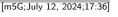
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Guidelines

Italian guidelines for the diagnosis and management of colonic diverticulosis and diverticular disease *

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ABSTRACT

Colonic diverticulosis and diverticular disease are among the most common gastrointestinal disorders encountered in clinical practice. These Italian guidelines focus on the diagnosis and management of diverticulosis and diverticular disease in the adult population, providing practical and evidence-based recommendations for clinicians. Experts from five Italian scientific societies, constituting a multidisciplinary panel, conducted a comprehensive review of meta-analyses, systematic reviews, randomised controlled trials, and observational studies to formulate 14 PICO questions. The assessment of the quality of the evidence and the formulation of the recommendations were carried out using an adaptation of the GRADE methodology. The guidelines covered the following topics: i) Management of diverticulosis; ii) Symptomatic uncomplicated diverticular disease: diagnosis and treatment; iii) Acute diverticulitis: diagnosis and treatment; iv) Management of diverticular disease.

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1. Introduction

Colonic diverticulosis is a common clinical condition, particularly in industrialised countries, with the highest rates recorded in Europe and the United States, where it is the 11th most common gastrointestinal (GI) disorder [1]. Most people (80%) with colonic diverticula remain asymptomatic throughout life (diverticulosis), and the diagnosis is often incidental during colonoscopy performed for other reasons, such as colorectal cancer screening. In contrast, approximately 20% develop a diverticular disease (DD) which encompasses a variety of clinical scenarios ranging from symptomatic uncomplicated diverticular disease (SUDD), characterised by recurrent abdominal pain often associated with changes in bowel habits and/or bloating, to the acute onset of symptoms and signs (e.g., acute and severe abdominal pain, fever and leucocytosis) configuring acute diverticulitis (AD) [2,3].

Several factors have been hypothesised to contribute to the pathogenesis of GI symptoms in patients with diverticulosis, such as low-grade inflammation, alteration of the intestinal microbiota, visceral hypersensitivity, nerve sprouting, and alteration of colonic motility [4–6].

On the other hand, AD is characterised by the inflammation of one or more diverticula and can manifest in either its un-

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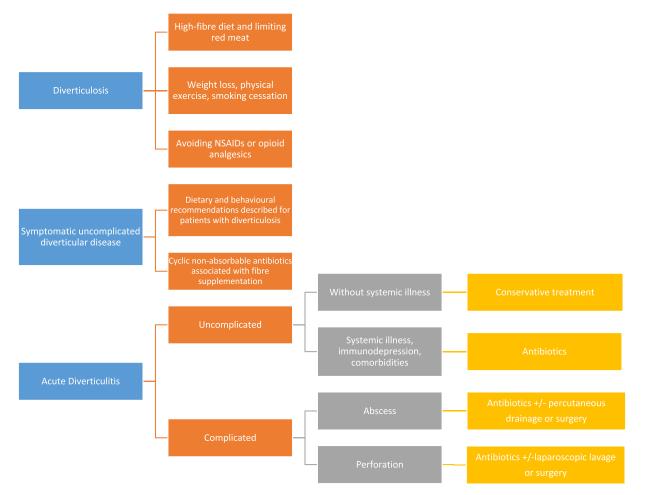


Fig. 1. Lifestyle changes, dietary modifications, and a stepwise therapeutic approach for managing diverticular disease. Legend to the Fig. 1: NSAIDs: non-steroidal anti-inflammatory drugs.

complicated or complicated form, with abscess, perforation, fistula, stenosis, or peritonitis. Approximately one quarter of affected patients may experience recurrent episodes of diverticulitis [7]. Lifestyle changes, dietary modifications, and a stepwise therapeutic approach for managing diverticular disease are summarised in Fig. 1.

Despite the significant epidemiological burden and economic impact of DD, knowledge of the condition and its natural history remains limited, leading to clinician uncertainty and patients dissatisfaction.

The aim of this document is to provide clinical guidelines for the appropriate definition, diagnosis and management of diverticulosis and DD in the adult population.

