle activity) although these studies are largely uncontrolled and have small numbers.[36–42] The Oxford EPIC study (European Prospective Investigation into Cancer and Nutrition) demonstrated a relative risk (RR) for hospitalization of 0.58 in people who consumed >25.5/g fiber per day.[43] This included all admissions with an ICD-10 code (primary or secondary) for any diverticular disease encompassing diverticulosis, diverticular bleeding, and diverticulitis. In the health professionals' follow-up study, Aldoori et al[44] found that the RR of developing symptomatic diverticular disease was 2.35 for men taking a low-fiber diet. However, it should be noted that the definition of symptomatic diverticular disease in this study was not objectively clarified in all cases and was self-reported by participants. Most recently, in a study borne out of the Million Women Study in the United Kingdom, Crowe et al[45] demonstrated that a high intake of dietary fiber is associated with a reduced risk of diverticular disease, and that this association varies by the source of the fiber (fruits and cereals). Again, the endpoint was patients admitted to hospital with an ICD-10 code of diverticular disease therefore it is difficult to tease out whether these patients had symptomatic disease.

Furthermore, there is little evidence to support a low-residue diet in preventing diverticulitis. It was previously thought that indigestible foods such as nuts and seeds could potentially cause diverticular trauma and perforation; however, these recommendations are unfounded. The health care professionals' follow-up study found an inverse relationship between high-residue consumption and the risk of diverticular disease (RR 0.8). In addition, this study did not demonstrate an increased incidence of diverticular bleeding associated with a high-residue diet.[21]

Overall, despite the plausibility of a low-fiber/low-residue hypothesis, evidence is still lacking to implicate fiber as a causative factor in the development of diverticular disease.

AGE AND GENDER

Age-related and gender-related differences in patients presenting with diverticulitis exist, with males more likely to develop diverticulitis at a younger age compared with a higher female predominance in older age. Data from Western populations suggest that up to one fifth of patients with diverticulitis are under the age of 50 (reported incidence 18% to 34%[19,46–48]). Although there was a concern that younger patients have a more virulent disease course and may require a more aggressive approach,[49–51] there is a lack of evidence to support this hypothesis. Recent studies would suggest that younger age is a risk factor for recurrent disease; however, these patients are just as likely to respond to conservative management.[52–55]

SMOKING

There have been a number of studies investigating the relationship between smoking and diverticular disease. The Swedish mammography cohort study investigated 36,000 women of whom 560 had an admission for diverticulitis during the study period.[22] After adjustment for multiple confounders, the authors found a 24% increased risk of hospitalization for diverticular disease in smokers and ex-smokers. In another northern European study of 7500 Swedish men, the RR of diverticulitis requiring hospitalization was 1.6.[56] The Oxford EPIC study found similar results (RR of 1.86).[43] Interestingly, there appears to be a higher incidence of strictures and perforation in smokers compared with nonsmokers[57] and a higher likelihood of abscess or perforation in female smokers compared with males.[58,59]

NSAIDs

NSAIDs may cause colonic injury via direct topical injury and/or impaired prostaglandin synthesis compromising mucosal integrity, increasing permeability and enabling the influx of bacteria and other toxins.[60] Several case-control studies have demonstrated an increased risk of diverticulitis and diverticular bleeding in patients taking aspirin or NSAIDS.[61–64] More robust data from the health professional follow-up study showed an increased incidence of uncomplicated diverticular disease in patients who used NSAIDs compared with their non-NSAID–using counterparts.[65]

