Left colon acute diverticulitis: An update on diagnosis, treatment and prevention

Walter Bugiantella a, b, *, Fabio Rondelli a, c, Maurizio Longaroni a, Enrico Mariani a, Alessandro Sanguinetti d, Nicola Avenia d

a General Surgery, “San Giovanni Battista” Hospital, AUSL Umbria 2, Via M. Arcamone, 06034, Foligno, Perugia, Italy
b University of Perugia, PhD School in Biotechnologies, Italy
c University of Perugia, Department of Surgical and Biomedical Sciences, Via G. Dottori, 06100 Perugia, Italy
d General and Specialized Surgery, “Santa Maria” Hospital, Via T. Di Ioannuccio, 05100 Terni, Italy

HIGHLIGHTS

- Diverticulosis of the colon represents significant costs for national health systems.
- Acute diverticulitis shows an increasing prevalence.
- Improvements have been achieved about diagnosis and treatment of acute diverticulitis.
- The timing of surgery has been reviewed recently both in urgency and in election.
- The antibiotic therapy seems to have a different role compared to past.

ABSTRACT

Diverticulosis of the colon is a common disease with an increasing incidence in Western Countries. It represents a significant burden for National Health Systems in terms of costs. Most people with diverticulosis remain asymptomatic, about one quarter of them will develop an episode of symptomatic diverticular disease and up to 5% an episode of acute diverticulitis (AD). AD shows an increasing prevalence.

Recently, progresses have been reached about the etiology, pathogenesis, natural course of diverticular disease and its complications; improvements about the diagnosis and treatment of AD have been achieved. However, the treatment options are not well defined because of a lack of solid evidence: there are few systematic reviews and well conducted trials to guide decision-making in the treatment of AD and in the prevention of its recurrences.

This review describes the recent evidence about diagnosis, treatment and prevention of AD.

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1. Introduction

Colonic diverticulosis is an acquired condition that results from the herniation of the mucosa through the muscle layer [1]. Its incidence greatly varies worldwide and it is higher in developed countries. The lack of fiber in the diet, as occurs in developed societies, and alimentary habits, has proved to be the main cause of the formation of diverticula [2,3]. The prevalence is difficult to define, since most patients affected by diverticulosis are asymptomatic, and it is age-dependent: it is uncommon in people under the age of 40 (about 5%) and it increases in those >65 years-old (up to 65%) [2,4].

About 80–85% of patients affected by diverticula remains asymptomatic for a lifetime, while 10–15% develops symptomatic diverticular disease and the approximately remaining 5% develops diverticulitis, which leads to complications (abscess formation, hemorrhage, fistula, obstruction) in a small part of them [5,6].
Colonic diverticula typically form in parallel rows between the taeniae coli because of the weakness of the muscle wall at sites of penetration of the vasa recta supplying the mucosa. In western populations diverticula mainly arise in the distal colon, with 90% of patients having sigmoid colon involvement and only 15% having right-side diverticula [4,7,8].

The causes of colonic diverticula formation traditionally include alteration in colonic wall resistance, disorder in colonic motility and dietary deficiency of fibers [9]. Diverticula formation is due to altered bowel motility leading to increased intraluminal pressure that causes mucosal pouching adjacent to the vasa recta.

The mechanism by which asymptomatic diverticula become inflamed and perforate is still not well known, but it is plausibly associated with altered gut motility and increased pressure combined with deranged colonic microenvironment. Recent ex vivo studies reported that the response of the colonic tissue from patients with diverticulitis was abnormal with increased hypercontractility and lower relaxation, when exposed to chemicals that contract or relax smooth muscle [10,11]. Neuropeptide abnormalities and altered histological appearance of muscle and nerves of the colonic wall (reduced serotonin transporter expression and fewer interstitial cells of Cajal) were found in patients with diverticulitis compared with healthy patients [12,13]. The ingestion of calcium channels blockers (which reduce the smooth muscle contractility) shown to reduce the risk of perforated diverticulitis compared with patients who did not take calcium blockers [14].