2. Methods

This position paper is endorsed by the Italian Society of Gastroenterology and Endoscopy (SIGE). Representative members from the SIGE, the Hospital Gastroenterologists and Endoscopists (AIGO), the Italian Society of Digestive Endoscopy (SIED), the Italian Society of Colon and Rectal Surgery (SICCR) and the Association of Dietetics and Clinical Nutrition (ADI) participated in the Delphi process to develop consensus statements on the diagnosis and management of colonic diverticulosis and diverticular disease [8].

The Core Working Group, composed of three panel members (M.Carabotti, C.Sgamato and R.Cuomo) with expertise in diverticular disease and Delphi consensus processes, identified 14 clinical questions to be answered by using the PICO format, which frames a clinical question by defining a specific population (P), intervention (I), comparator (C), and outcomes (O).

The consensus group consisted of 11 experts, including gastroenterologists, GI endoscopists, surgeons, and clinical nutritionists, who manage diverticular disease. Two participants (C. Severi, B. Annibale) were involved in the final review of the manuscript. The panel systematically searched the literature to answer each PICO and drafted statements with a summary of the evidence.

The following topics were reviewed: (1) management of diverticulosis; (2) symptomatic uncomplicated diverticular disease: diagnosis and treatment; (3) acute diverticulitis: diagnosis and treatment; (4) management of diverticular disease complications; (5) prevention of recurrent acute diverticulitis; (6) interventional management of diverticular disease.

In the context of diverticular disease, we decided not to include diverticular bleeding and segmental colitis associated with diverticulosis; these issues have recently been addressed in recent German guidelines [9].

The panel systematically searched the literature, reviewed statements based on the best available evidence, and reported graded statements and recommendations. The literature search included articles published in English using MEDLINE, EMBASE, Web of Science and the Cochrane Database of Systematic Reviews until October 1st, 2023. References were available in an online shared folder accessible to all members. Researchers prioritised data from systematic reviews and meta-analyses of randomised controlled trials (RCTs). If no RCTs evidence was available, a search for observational studies was performed. The level of evidence (LE) and the grade of

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the recommendation (GR) according to the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system were reported for each statement [10,11].

The GR was classified into three categories: strong (desirable effects outweigh undesirable effects), conditional (trade-offs are less certain), or consensus (the expert opinion supports the guideline recommendation even though the available scientific evidence did not provide consistent results, or controlled trials were lacking). The following definitions were used to rate the LE: high (further research is unlikely to change the confidence in the estimate), moderate (further research is likely to change the confidence in the estimate), low (further research is very likely to change confidence in the estimate), or very low (the estimate of the effect is very uncertain). The LE could be downgraded or upgraded according to several factors, such as limitations or implementations in the study design, imprecision of the estimates, variability of the results, indirectness of the evidence, publication bias, large magnitude of effects, dose-response gradient, or if all the plausible biases would reduce an apparent treatment effect. In addition, other factors such as alternative management strategies, variability in values and preferences, and costs were considered.

The final list of statements and recommendations with the summary of evidence was edited and discussed in a 1-day telematic meeting. Following the GRADE method, all participants were asked to vote on their agreement with the statements by using a 6-point Likert scale, that included one of the following: strongly agree (A+), agree with minor reservation (A), agree with major reservation (A-), disagree with major reservation (D-), disagree with minor reservation (D), or strongly disagree (D+) and to provide feedback on their clarity. We defined consensus as 80% of respondents strongly agree (A+) or agree with minor reservation (A). The agreement on all statements was reached after the first voting round. After voting, participants drafted and reviewed the manuscript for final approval. The final version of the document was then submitted for external review to improve the quality of the guidelines. All members submitted a conflict of interest statement by November-December 2023.

3. Results

All PICO and statements with the LE and GR and agreement are reported in Table 1.

3.1. Management of diverticulosis

PICO 1: What is the best strategy for preventing symptomatic colonic diverticular disease in subjects with colonic diverticulosis?

Statement 1.1. We suggest following a high-fibre diet and limiting the consumption of red meat to subjects with colonic diverticulosis.