Overlap With IBS

Although recent population-based studies demonstrate that lifestyle (diet, obesity, smoking, NSAID use) is a factor in developing diverticular disease, the etiology of this disease remains unknown. There is however a certain overlap between patients with chronic diverticular symptoms and that of IBS and inflammatory bowel disease. It could therefore be postulated that in certain cases of so called "smouldering" diverticular disease, a common etiology exists. It is recognized that patients with diverticular disease have abnormalities of neuromuscular function,[66–68] lower pain thresholds to colonic distension[69] and may have endoscopic and histological evidence of colitis.[70,71] Most

recently, efforts have been made to characterize a type of "post diverticulitis IBS."[72] As knowledge of the pathogenesis of IBD and IBS emerges, it is possible that patients with diverticular disease may have underlying abnormalities in gut immune function, brain gut axis, and dysbiosis.[73] Although very few studies have addressed this, there is limited evidence that modulation of colonic microbial flora with probiotics and nonabsorbable antibiotics may help to reduce symptomatic diverticular disease.[74]

SEGMENTAL COLITIS ASSOCIATED WITH DIVERTICULOSIS (SCAD)

SCAD is a chronic colitis that affects the diverticular segment but, by definition, with endoscopic and histological sparing of the rectum and proximal colon (right colon).[75] Presenting features include chronic diarrhea, abdominal pain, and rectal bleeding. It is thought to affect males more than females and usually occurs in patients over 60 years of age.[76] SCAD has been classified into types A, B, C, and D based on mucosal appearances at endoscopy. Types A and C demonstrate varying severity of mucosal inflammation, aphthous ulceration with sparing of the diverticulae. Types B and D are more like an ulcerative colitis-type pattern with loss of vascular pattern, mucosal edema, and hyperemia and diffuse erosions with contact bleeding.[77] The disease course is relatively benign although symptoms may recur despite treatment. SCAD has shown a response to 5-ASA compounds such as mesalazine or sulfasalazine,[75,78] as well as steroid treatment but evidence for their efficacy is confined to case series.

GENETICS

A genetic etiology to diverticular disease has often been dismissed as most studies have focused on diet and lifestyle factors. A study of the Swedish twin registry demonstrated an odds ratio of 7.15 of developing the disease given one's co-twin was affected. Monozygotic twins were more likely to be affected with a heritability estimated at 40% and the non shared environmental effects to 60%.[79] Familial diverticulosis has been reported in the literature however an underlying genetic defect has not been identified with the etiology being more attributable to abnormalities in collagen or elastin production.[80–82]

Figure 1 shows the factors implicated in diverticulitis.

DIAGNOSIS AND IMAGING

The classical presentation of acute diverticulitis includes left iliac fossa pain and tenderness, raised inflammatory markers (WCC and CRP) and fever. However, diagnosing diverticulitis on clinical grounds alone has a sensitivity of 40% to 70%.[83–85] In 2006, the American Society for Colon and Rectum Surgeons (ASCRS) advised that "computed tomography (CT) was the most appropriate imaging modality in the assessment of suspected diverticulitis"[86] with a sensitivity and specificity of 93% and 100%, respectively.[87] In addition, CT is useful in differentiating severe disease from mild uncomplicated diverticulitis and may be useful in predicting response to treatment as well as identifying patients who may develop complicated disease.[88]

Both ultrasound and magnetic resonance imaging play a role in the diagnosis of diverticulitis. Graded compression ultrasonography has been shown to have a sensitivity of 92% in diagnosing acute diverticulitis[89] although diagnostic

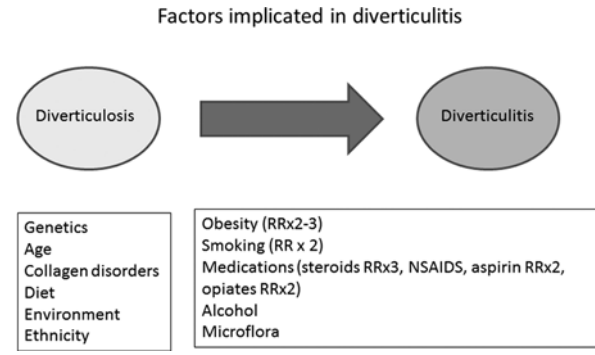

FIGURE 1. Factors implicated in diverticulitis: Representative diagram showing underlying factors associated with diverticulitis and relative risk (RR) in progressing to diverticulitis.

accuracy may be hampered by investigator experience, pain, and body habitus. Magnetic resonance imaging (although costly) is emerging as a valuable tool in GI imaging and may be superior to CT and ultrasound. Advantages include a lack of ionizing radiation, excellent contrast resolution, as well as the ability to perform fistulography and perhaps in time differentiate inflammation from cancer.[90,91]

CT criteria in acute diverticulitis is given in Table 1.