Recently, inflammation has been proposed to have a role in diverticular disease, since it was shown that patients with symptomatic diverticular disease often have microscopic inflammation of the mucosa close to diverticula [15]. In addition to that, endoscopic findings of diverticular inflammation (as erythema and edema of a diverticular orifice, pus coming out from a diverticular opening, a polypoid mass of granulation tissue in a diverticular orifice) in patients without clinical evidence of acute diverticulitis may be sometimes found during colonoscopy [16].

In some patients there may be extensive inflammation defined diverticulitis: most of them are over age 60 and show a segment of active inflammation upon endoscopic examination (patchy mucosal hemorrhage granularity and exudate without gross ulceration adjacent to multiple diverticular orifices) in an area of multiple diverticula causing hematochezia, altered bowel function and abdominal pain [17]. Endoscopic biopsies confirm chronic active colitis without granulomas [18]. To date, the pathogenesis of diverticulitis is unknown and its relation with the diverticula is unclear. It has been suggested that mucosal prolapse, relative ischemia, bacterial overgrowth, exposure to intraluminal toxins and antigens secondary to fecal stasis, and disorder of the enteral nervous system may be the causes [18–20].

Recurrent or chronic diverticulitis has been demonstrated to have chemical and histological similarities to inflammatory bowel disease and irritable bowel syndrome [21,22]. Although the mechanisms of inflammation are unknown, higher levels of histamine, tumor necrosis factor α and matrix metalloproteinases have been identified in colonic biopsies from patients with irritable bowel syndrome, inflammatory bowel disease and diverticulitis [23–25].

2. Methods

An unrestricted research was performed in Pubmed, Medline, Embase and Cochrane database up to 30th June 2014. All the keywords suited for the different databases were used in different order to use the maximum amount of papers. Only publications in English, Italian, French, German and Spanish were considered and publications before 2000 were excluded, thus resulting in 2790 articles for review. All studies designed to evaluate the diagnostic process, the treatment and the prevention of acute diverticulitis (AD) were considered. Two authors (WB and ML) independently performed the searches and reviewed all identified publications and abstracts for inclusion. Disagreements were resolved by consensus with a third investigator (FR) and by means of discussion.

Abstracts were reviewed and review articles, duplicated articles, commentary or opinion articles were excluded. Studies selected for inclusion were reviewed according to guidelines from the Strengthening the Reporting of Observational Studies in Epidemiology [26]. The level of evidence and the grade of recommendations were assessed according to the Oxford Centre for Evidence Based Medicine Levels of Evidence [27].

3. Results

3.1. Diagnosis

3.1.1. Clinical evaluation

The study by Toorevliet reported that the clinical evaluation in patients with suspected AD has a sensitivity of 64% and a specificity of 97% [28]. Laurell showed a sensitivity of 68% and a specificity of 98%, reporting that isolated left abdominal tenderness, signs of constipation and higher level of C-reactive protein were more frequent in patients with AD, whereas vomiting and right-sided abdominal pain were more frequent in non-specific abdominal pain [29].

3.1.2. Ultrasongraphy

The recent meta-analysis by Andeweg, performed on the high-quality prospective studies available to date [30–32], showed that the sensitivity and the specificity of graded compression US in detecting AD are 90% (95% CI: 76–98%) and 90% (95% CI: 86–94%) respectively [33].

3.1.3. Computed tomography

The meta-analysis by Andeweg, performed on 6 high-quality prospective studies available to date [32,34–38], reported that the sensitivity and the specificity of CT in detecting AD are 95% (95% CI: 91–97%) and 96% (95% CI: 90–100%) respectively [33].

The comparison of US and CT showed not significant differences about sensitivity (p = 0.86; OR 1.12; 95% CI 0.32–3.94), whereas specificity is significantly higher in CT (p = 0.04; OR 2.46; 95% CI: 1.01–5.96) [33]. Moreover, by analyzing those patients whose diagnosis was truly based on the initial US or CT findings, Andeweg reported that CT allows an accurate diagnosis of AD in 68% of patients whereas the US does it in 48%, with a similar percentage of false-positive and false-negative [33].