Agreement: 91% [A+ (73%); A (18%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Moderate; GR: Conditional

Summary of evidence: Dietary habits may play a role in the prevention of symptomatic DD. A recent systematic review showed that high dietary fibre intake was associated with a reduced risk of diverticulitis or hospitalisation due to DD, with a protective effect for fruit and cereal fibre, but not for vegetable fibre [12]. In a prospective cohort study, women in the highest quintile of dietary fibre intake had a reduced risk [adjusted HR=0.86 (95%CI: 0.78–0.95)] of developing diverticulitis compared with those in the lowest quintile [13]. Data from the Health Professional Follow-up Study (HPFS) prospective cohort found an increased risk [RR=1.58 (95% CI 1.19–2.11)] of developing diverticulitis in men in the highest quintile of red meat consumption compared with those in the

lowest quintile. This association was stronger for unprocessed red meat [RR=1.51 (95% CI: 1.12–2.03)] [14]. Finally, a Western dietary pattern (high intake of red and processed meat, refined grains, sweets, french fries, and high-fat dairy products) was associated with an increased risk of diverticulitis [HR=1.55 (95% CI:1.20–1.99)] compared with a prudent diet (high intake of fruits, vegetables, whole grains, legumes, poultry, and fish) [15]. Clinicians should be aware that subjects with diverticulosis often adopt restrictive dietary behaviours that avoid fibre-rich foods in the belief that they may cause diverticular complications or worsen GI symptoms [16]. Dietary counselling may be helpful in this context.

Statement 1.2. We suggest against the exclusion from the diet of seeds, nuts, corn, and fruit peels/skins in subjects with colonic diverticulosis.

Agreement: 100% [A+ (91%); A (9%); A- (0%); D-(0%); D(0%);D+(0%)]

LE: Low; GR: Conditional

Summary of evidence: Traditionally, physicians have often advised subjects with diverticulosis to avoid foods such as seeds, nuts, corn, and fruit peel, supporting the idea that high-residue foods could promote diverticular complications. However, this concept has now been revised. In the prospective HPFS cohort, an inverse association was found between nut and popcorn consumption and the risk of diverticulitis. Specifically, the multivariate HR for men with the highest intake of each food (at least twice a week) compared with men with the lowest intake (less than once a month) were 0.80 (95%CI:0.63–1.01) for nuts and 0.72 (95% CI: 0.56–0.92) for popcorn. Furthermore, no associations were found between corn consumption and diverticulitis, or between nut, corn, or popcorn consumption and diverticular bleeding or uncomplicated diverticulosis [17].

Statement 1.3. We suggest informing subjects with colonic diverticulosis that pharmacological treatment is unnecessary.

Agreement: 100% [A+ (91%); A (9%); A- (0%); D-(0%); D(0%);D+(0%)]

LE: unable to assess using GRADE methodology; GR: Consensus recommendation

Summary of evidence: Most subjects with colonic diverticulosis remain asymptomatic throughout their lives without progressing to symptomatic DD. It has been estimated that only 1–4% of patients with diverticulosis will develop AD over an 11-year follow-up period [18]. Colonic diverticulosis is often detected incidentally during radiological or endoscopic examinations (i.e., colonoscopy for colorectal cancer screening). Currently, there is no rationale for pharmacological treatment in this setting.

Statement 1.4. We suggest weight loss in case of overweight or obesity, physical exercise, and smoking cessation, as these reduce the risk of diverticular disease and diverticular complications.

Agreement: 91% [A+ (91%); A (0%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Low; GR: Conditional

Summary of evidence: A systematic review examined the relationship between body mass index (BMI), physical activity, and the risk of diverticular disease. Each five-unit increase in BMI was associated with a 28%, 31% and 20% increase in the relative risk of diverticular disease, acute diverticulitis and complications of DD, respectively. In addition, a higher levels of physical activity were associated with a 24% and 26% reduction in the risk of DD and acute diverticulitis, respectively [19]. The association between obesity and diverticulitis has also recently been confirmed in a cohort of Hispanic and Latin American individuals [20]. Tobacco smok-

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Table 1

PICO and statements with the level of evidence and grade of recommendation and agreement.