COLONOSCOPY

Guidelines recommend that patients with an attack of acute diverticulitis undergo a colonoscopy within 6 to 8 weeks to confirm the diagnosis and rule out a misdiagnosed malignancy. This dogma has been called into question and has formed the basis for several recent studies.[93,94] In patients who have a CT proven diagnosis of uncomplicated diverticular disease, the risk of an occult colorectal malignancy is low.[95,96] In a systematic review, the overall rate of malignancy was 1.6% (22/1970 patients).[97] However, these data must be carefully interpreted as the studies involved varied considerably in terms of design and methodology as well as including a very heterogeneous patient cohort. A systematic review recently publishes also claims a low incidence of malignancy in patients with uncomplicated diverticulitis (1.16%).[98] It should be recognized that in cases of complicated diverticulitis, the incidence of neoplasia is higher and this cohort should be considered "higher risk" in terms of harboring an underlying neoplasm.[97–100]

CHANGING CLASSIFICATION/CHANGING MANAGEMENT

Recently the nomenclature of diverticular disease has changed reflecting an acknowledgment that diverticular disease encompasses a spectrum of pathology ranging from diverticulosis, acute diverticulitis, and perforated diverticular disease to diverticular bleeding. Klarenbeek et al[101] proposed a classification system based on disease severity and duration of symptoms classifying diverticular disease into type A (uncomplicated diverticular disease), type B (chronic complicated disease), and type C (acute complicated diverticular disease). Others have classified diverticular disease into diverticulosis (the presence of diverticula) and diverticular disease (encompassing acute diverticulitis, symptomatic uncomplicated diverticular disease [SUDD]) and chronic diverticulitis (SCAD and recurrent diverticulitis).[102] SUDD is

TABLE 1. CT Classification of Acute Diverticulitis[92]

Moderate Diverticulitis	Severe Diverticulitis
Localized sigmoid colon wall thickening (> 5 mm) Inflammation localized to pericolic fat	Moderate diverticulitis plus any of: Abdomino-pelvic abscess Free extraluminal gas Extraluminal contrast extravasation

a subtype of diverticular disease in which there are persistent abdominal symptoms attributed to diverticula in the absence of macroscopically overt colitis or diverticulitis.[102] It is characterized by left lower quadrant abdominal pain in patients with diverticular disease, who do not manifest severe or acute symptoms, but rather low-level and indolent complaints.[103] Despite the fact that there is no universal classification system for diverticular disease, there is agreement that treatment differs depending on the severity of disease and that medical management is appropriate in the majority.

The classification systems for diverticular disease Table 2.

MEDICAL MANAGEMENT

There have been several, generally limited quality studies of 5-ASA compounds in the treatment and prevention of recurrence in diverticular disease, specifically in patients with SUDD. These studies however are limited by small numbers with poorly defined patient populations. Use of mesalamine/mesalazine an anti-inflammatory 5-ASA derivative has proven to be of potential benefit in achieving and maintaining remission in recurrent diverticulitis. It is difficult to tease out whether the response to mesalazine is secondary to controlling an element of diverticular colitis however results demonstrate lower rates of symptomatic relapse in the mesalazine group.[108,109] Results of the DIVA trial investigating mesalamine, probiotic or placebo for CT proven diverticulitis demonstrated a trend to reduced symptoms in the mesalamine group although overall results were not statistically significant.[110] Most recently, mesalamine did not prevent recurrent diverticulitis in phase 3 controlled trials.[111] The nonabsorbable antibiotic rifaximin has demonstrated promise in reducing some of the symptoms SUDD. The rational for its use is based on the hypothesis of a colonic bacterial overgrowth linked to fecal stasis in diverticular pockets. In a recent meta-analysis of 4 prospective randomized trials (1660 patients),[112] the authors found that up to two thirds (64%) of patients treated with rifaximin were symptom free at 1-year follow-up compared with only 35% in the control group.

