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Current Controversies in the Management of Diverticulitis: A Review

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Keywords

Diverticulitis · Diverticular disease · Treatment

Abstract

Background: Symptomatic diverticular disease is challenging for patients, clinicians and health services. The prevalence increases with age and BMI and as such, the burden of this disease is set to increase with higher rates of acute presentations already documented. The natural history of recurrent episodes, complications and symptom progression is not fully understood. Furthermore, medical and surgical management strategies are under constant appraisal, debate and evolution. *Methods:* A review of the contemporary literature was performed to examine the emerging trend towards conservative treatment. Results: Routine use of in-patient, intravenous antibiotics may not be required and outpatient management is possible for certain patients. Universal colonoscopy examination after uncomplicated acute diverticulitis is controversial but is mandatory after complicated episodes. Recent, high-profile, clinical trials suggest that less aggressive surgical management of both acute and chronic presentations may be feasible in some cases. Con-

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E-Mail karger@karger.com www.karger.com/dsu *clusions:* Diverticulitis is a common yet challenging topic that demands clinicians to provide an individualised yet evidence-based approach. © 2018 S. Karger AG, Basel

Introduction

Diverticulosis, the presence of outpouchings of the colonic mucosa, increases with age with a prevalence of 10% in adults under 40 years and up to 70% in those 80 years of age or older [1]. For most people, diverticulosis is asymptomatic; however, traditional teaching suggests that it becomes clinically significant in approximately 20% of patients [2, 3]. Diverticulitis, the macroscopic inflammation of diverticulae with related acute or chronic complications [4], continues to have an impact on patients and leads them to the use of health services. The number of presentations with this entity is increasing over time: In the NHS, acute admissions with diverticulitis increased by 16% in males and 12% in females over a 10-year period [5]. Similarly, epidemiological data from the United States reveals a 26% increase in presentations with acute

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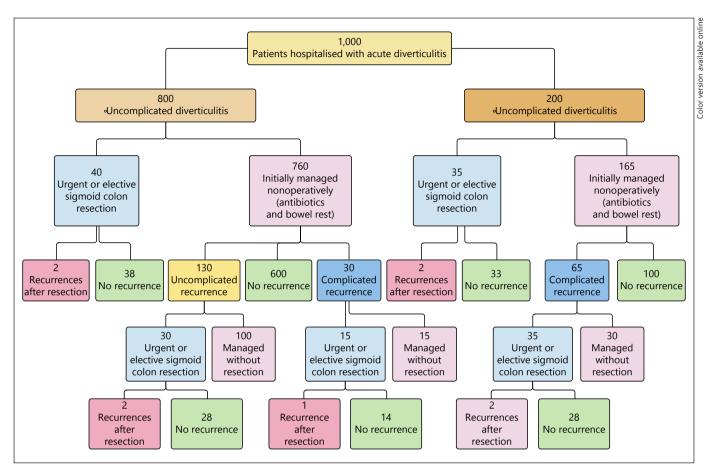


Fig. 1. The natural history of diverticulitis based on 1,000 hypothetical patients.

diverticulitis from 1998 to 2005 [6]. Of particular significance, rates of admission are increasing most rapidly in young patients (the rate of admission increased by 82% in patients aged between 18 and 44 years in one series [6]). Given that the prevalence of diverticulosis is related to both increasing age [7] and BMI [8], the burden of this disease is set to increase further, given the epidemic of obesity that is predicted and our ageing population.

The natural history of diverticulosis is poorly understood. A rate of symptomatic diverticulitis ranging from 10 to 25% was initially proposed in a review in 1975 by Parks [9]. With the emergence of population based colonoscopy, however, this has been revised. Current data from the American Gastroenterology Association (AGA) published in 2015 suggests that 4% of patients with diverticulosis develop diverticulitis; of these patients, 15% have complicated diseases [10]. There are multiple classification systems for complicated diverticulitis, of which the Hinchey Classification (Table 1) is most widely used [11]. Morris et al. [12] performed a systematic review of diver-

 Table 1. Hinchey classification [1]

Description
Phlegmon or localised paracolic abscess
Pelvic abscess
Purulent peritonitis
Feculent peritonitis

ticulitis, including the natural history, and illustrated their findings using a hypothetical cohort of 1,000 patients, which is reproduced, with permission, in Figure 1.This is consistent with a population-based Californian study in which 84% of patients with acute diverticulitis are successfully managed conservatively without them having to experience a second episode [13]. The outcomes of recurrent episodes of acute diverticulitis are particularly relevant for planning long-term management. Chapman found that the occurrence of more than

Nally/Kavanagh

2 episodes does not lead to poorer outcomes at subsequent presentations [14]. However, patients with a complicated initial presentation are more likely to have a second episode. In one series of 210 patients with a diverticular abscess, 60% had a second presentation that was frequently more severe than the initial presentation; 59% of these patients required surgery [15].

Furthermore, uncomplicated diverticulitis may not run a benign self-limiting course; up to 30% of patients without further episodes have ongoing abdominal symptoms labelled "smouldering" diverticulitis [16]. Strate et al. [4] disagree with the concept of diverticular disease as discrete isolated episodes and instead propose a model of chronic illness with a spectrum of manifestations. They propose a taxonomy defining the terms associated with chronic diverticulitis including segmental colitis associated with diverticulae, a clinicopathological entity akin to inflammatory bowel disease. New concepts of pathogenesis, implicating inflammation, microbiome shifts, visceral hypersensitivity, and abnormal motility are emerging and they are influencing the medical strategies for the management of diverticulitis [12].