3.1.4. Magnetic resonance imaging

The only prospective study available in literature to date, about the value of MRI in suspected AD, is by Heverhagen and it showed that sensitivity of MRI in diagnosing AD ranged 94–96% and specificity was 88% [39].

3.1.5. Contrast enema

The two comparative prospective studies available in literature showed that sensitivity and specificity of contrast enema in diagnosing AD ranged 80–83% and 81–100% respectively [34,35].

3.1.6. Colonoscopy

Colonoscopy is not recommended in the acute phase to diagnose AD (level 2b [40] and level 4 [41]). Abdominal pain, incomplete bowel preparation and bowel stenosis are the main
difficulties that hinder colonoscopy in the acute phase. Moreover, the hypotetic risk of perforation caused by the insufflation of air discourages to perform colonoscopy in the acute phase [42–44]. Colonoscopy is usually performed 6 weeks after an episode of AD in order to exclude a colonic malignancy, but routine performance of colonoscopy in asymptomatic patients after an episode of AD to exclude other diagnoses did not prove to be helpful (level 2b [40,45,46]).

3.1.7. Classification of acute diverticulitis

Since publication of the original Hinchey classification in 1978, several modifications and new grading systems have been developed. The new insights in the natural history of diverticular disease, emergence of the CT scan and new treatments led to evolving classifications.

The Hinchey classification has been used to distinguish four stages of complicated diverticulitis due to colonic perforation (I = localized abscess, II = pelvic abscess, III = purulent peritonitis, IV = feculent peritonitis) [47]. It was based on both clinical and surgical findings.

In 1999 Wasvary modified the Hinchey classification introducing stage 0 and differentiating stage I in Ia and Ib (Table 1) [48]. This broadened the original Hinchey classification by not only addressing perforated disease, but also by including mild clinical cases.

The increasing use of CT, as to become the gold standard in the diagnosis of AD, led to several radiologic classifications. The most used imaging classification was proposed by Kaiser in 2005: CT findings were correlated with the modified Hinchey scores to come to uniform reporting of CT findings (Table 1) [49].

3.2. Treatment of uncomplicated diverticulitis

Most patients with Hinchey 0 or Ia uncomplicated AD can be treated conservatively with antibiotics, fluid therapy and bowel rest; the literature reports a success rate of 93–100% (level 4 [50–54]).

There is no evidence that bed rest, dietary restrictions or laxatives positively influence the treatment outcome of AD. Parenteral feeding is recommended in patients who do not tolerate oral feeding when it is not to be expected within 3 days (level 5 [55]).

Almost all the international guidelines recommend the use of antibiotics for the treatment of diverticulitis [56–58]. However, there is no evidence that routine administration of antibiotics influences the course of uncomplicated AD (level 1b [59] and level 2b [45], grade B). A Cochrane review about antibiotics use in uncomplicated AD found that the best available data do not support the use of antibiotics [60]. A later review also found that antibiotics use has no effect on complications, need for surgery and recurrence rate [61]. A recent prospective RCT did not find a reduction of abscess formation, perforation and recurrence rates with the use of antibiotics [59].

The recent review by Tursi showed that outpatient treatment for uncomplicated AD is safe and effective in selected patients, allowing important cost saving to health systems (reducing health care costs by over 60%) without a negative influence on quality of life [62]. The study reported that less than 10% of patients, undergoing outpatient treatment for AD, required readmission to the emergency room for diverticulitis within 60 days of initial evaluation. However, if patients are unable to take oral therapy, have severe comorbidity or fail to improve with outpatient therapy, they must be treated in hospital with intravenous antibiotics. Moreover, the review stated that the efficacy of antibiotics use in AD is not “evidence-based”.

No difference seems to exist between oral and intravenous administration of antibiotics (level 2b [63]). Intravenous administration over 4 days is equally effective as 7 days (level 2b [52]). The use of antibiotics seem appropriate in patients showing signs of generalized infection or bacteremia or septicemia and in immuno-compromised patients (grade D [55]).