PICO	STATEMENT	Level of evidence	Grade of recommendation	Level of agreement
Management of diverticulosis 1. What is the best strategy for preventing symptomatic colonic diverticular disease in subjects with colonic diverticulosis?	1.1 We suggest following a high-fibre diet and limiting the consumption of red meat to subjects with colonic diverticulosis.	Moderate	Conditional	Agreement: 91% [A+ (73%); A (18%); A- (9%); D-(0%); D(0%);D+(0%)]
	1.2 We suggest against the exclusion from the diet of seeds, nuts, corn, and fruit peels/skins in subjects with colonic diverticulosis.	Low	Conditional	Agreement: 100% [A+ (91%); A (9%); A- (0%); D-(0%); D(0%);D+(0%)]
	1.3 We suggest informing subjects with colonic diverticulosis that pharmacological treatment is unnecessary	Unable to assess using GRADE methodology	Consensus recommendation	Agreement: 100% [A+ (91%); A (9%); A- (0%); D-(0%); D(0%);D+(0%)]
	1.4 We suggest weight loss in case of overweight or obesity, physical exercise, and smoking cessation, as these reduce the risk of symptomatic diverticular disease and diverticular complications.	Low	Conditional	Agreement: 91% [A+ (91%); A (0%); A (0%); A (9%); D-(0%); D(0%);D+(0%)]
	1.5 We suggest avoiding non-steroidal anti-inflammatory drugs (NSAIDs) or opioid analgesics because of the increased risk of diverticular complications (analgesic drugs such as paracetamol should be preferred).	Low	Conditional	Agreement: 91% [A+ (91%); A (0%); A (9%); D-(0%); D(0%);D+(0%)]
Symptomatic uncomplicated liverticular disease (SUDD): liagnosis and treatment				
 What symptoms and signs suggest a diagnosis of SUDD? 	2.1 We suggest suspecting SUDD in patients with recurrent abdominal pain mainly localised in the left lower quadrant, often associated with a change in bowel habits or bloating without evidence of diverticular inflammation.	Very low	Consensus recommendation	Agreement: 82% [A+ (73%); A (9%); A (9%); A (18%); D-(0%); D(0%);D+(0%)]
3. In which patients with suspected SUDD should nstrumental investigastions be performed?	3.1 We suggest against routinely prescribing instrumental investigations in patients with suspected SUDD unless other conditions are suspected, such as inflammatory or ischaemic colitis or colorectal cancer.	Unable to assess using GRADE methodology	Consensus recommendation	Agreement: 82% [A+ (73%); A (9%); A (9%); A (18%); D-(0%); D(0%);D+(0%)]
4. What is the most effective treatment for SUDD?	4.1 In SUDD patients, we suggest following dietary and behavioural recommendations described for subjects with diverticulosis.	Unable to assess using GRADE methodology	Consensus recommendation	Agreement: 91% [A+ (73%); A (18%); A- (9%); D-(0%); D(0%);D+(0%)]
	4.2 In SUDD patients, we suggest that cyclic non-absorbable antibiotics associated with fibre supplementation may be effective in relief of abdominal symptoms.	Low	Conditional	Agreement: 82% [A+ (73%); A (9%); A (18%); D-(0%); D(0%);D+(0%)]
	4.3 In SUDD patients, we suggest against using of mesalazine to relieve abdominal symptoms.	Low	Conditional	Agreement: 82% [A+ (64%); A (18%); A- (9%); D-(9%); D(0%);D+(0%)]
Acute Diverticulitis (AD): diagnosis and treatment 5. What symptoms and signs suggest a diagnosis of AD?	5.1 We recommend suspecting AD in patients with long-lasting and severe abdominal pain, more often localised in the left lower abdomen, associated with fever and/or change in bowel	Unable to assess using GRADE methodology	Strong	Agreement: 91% [A+ (73%); A (18%); A- (9%); D-(0%); D(0%);D+(0%)]
5. What are the referral criteria for urgent hospital evaluation in people with suspected AD?	habits. 6.1 We recommend referring the same day for urgent hospital evaluation if the patient with suspected AD complains of severe abdominal pain and/or signs of intra-abdominal abscess, perforation/ peritonitis, sepsis, bladder or vaginal fistula, and intestinal obstruction.	Unable to assess using GRADE methodology	Strong	Agreement: 91% [A+ (91%); A (0%); A (9%); D-(0%); D(0%);D+(0%)]
7. Which investigtions are iseful for patients with suspected AD who are referred for urgent hospital evaluation?	7.1 We recommend the assessment of vital signs (in particular body temperature), complete blood count, urea, electrolytes and C-reactive protein (CRP) in patients with suspected AD referred for	Low	Strong	Agreement: 100% [A+ (91%); A (9%); A- (0%); D-(0%); D(0%);D+(0%)]
	urgent hospital evaluation.			(continued on next p