Rationale/Aim of this Review

With the increase in presentations documented above and ambiguity regarding disease course, diverticulosis represents a challenge to the general surgical community. Moreover, optimal management generates considerable debate, with a movement towards an increasingly conservative approach with respect to hospital admission and antibiotic treatment. When surgery is required, a more limited intervention may be possible. Thus, diverticulitis remains a focus of prolific research with large volumes published on the topic on a regular basis. A review of the literature surrounding current controversies is a timely intervention to support clinicians involved in the management of this common, complex condition.

Medical Management Antibiotics

Our understanding of the pathophysiology of diverticulitis has recently expanded from a primarily infectious entity to an appreciation of the inflammatory nature of the condition, with increased expression of proinflammatory mediators [17, 18]. As a result, and with an increasing awareness of judicious antibiotic use, some clinicians are challenging established doctrines of antimicrobial therapy in acute diverticulitis. However, a Cochrane

Review in 2014 concluded that there was insufficient evidence to ensure the safety of omitting antibiotics and hence did not mandate a change in clinical guidelines at that time [19]. Recent studies, however, advocate the omission of antimicrobial therapy in acute diverticulitis: The AVOD study, a randomised controlled trial of 623 patients with CT proven diverticulitis, compared an antibiotic arm (at least a 7-day course of intravenous [IV] and oral antibiotics) with no antibiotic treatment (IV fluids only). They found that antibiotic treatment neither accelerated recovery nor reduced complications (sigmoid perforation or abscess formation) [20]. However, 32% of patients allocated to the no-antibiotic arm required antibiotic treatment because of increasing CRP level, fever or abdominal pain. Similarly, in the Diverticulitis Antibiotics or close Observation trial, 528 patients with a first episode of CT confirmed left-sided uncomplicated acute diverticulitis (including those with Hinchey stages 1a-b [abscess size up to 5 cm]) were randomised to antibiotic and no antibiotic arms. Those in the antibiotic arm received a 10-day course of antibiotics, initially intravenously with change to oral medication after 48 h based on clinical progress. Supportive care in the no-antibiotic treatment arm was not documented. The primary outcome, time to recovery, was defined as discharge from hospital, normal diet, temperature less than 38 °C, visual analogue score pain score below 4 (with no use of daily pain medication), and resumption of pre-illness working activities. This was similar between the 2 groups, as were secondary endpoints at longer-term follow-up [21]. Details of these trials are given in Table 2. This evidence is incorporated in the "2017 American Gastroenterological Association (AGA) Institute Guideline on the Management of Acute Diverticulitis" which promotes selective individualised as opposed to routine use of antibiotics in this presentation [22].

Mesalazine and Probiotics

As mentioned above, the postulated role of inflammation in the pathogenesis of diverticular disease, specifically in recurrent episodes, is gaining popularity. The role of anti-inflammatory, aminosalicyclate (5 ASA) compounds to counteract this, including mesalazine has been investigated. However, multiple placebo controlled trials have shown that they neither reduce recurrent episodes nor improve symptomatology [23, 24]. These findings are confirmed in a 2017 systematic review and meta-analysis of 8 randomised controlled trials. The studies included in this review have different methodologies including a variety of dosing regimens and the use of concomitant pro-

Paper	Year	Study design	Antibiotic arm	Supportive arm	Number of patients	Primary outcome	Findings
AVOD study [2]	2012	RCT	At least 10 days. Initially IV (2nd- or 3rd-generation cephalosporin + metronidazole OR Piperacillin/Tazobactam OR Carbapenem). Change to oral antibiotics (ciprofloxacin plus metronidazole) after admission or on discharge	Intravenous fluids only	623	Complications, need for surgery, hospital stay, abdominal pain, fever and abdominal tenderness	Complications: Supportive arm 1.9%; 1% in Antibiotic arm (p = 0.302). Median hospital stay: 3 days in both groups. Recurrent diverticulitis/ readmission in 1 year 16% in both groups $(p = 0.881)$
DIABLO [3]	2016	RCT	10-day course. IV amoxicillin– clavulanic for 48 h. Then oral route, if tolerated. In the event of allergy, ciprofloxacin + metronidazole	Observation as outpatient if certain criteria satisfied	528	Time to recovery during 6 months of follow-up	Median time (days) to recovery: observation 14 (IQR 6-35); antibiotic 12 (7-30; HR 0.91; p = 0.151)

Table 2. Randomised controlled trials (RCT) of the use of antibiotics in the treatment of acute diverticulitis

biotics. 5 ASA compounds were not superior to controls for preventing recurrent attacks (RR 0.86, 95% CI 0.63–1.17) [25].

Alterations in the microbiome of the colon and dysbiosis have also been implicated in recurrent attacks [26] and thence targeted as a treatment focus with probiotics: Rifaxamin, a poorly absorbed antibiotic, has been trialled both alone and in combination with fibre and/or mesalazine to modify this process. In a meta-analysis of 4 trials with 1,660 patients with symptomatic uncomplicated diverticular disease, treatment with rifaximin plus fibre supplementation was effective in obtaining symptom relief and preventing complications at 1 year with a number needed to treat equal to 3 [27]. The benefits of probiotics have been investigated. However, a systematic review of 11 studies by Lahner et al. [28] found that the included studies were of insufficient level of evidence to draw meaningful conclusions.