The RCT by Dughera showed that patients with AD treated with probiotics (polybacterial lysate suspension) plus rifaximin or ciprofloxacin reported significantly less abdominal pain, bloating and fever compared to those treated with antibiotics plus placebo [64].

Another important aspect of the therapy of AD is analgesia. There is no evidence that acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs) or morphinomimetics have a negative effect on the course of an episode of AD. The adverse effects of NSAIDs as analgesic in uncomplicated AD has not been studied [55]. On the other hand, home NSAIDs medication has been shown to increase complicated diverticulitis (level 4 [65–67]). Morphinomimetics can be safely administered without negatively affecting the diagnostic accuracy of clinical evaluation (level 1b [68,69]).

3.3. Treatment of complicated diverticulitis

3.3.1. Hinchey Ib and II

In literature there are no high-quality papers about the treatment of patients affected by AD with abscess formation (Hinchey Ib and II). Conservative treatment with antibiotics is successful in up to 73% of patients with an abscess of less than 4–5 cm in diameter (level 4 [70–73]). When the conservative treatment fails, US- or CT-guided percutaneous drainage should be performed, with a success up to 81% of patients (level [49,71–73]). The risk of failure of the conservative treatment is higher in patients with abscess larger than 4–5 cm (level 4 [49,71–73]).

3.3.2. Hinchey III and IV

Peritonitis is the most dreadful complication of AD with a mortality rate up to 14% [74,75]. The inflammation of the colonic wall may result in a perforation to the intra-abdominal cavity causing purulent or fecal peritonitis. The perforation is rare occurring in 3.5 per 100,000 patients per year, and in 1.5% of patients with AD [76,77]. Peritonitis leads to bacteremia and sepsis by progressive organ dysfunction or failure up to the death.

The early treatment, by eliminating the source of infection, administering broad spectrum antibiotics and supporting the vital functions, is the milestone of the management of peritonitis [78]. Here is no evidence-based advice in literature regarding indications
for surgery in perforated diverticulitis, but this indication is self-evident and may be inferred by clinical practice.

Many surgical procedures may be performed in Hinchey III and IV peritonitis: peritoneal toilette and drainage, colonic resection with primary anastomosis (with or without a protective ileostomy or colostomy), Hartmann’s procedure, diverting colostomy, both with laparotomic and laparoscopic approach. The most performed is Hartmann’s procedure consisting in the resection of the diseased colon, the closure of the distal rectal stump and the construction of an end colostomy that will be reversed in a second stage. However, the restoration of the colon continuity is not performed in up to 55% of patients due to operating risk and clinical conditions [79,80].

Studies comparing post-operative complications of Hartmann’s procedure and primary anastomosis did not show any significant differences (although in most studies patients were not randomized for the two procedures and the two groups were not comparable according to patients’ characteristics and disease severity). Nevertheless, there are indications that Hartmann’s procedure and primary anastomosis have comparable outcomes (level 2b [81–83]).

It is likely that the choice of the surgical procedure is influenced by patient’s conditions and perioperative findings. Therefore, in case of critically ill subjects and hemodynamic instability it is reasonable that the primary anastomosis could be avoided, whereas in hemodynamically stable patients primary anastomosis, with or without faecal diversion, may be preferred over Hartmann’s procedure (grade B [55]).

Purulent peritonitis may be treated with laparoscopic toilette and drainage of the abdominal cavity without colon resection. There are only not-RCTs about this issue showing that laparoscopic toilette and drainage accompanied by intravenous antibiotics seems to be effective and safe for Hinchey III patients (level 4 [28,84], grade C).

3.4. Elective surgery

In 2000 the American Society of Colon and Rectal Surgeons recommended elective surgery after two episodes of AD [85]. In 2006 the same group stated that elective colonic resection after AD should be performed on a case-by-case basis [59]. This change in orientation may be explained by the fact that the majority of recurrent episodes of AD have a benign course and only 5.5% of patients due to operating risk and clinical conditions [79,80].