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Table 1 (continued)

PICO	STATEMENT	Level of evidence	Grade of recommendation	Level of agreement
	7.2 In patients with suspected AD, we recommend performing a contrast-enhanced computed tomography (CT) scan to confirm the diagnosis and guide management. If contrast is contraindicated, we recommend performing non-contrast CT, Magnetic Resonance Imaging	Moderate	Strong	Agreement: 100% [A+ (100%); A (9%) A- (0%); D-(0%); D(0%);D+(0%)]
3. Which investigations are nelpful to perform in patients with suspected AD who are not referred for urgent nospital assessment?	(MRI), or ultrasound based on local expertise. 8.1 We suggest careful evaluation of gastrointestinal symptoms, conducting a physical examination, assessing body temperature, and performing blood tests, including leukocyte count and CRP, in patients with suspected AD who are not referred for urgent hospital assessment.	Unable to assess using GRADE methodology	Conditional	Agreement: 91% [A+ (91%); A (0%); A (9%); D-(0%); D(0%);D+(0%)]
9. What are the most clinically effective treatments for managing AD?	9.1 We suggest a no-antibiotic prescribing strategy and a conservative approach with simple analgesia in patients with acute uncomplicated CT-proven diverticulitis without signs of systemic illness. Patients can be managed on an outpatient basis and should be advised of the need to be re-evaluated if the symptoms persist or worsen.	Moderate	Conditional	Agreement: 82% [A+ (64%); A (18%); A- (9%); D-(9%); D(0%);D+(0%)]
	9.2 We suggest an antibiotic prescribing strategy for immunocompromised patients with uncomplicated AD or those presenting with signs and/or symptoms of sepsis along with signs of systemic impairment or significant comorbidities.	Moderate	Conditional	Agreement: 91% [A+ (91%); A (0%); A (9%); D-(0%); D(0%);D+(0%)]
	9.3 We suggest an intravenous antibiotics prescribing strategy in patients admitted to secondary care with complicated AD. <i>Re</i> -evaluate therapy with intravenous antibiotics within 48 hours or after re-scanning and shift to oral antibiotics where possible.	Low	Strong	Agreement: 100% [A+ (100%); A (0%) A- (0%); D-(0%); D(0%);D+(0%)]
	9.4 We recommend urgent surgical evaluation of patients with AD complicated by sepsis, overt perforation, diffuse peritonitis or those who fail to improve despite medical therapy and/or percutaneous drainage.	Very low	Strong	Agreement: 100% [A+ (100%); A (0%) A- (0%); D-(0%); D(0%);D+(0%)]
Management of diverticular disease complications 10. What are the most effective treatments for patients with intra-abdominal diverticular abscess?	10.1 We recommend contrast-enhanced CT results to guide abscess management according to its location and size. If contrast is contraindicated, we suggest performing non-contrast CT, MRI, or ultrasound based on local expertise.	Very low	Conditional	Agreement: 91% [A+ (91%); A (0%); A (9%); D-(0%); D(0%);D+(0%)]
	10.2 We suggest considering an initial trial of antibiotics alone for abscesses < 3 cm in size. There is no indication for elective surgery after successful conservative therapy.	Low	Conditional	Agreement: 91% [A+ (82%); A (9%); A (9%); D-(0%); D(0%);D+(0%)]
	10.3 We suggest considering percutaneous drainage (if anatomically feasible and local expertise available) or surgery for abscesses ≥ 3 cm not responsive to antibiotics alone. The choice of treatment should consider factors such as the patient's age, comorbidity, and performance status. If percutaneous drainage is performed, a pus sample should be sent to a microbiology laboratory to guide antibiotic treatment.	Low	Conditional	Agreement: 91% [A+ (82%); A (9%); A (9%); A (9%); D-(0%); D(0%);D+(0%)]
	10.4 We suggest re-imaging if the clinical condition does not improve or worsen in patients with CT-confirmed abscesses to address the therapeutic strategy.	Very low	Conditional	Agreement: 91% [A+ (91%); A (0%); A (9%); D-(0%); D(0%);D+(0%)]
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PICO	STATEMENT	Level of evidence	Grade of recommendation	Level of agreement
11. What is the most effective treatment for patients with generalised peritonitis due to diverticular perforation?	11.1 We suggest considering colon resection with primary anastomosis (with or without a diverting ileostomy) in haemodynamically stable/immunocompetent patients with generalised peritonitis due to diverticular perforation. A potential alternative therapeutic strategy in selected patients (Hinchey III) is laparoscopic peritoneal lavage and drainage. However, if faecal peritonitis is identified intraoperatively, proceed to resectional surgery.	Low	Conditional	Agreement: 91% [A+ (82%); A (9%); D-(0%); D(0%);D+(0%)]
	11.2 We suggest considering Hartmann's procedure in haemodynamically unstable patients with multiple comorbidities or immunodepression and diffuse peritonitis due to diverticular perforation.	Low	Conditional	Agreement: 91% [A+ (82%); A (9%); D-(0%); D(0%);D+(0%)]
12. What is the most appropriate surgical approach for patients with generalised peritonitis due to diverticular perforation?	12.1 We suggest a laparoscopic approach in haemodynamically stable patients with generalised peritonitis due to diverticular perforation.	Very low	Consensus	Agreement: 82% [A+ (64%); A (18 A- (9%); D-(9%); D(0%);D+(0%)]
	12.2 We suggest an open approach in haemodynamically unstable patients with generalised peritonitis due to diverticular perforation. When adequate expertise is available, the laparoscopic approach may be considered in selected patients (responders to fluid resuscitation).	Very low	Consensus	Agreement: 91% [A+ (82%); A (9%); D-(0%); D(0%);D+(0%)]
Prevention of recurrent AD 13. What is the most clinically effective pharmacological strategy to prevent recurrent acute diverticulitis?	13.1 We recommend against the use of aminosalicylate to prevent recurrent AD.	Moderate	Strong	Agreement: 91% [A+ (82%); A (9% (9%); D-(0%); D(0%);D+(0%)]
	13.2 We recommend against the routine use of non-absorbable antibiotics to prevent recurrent	Very low	Conditional	Agreement: 82% [A+ (64%); A (18 A- (9%); D-(9%); D(0%);D+(0%)]