Inpatient verses Outpatient

In keeping with the theme of conservative management, the suitability and safety of outpatient management have been examined. A recent systematic review of 10 studies from centres in Spain and the United States found that failure rates for primary treatment and recurrence rates are similar when treated on an inpatient or outpatient basis [29]. This paper defines ambulatory care as an in-patient hospital stay up to 24 h only, with discharge to continue treatment at home in an out-patient setting either on oral antibiotics or with an outpatient IV service. This is confirmed by a recent paper by Joliat et al. [30] who employed a similar outpatient treatment strategy. These authors found that factors including increasing time to admission CT, Ambrosetti score of 4 and free air around the colon were predictive of treatment failure [30]. Assuming equivalent patient outcomes, it follows that outpatient treatment can lead to significant savings on health care costs: An Italian group quantified the economic burden of diverticulitis as EUR 3,826 per patient per year, of which, EUR 3,653 for hospital fees, might be avoided. Similarly, researchers in Spain found that outpatient management can generate up to a 60% saving in health care costs [31]. Moya et al. [32] demonstrated a saving of EUR 1,600 per patient. This potential for saving is particularly relevant to health care budgets, given the anticipated increase volume of disease outlined above.

Follow-Up (Interval) Colonoscopy

Clinical practice guidelines recommend an interval colonoscopy after an episode of diverticulitis [10]. This originates from historical data on the inaccuracy of barium studies: in a 1984 series of 65 patients, follow-up colonoscopy revealed polyps in 8 and carcinoma in 3 where a barium enema showed diverticulitis only [33]. However, colonoscopy is invasive with concomitant risks and is a burden on health care budgets [34]. Additional arguments against colonoscopy include the extensive use of modern, higher resolution CT scans and a diagnostic yield from colonoscopy in Hinchey I and II diverticulitis that is similar to that of the general population [35]. However, concern remains regarding occult malignancies and the possible association between diverticulitis and colorectal cancer. A 2004 paper from Sweden reviewed 7,159 cases of diverticulitis from 1965 to 1983 and found 64 cancers. When matched to patients with diverticulosis but no diverticulitis there was increased risk of colon cancer (OR 4.2, 95% CI 1.3-13.0) [36]. A Systematic Review and metaanalysis on the subject, including 11 studies from 7 countries, which pooled 1,970 patients, found 22 cancers that equated to a pooled proportional estimate of malignancy of 1.6% (95% CI 0.9-2.8). When categorised into uncomplicated and complicated diverticulitis, the pooled proportional estimates of malignancy were 0.7% (95% CI 0.3-1.4) and 10.8% (95% CI 5.2-21.0) respectively [37]. A further consideration is the detection of non-malignant polyps in 19.5%, which would otherwise not be removed. In a recent Danish population-based cohort study including 40,000 patients admitted with diverticulitis, the incidence of colon cancer at 4.3% was significantly higher than that in patients without diverticulitis (2.3%). Of note, patients had full colonoscopies, but the severity of the diverticulitis and hence any variation in the rate of cancers in simple and complicated diverticulitis is not captured in this paper [38]. The authors propose the inflammation associated with diverticulitis as a propagating factor for colorectal cancer. The results of primary studies have been synthesised in the 4 systematic reviews provided in Table 3. These studies show that the merit of interval colonoscopy following an episode of simple uncomplicated diverticulitis is debatable, but endoscopic evaluation after an episode of complicated diverticulitis is essential. Surgical intervention in diverticular disease is discussed below, but at this juncture, it is worth considering the possibility that a trend towards a non-resectional approach - both acutely and electively - might increase the risk of undiagnosed colorectal malignancies. This must be factored into follow-up endoscopy protocols in the future.

Surgical Management

Laparoscopic Lavage

An algorithm for the treatment of complicated diverticulitis, including interventional radiology and surgery is presented in Figure 2. One of the most controversial aspects of diverticulitis in recent years is the role of laparoscopic lavage, particularly in Hinchey III diverticulitis. Initial case series including the one by Myers et al. [39] suggested that this was a feasible approach, and a systematic review in 2010 found laparoscopic lavage to be successful in up to 95% of such cases [40]. The included studies, however, were level III evidence, (retrospective, cohort studies or case series) at risk of selection bias. Randomised controlled trials have subsequently reported conflicting results. The SCANDIV trial, a multicentre randomised controlled trial involving 199 participants, randomised patients with suspected perforated diverticular disease to undergo either laparoscopic lavage or colonic resection [41]. The primary endpoint was severe postoperative complications (defined as Clavien-Dindo complication of >IIIa) at 90 days. This was seen in 30.7% in the laparoscopic lavage group and 26.0% in the colon resection group (difference, 4.7% [95% CI -7.9 to 17.0]; p = 0.53), with a higher reoperation rate (12.9 vs. 8.3%) and 4 missed sigmoid cancers in the laparoscopic lavage group. The authors conclude that laparoscopic lavage does not reduce serious complication rates and has poorer secondary outcomes. For these reasons, they do not favour a lavage strategy.