ANTIBIOTICS AND AMBULATORY TREATMENT

According to current guidelines, bowel rest or intake of oral fluids and a 7- to 10-day regimen of broad-spectrum antibiotics is recommended in patients with uncomplicated diverticulitis.[113] However, there is no consensus on the most appropriate antibiotic regimen or route (oral/intravenous) although broad-spectrum agents targeting gram-negative organisms (*Escherichia coli*) are advised. In cases of symptomatic uncomplicated diverticular disease, treatment can be safely provided on an outpatient basis as long as patients are able to tolerate oral intake.[114–116] Interestingly, there is little evidence on whether mild cases of diverticulitis require antibiotic therapy at all. Current recommendations are based on expert opinion however a recent open, randomized, multicenter trial (AVOD trial, 669 patients)

TABLE 2. Classification Systems for Diverticular Disease

	Hinchey Classification[104]	Köhler Modification[105]	Modified Hinchey[106]	Hansen/ Stock[107]
			0—Mild clinical diverticulitis	0 Diverticulosis
Stage I	Pericolic abscess confined by the mesocolon	Pericolic abscess	I—Pericolic abscess or phlegmon Ia—Colonic wall thickening/ Confined pericolic inflammation Ib—Confined small (< 5 cm) pericolic abscess	Acute uncomplicated diverticulitis
Stage II	Pelvic abscess, distant from area of inflammation	IIa—distant abscess amenable to percutaneous drainage IIb—complex abscess with/ without associated fistula	II—Pelvic, distant intra-abdominal, or retroperitoneal abscess	Acute complicated diverticulitis IIa—Phlegmon, peri-diverticulitis IIb—Abscess, sealed perforation IIc—Free perforation
Stage III	Generalized peritonitis resulting from pericolic/pelvic abscess rupture into peritoneal cavity	Generalized purulent peritonitis	III—Generalized purulent peritonitis	Recurrent diverticulitis
Stage IV	Fecal peritonitis resulting from free perforation of colonic diverticulum	Fecal peritonitis	IV—Generalized fecal peritonitis	N/A

found no significant difference in complication rate ($P = 0.3$), length of stay or recurrent diverticulitis ($P = 0.88$) in patients treated without antibiotics.[117] A second multicenter randomized trial investigating the cost-effectiveness of treatment strategies with or without antibiotics for uncomplicated acute diverticulitis (DIABOLO) is underway and results are eagerly awaited.[118]

ARE WE OVERTREATING THIS DISEASE? ELECTIVE RESECTION

Outdated guidelines propose elective resection to patients who suffered more than 2 attacks of diverticulitis as it was thought that the risk of perforation was higher in those with relapsing disease.[113] However, sigmoid colectomy is not without risk and has a reported mortality of 1%, a 30% to 50% morbidity, with up to 10% receiving a stoma (at least in the short term).[119–121] Furthermore, elective resection is not curative in all patients, with recurrence rates after surgery estimated at 2.6% to 10%.[122–124]

The natural history of diverticulitis is such that the rate of recurrence is estimated at 2% per year while the risk of requiring emergency surgery after diverticulitis is calculated to be 1 in 2000 patient-years.[125] Consistently, studies have demonstrated that approximately 20% to 30% of patients will have a recurrence.[126–131] Interestingly, patients are more likely to present with perforated disease and severe sepsis on their index admission.[129,131–139] In terms of cost-effectiveness, expectant surgical management of recurrent diverticular disease gives rise to fewer deaths, fewer colostomies and more quality-adjusted life years.[140,141]

Table 3 shows the outcomes following an episode of acute diverticulitis.