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3.5. Prevention of recurrent diverticulitis

The goal of therapy in diverticular disease is to improve symptoms and to prevent the recurrence of episodes of AD. Several therapies have been proposed, such as high-fiber diet, modification in lifestyle, antibiotics, 5-aminosalicylic acid and probiotics.

3.5.1. Dietary fiber

Traditionally, high-fiber diets have been considered to prevent AD recurrence, but RCTs on fiber-enriched diets, carried on patients with diverticular disease and episodes of AD, showed inconsistent results [99]. Moreover, the recent systematic review by Unlu, about the medical therapy to prevent recurrent diverticulitis, did not include any studies about the use of high-fiber diet and concluded that recommendations for ingestion of dietary fiber are based on inconsistent level 2 and 3 evidence [100].

3.5.2. Lifestyle

Obesity and smoking are associated with an increased risk of complications of diverticulitis (level B [101,102]). However, there is no evidence in literature about lifestyle advice to prevent recurrent AD, but it is likely that same advice might also apply after an episode of AD [55]. A correct lifestyle, including physical activity, fiber-rich diet, little intake of red meat, low alcohol consumption and nonsmoking habits, is recommended in patients after an episode of AD (level 2a [103] and level 4 [104], grade D).

3.5.3. Antibiotics

The discontinuous administration of the non-absorbable antibiotic rifaximin after an episode of AD proved to decrease the chance of readmission by 50% and of recurrent diverticulitis by 73% (level 2b [105], grade C). However, the systematic review by Unlu did not include any studies about the use of antibiotics, because none of them met the inclusion criteria [100].

3.5.4. 5-aminosalicylic acid

The use of 5-aminosalicylic acid (Mesalazine) 800 mg bid combined with rifaximin 400 mg bid (for 7 days every month) showed to be more effective in preventing AD recurrence, if compared to rifaximin alone (level 1b [106] and level 2b [107], grade B).

3.5.5. Probiotics

The rationale for use of probiotics in diverticular disease is based on the theory that a deranged colonic microenvironment, including abnormal gut flora, accelerates chronic inflammation and recurrent disease. The use of probiotics (oral polybacterial lyase suspension of Escherichia Coli and Proteus Vulgaris administered bid for 2 weeks every month within 3 months after an acute attack) proved to be more effective in preventing AD recurrence, if compared to no treatment (level 1b [64]).

4. Discussion

Left colon diverticulitis is an increasingly common and costly disease, endemic in industrialized nations. Between 1998 and 2005 the costs for hospital admissions for AD increased by 26% and elective operations by 29% in US [108].

The understanding and the management of AD are evolving. Recent studies indicate a pathogenetic role for inflammation that may be similar to that of irritable bowel syndrome and inflammatory bowel disease, based on common histologic findings such as...
granulomas, infiltrating lymphocytes, tumor necrosis factor, histamine and matrix metalloproteinases.

The clinical evaluation should be considered the mainstream of the diagnostic process in AD. The meta-analyses by Lameris and Andeweg showed comparable results about accuracy of graded compression US and CT in diagnosing AD: comparable sensitivity, with higher specificity in favor of CT in the study by Andeweg [33,109]. Therefore, the recent study by Lameris proposed the performing of CT after inconclusive or negative US, resulting in the highest overall sensitivity and the lowest overall exposure to radiation [110]. This step-up approach seems to be logical and safe. The first step of the diagnostic process is an estimation of AD probability based on clinical evaluation and laboratory findings. US examination is the second step. In case of inconclusive or negative US, a CT scan is made. This step-up approach may differ because of personal and geographic preferences. The two surveys carried out among colorectal surgeons in the UK and USA, showed that in one-third of patients with suspected AD, US was the initial imaging technique in the UK, compared to only 7% in USA. The reasons of this difference may be searched in patients characteristics (obesity may make US exploration difficult) and in the advantages of CT scan (reproducibility of images, ability to identify an alternative diagnosis, practicability of therapeutic interventional procedures). Since in 90% of patients with AD the disease follows a rather indolent course and CT images lead to modifications in management in only 7% of patients with suspected AD, the use of CT in suspected uncomplicated AD should not be recommended [28,52]. Otherwise, the step-up approach should not be applied to critical patients with signs of sepsis which might be due to complicated AD [55,78].