The Ladies trial is a parallel group, multicentre (34 hospitals in Belgium, Netherlands, and Italy) randomised trial investigating the acute surgical management of diverticulitis. There are 2 arms: DIVA, which is ongoing, compares resection plus end colostomy (Hartman's Procedure) to resection plus primary anastomosis; the LOLA arm of this trial compared laparoscopic lavage to Hartman's procedure [42]. In this latter study, 90 patients with purulent perforated diverticulitis were randomised to undergo either laparoscopic lavage or Hartman's procedure [43]. The primary outcome was a composite endpoint of major morbidity and mortality within 12 months. Recruitment terminated early after interim analysis of results demonstrated poorer outcomes in the laparoscopy group: At 30 days, the combined primary outcome was 39% in the laparoscopic lavage group compared with 19% in the sigmoid colectomy group. Surgical re-interventions accounted for most of these adverse events. Followup continued to 12 months at which time the primary outcome measures were 60 and 67% between laparoscopic and open groups, respectively, with an OR of 1.28 (95%

[4]201210Studies of patients with CT diagnosis of acute diverticulitis who underwent colonoscopy, surgery, or buthin 24 weeksNot stated studies with both both studies with studies with studies with made on clinical and non- diagnosis of made on clinical and non- diagnosis was sigmoidoscopy, CT colonoscopy, or barium enemasNot stated studies with both made on clinical and non- complicated and non- colonoscopy, or barium enemasVries 20149Rc1 and idagnosis was econolic evaluation with colonoscopy, CT colonoscopy, or barium enemasDucomplicated and non- complicated diagnosis of made on clinical and non- conplicated observational diverticulitisDucomplicated and non- complicatedVries 20149RCT and barium enemasPatients <18 vervexs, and non- conplicatedUncomplicatedVries 20149RCT and barium enemasPatients <18 vervexs, teatures only or colonoscopy, or colonoscopyUncomplicatedVries 20148Studies with hartative colonoscopyUncomplicatedVries 20148Studies with or olonoscopy, or colonoscopyUncomplicatedVries 20148Studies with or olonoscopy, or colonoscopyUncomplicatedVries 20148Noroscopy or olonoscopyUncomplicatedVries 20148Studies with or olonoscopyUncomplicatedVries 20148Noroscopy or olonoscopyUncomplicatedVries 20148Noroscopy or o	Complicated or Patients Percentage uncomplicated who underwent endoscopy	Percentage with malignancy	Percentage of patients with nonmalignant colonic polyps/ neoplasia	Comments	Author's conclusion
11Studies including patients with patients with studies where diverticulitis who diverticulitis who diverticulitis who diverticulitis who diverticulitis who diverticulitis who features only received direct colonic evaluation with colonoscopy, CT colonography, or barium enemasBoth: subgroup and non- complicated and non- complicated9RCT and observational studies with colonoscopy, CT colonoscopyPatients <18 voncomplicated9RCT and observational studies with colonoscopyPatients <18 voncomplicated8zStudies with oution diverticulitisColonoscopy 	771 56% (remainder had alternative evaluation)	Pooled r prevalence 2.1%	Not specified	2 studies included patients with suspicious lesions on CT	Limited data supports the recommendation to perform colonoscopy after acute diverticulitis
RCT andPatients <18observationalyears, casestudies withreports,routinenarrativecolonoscopyreviews,acute diverticulitispatients withacute diverticulitiscomplicateddiverticulitisstudies withoutwith follow-upcolonoscopyafter US- orbut with CT-CT-provencolonography orleft-sidedcontrast bariumdiverticulitison stread oron stread orwith outcome based	up 3,358 59%	1.12% crude 1.6% pooled	Non-malignant polyps 19.5% (crude)	Crude rate of malignancy in complicated 7.6% Crude rate of malignancy in uncomplicated 0.3%	In the absence of other indications, routine colonoscopy may not be necessary, but those with complicated diverticulitis still have a significant risk of CRC
8z Studies dealing Studies without with follow-up follow-up colonoscopy colonoscopy after US- or but with CT- CT-proven colonography or left-sided contrast barium diverticulitis enemas instead or with outcome based	ted 2,490 59%	1.16%	Hyperplastic polyps 10.6% Low-grade adenoma 6.1% Advanced adenoma 2.2%	AA = adenoma >10 mm or greater and/or more than 25% villous components and/or severe dysplasia	Routine colonoscopy in the absence of other clinical signs of CRC is not required
obtained pathology specimens	ted 1,796 100%	1.60%	At least 1 polyp 20.2% Advanced adenoma 3.6% Advanced adenoma OR colorectal cancer 4.9%	AA = adenoma ≥10 mm, ≥25% villous features or with high-grade dysplasia	Recommend a refined approach targeting a complicated diverticulitis, suspicious radiologic findings, protracted clinical course or those due screening

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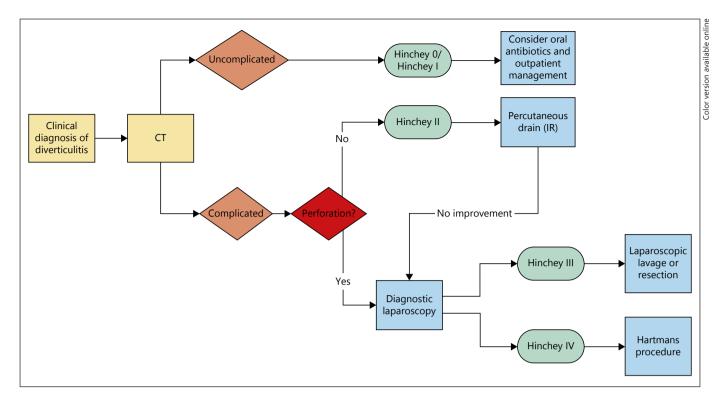


Fig. 2. Proposed treatment algorithm for diverticulitis based on severity. CT, computerised tomography; IR, interventional radiology.

CI 0.54–3.03, p = 0.58) for the primary outcome in the laparoscopic lavage group. This includes 4 patients (9%) and 6 patients (14%) in the lavage and resection groups, respectively, who died during the study period (OR 0.53, 95% CI 0.13–2.15, p = 0.38).