What has emerged from the literature is that there are certain high-risk groups who should be considered for elective resection. Immunocompromised patients, those with renal failure or collagen-vascular disorders (rheumatoid arthritis) and perhaps patients following abscess drainage may warrant sigmoid resection in an elective setting.[146,147] The only strict criteria for elective resection should be fistulating disease, diverticular stricture, disease refractory to conservative management, recurrent diverticular bleeding, or if there is a strong suspicion of malignancy. At present the ASCRS recommend that elective resection should be decided on a case-by-case basis.

ABSCESS DRAINAGE

Before the introduction of radiological drainage, up to 15% of operations for complicated diverticular disease were for abscess drainage.[148] Despite the fact that percutaneous drainage has become the standard of care in the management of large abscesses, its role is limited to minimizing intra-abdominal sepsis preceding definitive surgery. Interestingly, there is no clear international consensus on whether all abscesses require drainage and whether a definitive procedure (sigmoid resection) is required.

Not all diverticular abscesses require drainage. In a study by Siewert et al[149] of 31 diverticular abscesses, those <4 cm were treated successfully with antibiotics. In the same study, patients with an abscess >4 cm were treated with CT-guided drainage with 40% of patients avoiding surgery. In study by Singh et al,[150] 50% of patients (16 patients in total) undergoing percutaneous abscess drainage avoided surgery. In this cohort, the median abscess size was 8.5 cm. The largest study conducted by Ambrosetti et al[151] in 2005 retrospectively analyzed 76 patients with diverticular abscess. After a follow-up period of 43 months they found that 41% did not require surgery after conservative management. Antibiotics alone were curative in 30 cases and mesocolic abscess had a better prognosis with higher avoidance of surgery compared with pelvic abscess.

MINIMALLY INVASIVE APPROACH

Over the last number of years a minimally invasive approach to the surgical management of diverticular disease has been adopted in both the elective and emergency setting.

ELECTIVE SURGERY—LAPAROSCOPIC OR OPEN?

Elective surgery for diverticular disease is indicated for patients with a diverticular stricture or fistula (colo-vesical/colo-vaginal) or for patients with disease refractory to medical management (persistent symptoms and chronic pain). Although the open approach to elective sigmoid resection has been the mainstay of treatment, laparoscopic sigmoid resection has emerged as a viable alternative with lower rates of morbidity, mortality, cost, and hospital stay in the reported literature. The Sigma trial[152] (104 patients, prospective, multicenter, double-blind, parallel-arm, randomized controlled trial) demonstrated equivalent outcomes in terms of morbidity between laparoscopic sigmoid resection and open sigmoid resection. However, the laparoscopic group had less major complications, less blood loss, shorter hospital stay, and better quality of life (as assessed by SF-36) and pain scores. In a second randomized single-blind trial of 113 patients[153] there was a significant difference in postoperative ileus, length of stay, and postoperative pain compared with the open group. Interestingly, this study did not show a difference in major postoperative complications between groups. Data from meta-analyses comparing laparoscopic to open sigmoid

TABLE 3. Outcomes of Patients Presenting with Acute Diverticulitis

Study	Total	Conservative	Drainage	Surgery
Abbas[142]	639	566 (88%)	14 (2.1%)	59 (9.2%)
Rogers[143]	28,480	26,025 (91%)	N/A	2455 (8.6%)
Masoomi[19]	840,157	85.9%	1.88%	102,245 (12.1%)
Makela[144]	695	625 (90%)	N/A	70 (10%)
Etzioni[145]	165,826	83.1%	2.5%	14.4%
Jeyarajah[23]	176,528	154,602 (87.6%)	N/A	21,926 (12.4%)
Anaya[127]	25,058	20,136 (80.3%)	N/A	4922 (19.6%)

Overall, approximately 85% of patients with acute diverticulitis will be successfully managed with conservative treatment. The remaining 15% will either require surgical intervention or may be treated with percutaneous drainage (2%).