For post-acute patients who recover from an initial episode of diverticulitis with non-operative therapy, many authors recommended endoscopic evaluation to confirm the diagnosis of diverticulitis and exclude other common causes of segmental colitis such as neoplasm, Crohn disease and ischemic colitis. Indications of flexible colonoscopy after AD are still not established, it is suggested for any patients who have not recently undergone colorectal cancer screening [111].

There is no evidence that bed rest, dietary restrictions or laxatives influence the treatment of AD. There is no evidence that antibiotics should be routinely administrated to patients with uncomplicated AD. Recent literature found that antibiotic treatment was not superior to simple support therapy in terms of obtaining clinical resolution and preventing recurrence of diverticulitis [55,62]. The outpatient treatment of uncomplicated AD may be considered a safe and effective approach in the vast majority of patients, thus allowing important cost-saving policies to health care systems [62].

AD complicated with abscesses <4–5 cm can be treated with antibiotic therapy alone, whereas percutaneous drainage plus antibiotic can be the best treatment of larger abscesses. Hinchee III and IV AD should be treated with surgery: in hemodynamically stable patients primary anastomosis with or without fecal diversion is preferred over Hartmann's procedure. Elective surgery with sigmoid resection should be performed according to patient-related factors; laparoscopy should be favored over laparotomy in terms of short-term outcome, although long-term benefits have not been reported [55].

The reviewing of literature has shown a change in the last decade evidence about the role of surgery for AD, thus reducing the use of urgent operations for AD and restricting the indications for prophylactic surgery in recurrent diverticulitis. In 2000, elective surgery was recommended after 2 episodes of AD whereas from 2006 the timing of surgery has been individualized according to the characteristics of each patient. The available data in literature do not support a routine policy of prophylactic sigmoidectomy on clinical grounds alone, since the risk of recurrence among patients with uncomplicated AD ranges 13–36% and the risk of future emergency surgery ranges 4–7% [111]. Data from literature show that elective surgery does not prevent recurrence or treat chronic disease [55].

With regards to prevention, there is no evidence that increased fiber ingestion reduces the recurrences of AD. Recent data suggest that combined medical therapy with rifaximin and mesalamine may contribute to reduce symptoms in chronic disease and AD recurrences [55,112]. Throughout the review the level of evidence was lower, thereby limiting interpretation and conclusions. Retrospective and epidiemologic studies account for nearly the entire evidence basis from which current practice standards derive. The available trials about therapy were largely observational and subject to selection bias: variability in surgical technique, diagnostic criteria, duration and method of follow-up made the analysis and the comparisons between the studies difficult.

5. Conclusion

Diverticulitis is a common, morbid and costly condition whose optimal treatment and prevention remain controversial. The current data support a substantially decreasing role of aggressive antibiotic therapy and surgical intervention in acute and recurrent diverticulitis. The results of RCTs are needed in order to address the optimal treatment of AD episodes and the prevention of recurrences.

Ethical approval

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Author contribution

Bugiantella Walter: Participated substantially in conception, design and execution of the study, and in the analysis and interpretation of the data; also participated substantially in the drafting and editing the manuscript.
Rondelli Fabio: Participated substantially in conception, design and execution of the study, and in the analysis and interpretation of the data.
Longaroni Maurizio: Participated substantially in conception, design and execution of the study, and in the analysis and interpretation of the data.
Mariani Enrico: Participated substantially in the analysis and interpretation of data.
Sanguinetti Alessandro: Participated substantially in the interpretation of the data and in the editing the manuscript.
Avenia Nicola: Finally reviewed the manuscript.

Conflict of interests

None.

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