Conversely, an initial report from the DILALA study, a randomised controlled trial from 9 centres in Sweden and Denmark, revealed findings in favour of laparoscopic lavage. In this study, 83 patients with purulent peritonitis at an initial diagnostic laparoscopy were randomised into laparoscopic lavage or Hartman's Procedure arms [44]. The primary outcome of the study, reoperation rates at 12 months, is not yet reported, but short-term results at 3 months demonstrate similar rates of mortality (7.7 and 11.4%; p = 0.58) and reoperation rates (13.2 vs. 17.1%; p = 0.63) in lavage and resectional arms, respectively, while there was a shorter operation time, recovery and hospital stay in patients undergoing laparoscopic lavage.

Details of these three trials are provided in Table 4. The major differences between these studies are dependent on the re-intervention rate, which varies on the basis of when results are reported (prior to the time of expected stoma closure) or if stoma closure is specifically excluded. A further consideration when comparing the or after a diagnostic laparoscopy, which might change the diagnosis and account for variation in results. Three meta-analyses of the results of these trials have been published by Ceresoli [45], Angenete (the primary author of DILALA) [46] and Cirocchi et al. [47]. The former group concludes that washout is associated with more morbidity and reoperation at index admission, without differences in terms of mortality. In the longer term, laparoscopic lavage is associated with fewer reoperations. The authors conclude that the available evidence is inconclusive to favour one treatment over the other. Conversely, Angenete assert that the lower, 12-month re-intervention rates for laparoscopic washout favours this intervention [46]. Based on a cost analysis paper published elsewhere by the same research group, they also conclude that laparoscopic lavage is a more economical approach. In their meta-analysis, Cirocchi et al. [47] found a higher rate of postoperative, intraabdominal abscess in the lavage group (RR 2.54, 95% CI 1.34-4.83) and consequently adopted the position that, by generating more abscesses, laparoscopic washout negates the objective of sepsis control and hence is less preferable. The meta-analysis by Cirocchi et al. [47] also demonstrated the presence of a

studies is whether randomisation was performed before

Table 4. $ m R_i$	andon	nised contro	olled trials c	Table 4. Randomised controlled trials comparing outcomes from laparoscopic lavage and resection	tparoscopic lav	vage and resection		
Name of Year Location study	í ear	Location	Number of patients	Number of Arms (total patients numbers recruited)	Time of randomisation	Primary outcomes	Secondary outcome	Primary outcomes findings
SCANDIV 2 [8]	2015	SCANDIV 2015 Norway and 199 [8] Sweden	199	 Laparoscopic lavage (101) Colonic Resection (98) (lap/open/Hartman's/PRA as per surgical preference 	Before laparoscopy	Severe complication (>CD IIIa) at 90 days	 Length of operating time Postoperative LOS Post-operative LOS Post-operative complications individually, resection, difference 4.7% including those resulting in reoperation 90-day postoperative QoL 	Severe complications: 30.7% lap lavage; 26% in resection, difference 4.7% (95% CI -7.9 to 17.0 ; $p = 0.53$)
LOLA [9] 2015		Belgium, Italy, The Netherlands	90	 Laparoscopic lavage (47) Sigmoidectomy Hartman's procedure (21) Primary anastomosis (22) 	After laparoscopy	Composite endpoint including major morbidity and mortality within 12 months.	 Operating time LOS LOS Days alive and outside the hospital Short-term morbidity and mortality, Incisional hernia, Reinterventions within 12 months Health-related QoL 	Composite endpoint: 67% lap lavages; $60%$ in sigmoidectomy ($p = 0.5804$)
DILALA 2 [10]	2016	2016 Sweden and Denmark	83	– Laparoscopic lavage (43) – Open Hartman's procedure (40)	After laparoscopy	Reoperations within 12 months postoperatively	– Morbidity – Readmissions, – Reoperations – Mortality	Primary outcomes not yet reported
PRA, pri	mary r	esection anast	omosis; CD,	PRA, primary resection anastomosis; CD, Clavien Dindo; QoL, quality of life; LOS, length of stay.	fe; LOS, length of	f stay.		

stoma at 12 months to be lower in the laparoscopic group than that in the Hartman's procedure (RR 0.5, 95% CI 0.14–1.75).

Surgical Resection

The operative strategy for diverticular perforation with purulent or feculent peritonitis (Hinchey III and IV) has changed. Initially a 3-stage operation was performed: (1) diversion with a proximal colostomy and drainage of the perforated area; (2) resection of the affected area; and (3) reversal of stoma. In 1976, Classen published a 10-year experience with this approach with 208 patients and cited an overall mortality rate of 11% (78% of these deaths were related to the first procedure) [48]. This sequence, however, initially leaves the perforated colon (and faeces) in situ as a focus for sepsis and so it was condensed into a 2-stage, Hartman's procedure in which the diseased segment was removed during the initial laparotomy [49]. This became, and possibly still remains the standard of care, but the mortality of this operation has been cited as 15% based on a series of 199 patients undergoing this operation from 1999 to 2010 [50]. Furthermore, a Hartman's procedure is limited by the mortality and morbidity of colostomy reversal or the lifestyle implications of a permanent stoma for up to 60% of patients [51]. A onestage resection with restoration of continuity avoids some of these challenges but also generates concern about performing an anastomosis in a contaminated environment for a critically unwell patient. Intuitively this would require a very selective approach. In 2004, Salem et al. [52] performed a systematic review of these 2 strategies (including 98 studies and a total of 1,051 Hartman's procedures and 569 primary anastomoses). The cited overall mortality rate was 9.9 and 18.8% for primary anastomosis and Hartman's, respectively, with an overall anastomotic leak rate for a primary anastomosis of 13.9%. Meta-analysis and direct comparisons could not be drawn due to heterogeneity [52]. This clinical question will be clarified further when the DIVA arm of the LADIES trial, a randomised controlled trial comparing these 2 treatment modalities reports [42].