colectomy add further weight to a laparoscopic approach. Siddiqui et al[154] (22 comparative studies involving 10,898 patients were analyzed; 1538 patients were in the laparoscopic group and 9360 were in the open group) demonstrated a statistically lower overall morbidity, blood loss, and hospital stay in patients undergoing laparoscopic sigmoid resection. Data from the American nationwide inpatient sample also demonstrate significantly superior outcomes for elective laparoscopic sigmoid resection in terms of postoperative mortality, morbidity, and hospital stay.[155]

EMERGENCY SURGERY FOR PERFORATED DIVERTICULAR DISEASE (FECULENT/ NONFECULENT PERITONITIS)

The traditional dogma has always advocated against performing a primary anastomosis in the presence of peritonitis due to the risk of persistent sepsis and anastomotic leak. Based on these teachings, HP (resection of the diseased segment [sigmoid colon], oversewing of the rectal stump and formation of a proximal end colostomy) became the gold standard in the surgical management of perforated sigmoid diverticulitis. The benefits of an HP include a quick, relatively straightforward operation in sick or unstable patients. However, an increasing number of reports demonstrate that primary anastomosis is a worthy alternative even in the presence of peritonitis.[156,157] A systematic review published in 2007 demonstrated favorable outcomes of primary resection and anastomosis compared with HP in terms of mortality and perioperative complications.[158] However, the majority of published studies are retrospective in nature and contain selection bias as the sickest patients tend to undergo an HP which may inflate the complication rates associated with this operation. To date, there has only been one randomized controlled trial

TABLE 4. Noteworthy Trials in Acute Diverticulitis

Name	Study	Objective	Inclusion Criteria	Study Number	Results
DIABOLO trial The Netherlands[118]	A multicenter randomized clinical trial investigating the cost-effectiveness of treatment strategies with or without antibiotics for uncomplicated acute diverticulitis	To establish whether antibiotics are necessary in the primary treatment of acute mild diverticulitis	Hinchey Ia or Ib determined by CT criteria No systemic sepsis	533	Currently recruiting
AVOD Sweden/ Iceland[117]	Open multicenter randomized controlled trial 2003-2010	Antibiotics in uncomplicated diverticulitis	Uncomplicated diverticulitis Clinical signs of diverticulitis, without sepsis, with an increased body temperature and inflammatory parameters, verified by computed tomography (CT), and without any sign of complications such as abscess, free air or fistula	669	No significant difference in complication rate ($P = 0.3$), length of stay or recurrent diverticulitis ($P = 0.88$) between groups No antibiotics (1.9% vs. 1% antibiotic group, $P = 0.3$)
SIGMA The Netherlands[152]	Prospective, multicenter, double-blind, parallel-arm, randomized control trial	Laparoscopic vs. open sigmoid resection for diverticular disease	Recurrent disease Hinchey I, IIa, IIb, symptomatic stricture, or severe rectal bleeding	104	Laparoscopic sigmoid resection had a 15.4% reduction in the rate of major complications. Also less pain, improved quality of life, and shorter hospitalization with laparoscopic approach
LADIES The Netherlands[166]	Multicenter two armed randomized trial LOLA arm; laparoscopic lavage, Hartmann's or resection and anastomosis (2:1:1) DIVA arm: for feculent peritonitis Hartmann's or resection/ anastomosis (1:1)	Patients with generalized peritonitis caused by perforated diverticulitis are randomized to undergo either laparoscopic lavage and drainage or resectional surgery by laparotomy.	Free gas on CT, or upon the finding of peritonitis with diffuse fluid or gas on CT	LOLA arm: 264 DIVA arm: 212	Recruitment commenced 2009.
LapLAND Ireland[167]	Multicenter randomized trial	Laparoscopic lavage for perforated nonfeculent diverticulitis vs. Hartmann's or resection and anastomosis	Patients with generalized peritonitis and radiological evidence of free air on CT	300	Recruitment commenced 2010