Elective Surgery for Diverticulitis

As discussed above, 15–30% of patients have recurrent episodes of diverticulitis and up to 30% have ongoing pain. There are 2 distinct indications for elective surgery. First, prophylaxis against recurrent attacks and complications and second, surgery for ongoing symptoms that impact quality of life (QoL). An initial enthusiasm for liberal preemptive elective surgery has waned somewhat. Guidelines from the American Society of Surgeons of Colon and Rectal surgeons from 2000 recommended an elective resection after 1 or 2 episodes of acute uncomplicated diverticulitis [53]. At present, professional bodies including the AGA advise against routine resection and instead propose an individualised approach [10]. This, in part, reflects an appreciation that complications of diverticulitis typically manifest on the initial presentation and the morbidity and mortality of elective procedures for diverticulitis can be significant [54].

Conversely, elective surgery to enhance QoL is coming more to the fore. A systematic review by Andeweg et al. [55] with 21 studies and over 1,800 patients found that patients report higher QoL scores and reduced abdominal symptoms after laparoscopic resections, but there were no direct comparisons with conservative management. The recently reported, multicentre, randomised DIRECT trial by Dutch investigators may provide stronger evidence in favour of resection. In this study, 109 patients with recurrent episodes (3 or more presentations in 2 years) or persistent abdominal complaints were allocated to sigmoid resection (ideally laparoscopic with primary anastomosis) or conservative management (intensive monitoring, lifestyle modification including supplementary dietary fibre, and analgesics or laxatives as required). The primary endpoint was health-related QoL, measured by the Gastrointestinal QoL Index, in which a change of 10 points is considered clinically significant. At 6 months, the mean Gastrointestinal QoL Index score was significantly higher in the surgical group with a mean difference of 14.2 (95% CI 7.2–21.1; p < 0.0001) [56]. Furthermore, 23% of 56 patients initially allocated to conservative management group eventually underwent surgery. There was an overall 12% anastomotic leak rate. Twentyone percent of patients received a stoma; at 6 months, 82% of stomas were reversed. Of note, this study terminated early and recruited approximately half of the 214 participants stipulated by power calculations. It has been previously documented that stopping such trials early overestimates treatment effect, despite statistical compensation [57].

The Association of Coloproctologists of Great Britain and Ireland clearly differentiate between these indications for surgery and reject the need for universal elective resection [58]. This position is constant across age groups, as previously it was held that younger patients had a more virulent course.

Conclusion

Symptomatic diverticular disease is becoming increasingly prevalent and this challenges clinicians to consistently provide the highest level of care. This review provides a comprehensive yet succinct summary of numerous pertinent issues, thereby assisting with clinical decision making. An individualised approach to each patient depending on the specifics of presentation is required. This topic remains dynamic, and further highquality research is required to support clinicians as they seek to provide excellent, evidence-based care, thereby optimising patient outcomes.

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

References

- 1 Jacobs DO: Clinical practice. Diverticulitis. N Engl J Med 2007;357:2057–2066.
- 2 Kohler L, Sauerland S, Neugebauer E: Diagnosis and treatment of diverticular disease: results of a consensus development conference. The Scientific Committee of the European Association for Endoscopic Surgery. Surg Endosc 1999;13:430–436.
- 3 Martel J, Raskin JB; NDSG: History, incidence, and epidemiology of diverticulosis. J Clin Gastroenterol 2008;42:1125– 1127.
- 4 Strate LL, Modi R, Cohen E, Spiegel BM: Diverticular disease as a chronic illness: evolving epidemiologic and clinical insights. Am J Gastroenterol 2012;107:1486–1493.
- 5 Kang JY, Hoare J, Tinto A, Subramanian S, Ellis C, Majeed A, et al: Diverticular disease of the colon – on the rise: a study of hospital admissions in England between 1989/1990 and 1999/2000. Aliment Pharmacol Ther 2003;17: 1189–1195.
- 6 Etzioni DA, Mack TM, Beart RW Jr, Kaiser AM: Diverticulitis in the United States: 1998– 2005: changing patterns of disease and treatment. Ann Surg 2009;249:210–217.
- 7 Comparato G, Pilotto A, Franze A, Franceschi M, Di Mario F: Diverticular disease in the elderly. Dig Dis 2007;25:151–159.
- 8 Aune D, Sen A, Leitzmann MF, Norat T, Tonstad S, Vatten LJ: Body mass index and physical activity and the risk of diverticular dis-

ease: a systematic review and meta-analysis of prospective studies. Eur J Nutr 2017;56:2423–2438.

- 9 Parks TG: Natural history of diverticular disease of the colon. Clin Gastroenterol 1975;4: 53–69.
- 10 Stollman N, Smalley W, Hirano I: American gastroenterological association institute guideline on the management of acute diverticulitis. Gastroenterology 2015;149:1944–1949.
- 11 Hinchey EJ, Schaal PG, Richards GK: Treatment of perforated diverticular disease of the colon. Adv Surg 1978;12:85–109.
- 12 Morris AM, Regenbogen SE, Hardiman KM, Hendren S: Sigmoid diverticulitis: a systematic review. JAMA 2014;311:287–297.

Current Controversies in the Management of Diverticulitis: A Review

- 13 Rose J, Parina RP, Faiz O, Chang DC, Talamini MA: Long-term outcomes after initial presentation of diverticulitis. Ann Surg 2015; 262:1046–1053.
- 14 Chapman JR, Dozois EJ, Wolff BG, Gullerud RE, Larson DR: Diverticulitis: a progressive disease? Do multiple recurrences predict less favorable outcomes? Ann Surg 2006;243:876– 880; discussion 880–883.
- 15 Devaraj B, Liu W, Tatum J, Cologne K, Kaiser AM: Medically treated diverticular abscess associated with high risk of recurrence and disease complications. Dis Colon Rectum 2016; 59:208–215.
- 16 Boostrom SY, Wolff BG, Cima RR, Merchea A, Dozois EJ, Larson DW: Uncomplicated diverticulitis, more complicated than we thought. J Gastrointest Surg 2012;16:1744– 1749.
- 17 Floch MH: A hypothesis: is diverticulitis a type of inflammatory bowel disease? J Clin Gastroenterol 2006;40(suppl 3):S121–S125.
- 18 Tursi A, Elisei W, Brandimarte G, Giorgetti GM, Inchingolo CD, Nenna R, et al: Musosal tumour necrosis factor α in diverticular disease of the colon is overexpressed with disease severity. Colorectal Dis 2012;14:e258– e263.
- 19 Shabanzadeh DM, Wille-Jorgensen P: Antibiotics for uncomplicated diverticulitis. Cochrane Database Syst Rev 2012;11:CD009092.
- 20 Chabok A, Påhlman L, Hjern F, Haapaniemi S, Smedh K; AVOD Study Group: Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. Br J Surg 2012;99: 532–539.
- 21 Daniels L, Ünlü Ç, de Korte N, van Dieren S, Stockmann HB, Vrouenraets BC, et al: Randomized clinical trial of observational versus antibiotic treatment for a first episode of CTproven uncomplicated acute diverticulitis. Br J Surg 2017;104:52–61.
- 22 Shah SD, Cifu AS: Management of acute diverticulitis. JAMA 2017;318:291–292.
- 23 Raskin JB, Kamm MA, Jamal MM, Marquez J, Melzer E, Schoen RE, et al: Mesalamine did not prevent recurrent diverticulitis in phase 3 controlled trials. Gastroenterology 2014;147: 793–802.
- 24 Kruis W, Kardalinos V, Eisenbach T, Lukas M, Vich T, Bunganic I, et al: Randomised clinical trial: mesalazine versus placebo in the prevention of diverticulitis recurrence. Aliment Pharmacol Ther 2017;46:282–291.
- 25 Urushidani S, Kuriyama A, Matsumura M: 5-aminosalicylic acid agents for prevention of recurrent diverticulitis: a systematic review and meta-analysis. J Gastroenterol Hepatol 2018;33:12–19.
- 26 Dughera L, Serra AM, Battaglia E, Tibaudi D, Navino M, Emanuelli G: Acute recurrent diverticulitis is prevented by oral administration of a polybacterial lysate suspension. Minerva Gastroenterol Dietol 2004;50:149–153.
- 27 Bianchi M, Festa V, Moretti A, Ciaco A, Mangone M, Tornatore V, et al: Meta-analysis: long-term therapy with rifaximin in the man-

agement of uncomplicated diverticular disease. Aliment Pharmacol Ther 2011;33:902–910.

- 28 Lahner E, Bellisario C, Hassan C, Zullo A, Esposito G, Annibale B: Probiotics in the treatment of diverticular disease. A systematic review. J Gastrointestin Liver Dis 2016;25:79–86.
- 29 Balasubramanian I, Fleming C, Mohan HM, Schmidt K, Haglind E, Winter DC: Out-patient management of mild or uncomplicated diverticulitis: a systematic review. Dig Surg 2017;34:151–160.
- 30 Joliat GR, Emery J, Demartines N, Hubner M, Yersin B, Hahnloser D: Antibiotic treatment for uncomplicated and mild complicated diverticulitis: outpatient treatment for everyone. Int J Colorectal Dis 2017;32:1313– 1319.
- 31 Lorente L, Cots F, Alonso S, Pascual M, Salvans S, Courtier R, et al: [Outpatient treatment of uncomplicated acute diverticulitis: Impact on healthcare costs]. Cir Esp 2013;91: 504–509.
- 32 Moya P, Arroyo A, Perez-Legaz J, Serrano P, Candela F, Soriano-Irigaray L, et al: Applicability, safety and efficiency of outpatient treatment in uncomplicated diverticulitis. Tech Coloproctol 2012;16:301–307.
- 33 Boulos PB, Karamanolis DG, Salmon PR, Clark CG: Is colonoscopy necessary in diverticular disease? Lancet 1984;1:95–96.
- 34 Levin TR, Zhao W, Conell C, Seeff LC, Manninen DL, Shapiro JA, et al: Complications of colonoscopy in an integrated health care delivery system. Ann Intern Med 2006;145:880– 886.
- 35 Walker AS, Bingham JR, Janssen KM, Johnson EK, Maykel JA, Ocampo O, et al: Colonoscopy after Hinchey I and II left-sided diverticulitis: utility or futility? Am J Surg 2016; 212:837–843.
- 36 Stefansson T, Ekbom A, Sparen P, Pahlman L: Association between sigmoid diverticulitis and left-sided colon cancer: a nested, population-based, case control study. Scand J Gastroenterol 2004;39:743–747.
- 37 Sharma PV, Eglinton T, Hider P, Frizelle F: Systematic review and meta-analysis of the role of routine colonic evaluation after radiologically confirmed acute diverticulitis. Ann Surg 2014;259:263–272.
- 38 Mortensen LQ, Burcharth J, Andresen K, Pommergaard HC, Rosenberg J: An 18-year Nationwide cohort study on the association between diverticulitis and colon cancer. Ann Surg 2017;265:954–959.
- 39 Myers E, Hurley M, O'Sullivan GC, Kavanagh D, Wilson I, Winter DC: Laparoscopic peritoneal lavage for generalized peritonitis due to perforated diverticulitis. Br J Surg 2008;95: 97–101.
- 40 Toorenvliet BR, Swank H, Schoones JW, Hamming JF, Bemelman WA: Laparoscopic peritoneal lavage for perforated colonic diverticulitis: a systematic review. Colorectal Dis 2010;12:862–867.