TABLE 5. Diverticular Hemorrhage Diagnosis and Treatment

Modality	Sensitivity	Therapy	Outcome
Nuclear scintigraphy	0.1 mL/min	N/A (purely diagnostic)	Reported to localize bleeding in 45%-94% of cases[176,177]
Colonoscopy	Mild/moderate bleeding	Endoscopic clipping Rubber band ligation	Cessation of bleeding in 85%[178]
Angiography	1.0-1.3 mL/min	Vasopressin infusion Embolization	Diagnostic yield 40%-86%[179] 90% success rate (vasopressin) 85% success rate (embolization)

comparing HP to primary resection, anastomosis and defunctioning ileostomy. Results from this multicenter trial of 62 patients demonstrated equivalent results in terms of postoperative mortality and morbidity but a lower rate of serious complications, decreased hospital stay, and a higher rate of stoma reversal in the primary anastomosis group.[159] In a decision analysis study between HP and primary anastomosis with diverting ileostomy (PADS), the authors concluded that PADS may be the procedure of choice for perforated diverticular disease when the risk of postoperative complications is reasonable (in the region of 40%). When long-term outcomes are considered, PADS is the preferred option (better quality of life) reflecting the fact that patients undergoing HP are often left with a permanent stoma (27.4%).[160]

LAPAROSCOPIC LAVAGE FOR PURULENT PERITONITIS

In addition to colonic resection for diverticular disease with peritonitis, there has been an adoption of a minimally invasive approach in select circumstances. Laparoscopic lavage has emerged as a useful diagnostic adjunct as well as an attractive therapeutic procedure in patients with purulent peritonitis. It should be recognized however that purulent peritonitis (Hinchey III) likely represents rupture of an abscess into the abdominal cavity rather than an actual perforation of the colon. Therefore, in these circumstances, peritoneal lavage and washout allows for an organ preserving approach with lower rates of morbidity (avoidance of stoma) and mortality (< 5%) compared with standard sigmoid resection.[143,161–165]

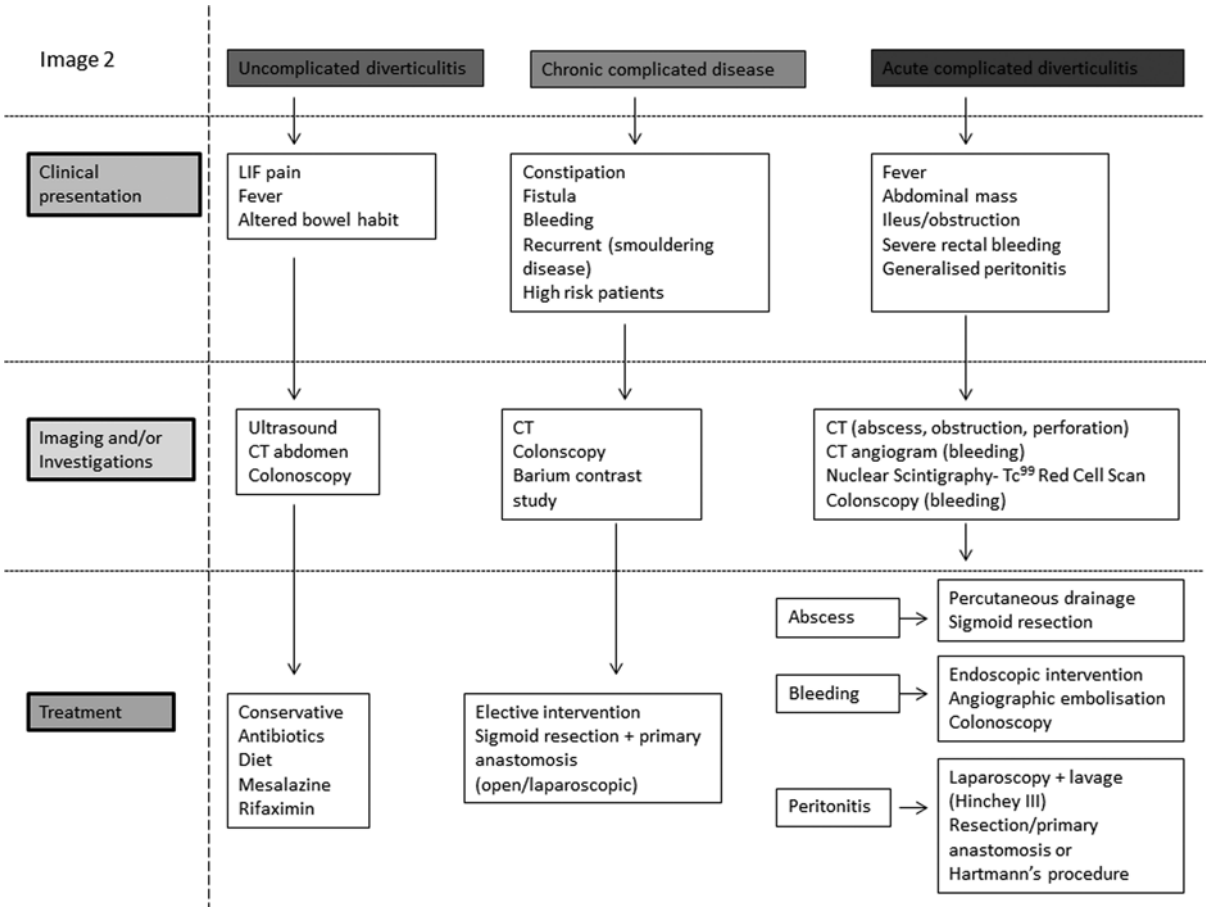

FIGURE 2. Clinical algorithm for the management of diverticular disease. CT indicates computed tomography; LIF, left iliac fossa;

Table 4 lists the noteworthy trials in diverticulitis.

DIVERTICULAR HEMORRHAGE

Lower GI tract bleeding has a hospitalization rate of approximately 36/100,000 in the United States.[168] Diverticular disease is thought to be responsible in approximately 30% of cases[169] estimated at fewer than 1 in 2000 person-years events (383 bleeds with only 70 requiring transfusion or intervention in 730,446 person-years or follow-up).[21] Bleeding is usually of sudden onset, painless and is generally self-limiting in the majority of cases (80%)[170] although re-bleeding may occur in 20%.[171] Hemorrhage is thought to be due to rupture of the vasa recta into the colonic lumen as they course over protruding diverticula. Histological features demonstrate nonuniform intimal thickening of vasa recta usually in the absence of luminal inflammation.[172] Patient factors associated with diverticular bleeding include aspirin and NSAID use,[65] anticioagulant use, obesity,[173] advanced age, and hypertension.[174] Although left-sided diverticula are most common in western populations, bleeding most often originates from the right side.[175] Methods for investigating diverticular hemorrhage include nuclear scintigraphy (diagnostic), angiography with embolization, and colonoscopy. Surgery may be offered as a final resort although these patients often have considerable comorbidities and may require a total colectomy if a preoperative bleeding source cannot be identified.

The management of diverticular hemorrhage is given in Table 5.

Summary of management strategies in diverticular disease is shown in Figure 2.

CONCLUSIONS

A renewed interest in the epidemiology, pathogenesis, and management of diverticular disease has emerged over the last decade. With the development of improved antimicrobial therapy and widespread access to critical care, as well as accurate diagnostic imaging and minimally invasive surgery (including percutaneous drainage), the morbidity and mortality from diverticulitis has dramatically decreased. Large-scale epidemiological studies have yielded etiological factors (eg, obesity, smoking, genetics, and ethnicity) which may contribute to the pathogenesis of this disease. Armed with this new evidence we are now in a position to challenge the outdated poor quality evidence which has governed the management of diverticulitis for the last 50 years.

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