- 41 Schultz JK, Yaqub S, Wallon C, Blecic L, Forsmo HM, Folkesson J, et al: Laparoscopic lavage vs primary resection for acute perforated diverticulitis: the SCANDIV randomized clinical trial. JAMA 2015;314: 1364–1375.
- 42 Swank HA, Vermeulen J, Lange JF, Mulder IM, van der Hoeven JA, Stassen LP, et al: The ladies trial: laparoscopic peritoneal lavage or resection for purulent peritonitis and Hartmann's procedure or resection with primary anastomosis for purulent or faecal peritonitis in perforated diverticulitis (NTR2037). BMC Surg 2010;10:29.
- 43 Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, et al: Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial. Lancet 2015;386: 1269–1277.
- 44 Thornell A, Angenete E, Gonzales E, Heath J, Jess P, Lackberg Z, et al: Treatment of acute diverticulitis laparoscopic lavage vs. resection (DILALA): study protocol for a randomised controlled trial. Trials 2011;12:186.
- 45 Ceresoli M, Coccolini F, Montori G, Catena F, Sartelli M, Ansaloni L: Laparoscopic lavage versus resection in perforated diverticulitis with purulent peritonitis: a meta-analysis of randomized controlled trials. World J Emerg Surg 2016;11:42.
- 46 Angenete E, Bock D, Rosenberg J, Haglind E: Laparoscopic lavage is superior to colon resection for perforated purulent diverticulitisa meta-analysis. Int J Colorectal Dis 2017;32: 163–169.
- 47 Cirocchi R, Di Saverio S, Weber DG, Tabola R, Abraha I, Randolph J, et al: Laparoscopic lavage versus surgical resection for acute diverticulitis with generalised peritonitis: a systematic review and meta-analysis. Tech Coloproctol 2017;21:93–110.
- 48 Classen JN, Bonardi R, O'Mara CS, Finney DC, Sterioff S: Surgical treatment of acute diverticulitis by staged procedures. Ann Surg 1976;184:582–586.
- 49 Cirocchi R, Afshar S, Di Saverio S, Popivanov G, De Sol A, Gubbiotti F, et al: A historical review of surgery for peritonitis secondary to acute colonic diverticulitis: from Lockhart-Mummery to evidence-based medicine. World J Emerg Surg 2017;12:14.
- 50 Ince M, Stocchi L, Khomvilai S, Kwon DS, Hammel JP, Kiran RP: Morbidity and mortality of the Hartmann procedure for diverticular disease over 18 years in a single institution. Colorectal Dis 2012;14:e492– e498.
- 51 Banerjee S, Leather AJ, Rennie JA, Samano N, Gonzalez JG, Papagrigoriadis S: Feasibility and morbidity of reversal of Hartmann's. Colorectal Dis 2005;7:454–459.
- 52 Salem L, Flum DR: Primary anastomosis or Hartmann's procedure for patients with diverticular peritonitis? A systematic review. Dis Colon Rectum 2004;47:1953–1964.

Nally/Kavanagh

- 53 Wong WD, Wexner SD, Lowry A, Vernava A 3rd, Burnstein M, Denstman F, et al: Practice parameters for the treatment of sigmoid diverticulitis – supporting documentation. The Standards Task Force. The American Society of Colon and Rectal Surgeons. Dis Colon Rectum 2000;43:290–297.
- 54 Van Arendonk KJ, Tymitz KM, Gearhart SL, Stem M, Lidor AO: Outcomes and costs of elective surgery for diverticular disease: a comparison with other diseases requiring colectomy. JAMA Surg 2013;148:316–321.
- 55 Andeweg CS, Berg R, Staal JB, ten Broek RP, van Goor H: Patient-reported outcomes after conservative or surgical management of recurrent and chronic complaints of diverticulitis: systematic review and meta-analysis. Clin Gastroenterol Hepatol 2016;14:183– 190.
- 56 van de Wall BJM, Stam MAW, Draaisma WA, Stellato R, Bemelman WA, Boermeester MA, et al: Surgery versus conservative management for recurrent and ongoing left-sided diverticulitis (DIRECT trial): an open-label,

multicentre, randomised controlled trial. Lancet Gastroenterol Hepatol 2017;2:13–22.

- 57 Bassler D, Briel M, Montori VM, Lane M, Glasziou P, Zhou Q, et al: Stopping randomized trials early for benefit and estimation of treatment effects: systematic review and meta-regression analysis. JAMA 2010;303:1180– 1187.
- 58 Fozard JB, Armitage NC, Schofield JB, Jones OM: ACPGBI position statement on elective resection for diverticulitis. Colorectal Dis 2011;13:1–11.