AD. Interventional management of diverticular disease 14. What are the indications 14.1 Verv low Strong Agreement: 100% [A+ (91%); A (9%); for elective surgery in patients We recommend against elective sigmoid resection A- (0%); D-(0%); D(0%);D+(0%)] with AD, complicated or not? in asymptomatic patients who have recovered from an episode of uncomplicated AD. 142 Very low Conditional Agreement: 91% [A+ (82%); A (9%); A-We suggest that elective sigmoid resection should (9%); D-(0%); D(0%);D+(0%)] be considered on a case-by-case basis in patients who have recovered from AD with persistent symptoms or recurrent diverticulitis, residual fistula or chronic obstruction due to stricture.

ing has also been associated with DD and related complications. A meta-analysis found an increased risk for the developing DD or complications of acute diverticulitis in current [RR 1.36 (95% CI 1.15-1.61)], former [RR 1.17 (95% CI 1.05-1.31)] and ever smokers [RR 1.29 (95% CI 1.16-1.44)]. There is evidence that smoking also increases the risk of complications of DD, although the number of studies analysing this item was small [21].

Statement 1.5. We suggest avoiding non-steroidal antiinflammatory drugs (NSAIDs) or opioid analgesics because of the increased risk of diverticular complications (analgesic drugs such as paracetamol should be preferred).

Agreement: 91% [A+ (91%); A (0%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Low; GR: Conditional

Summary of evidence: A recent systematic review and metaanalysis showed that NSAIDs and acetylsalicylic acid (ASA) increased the risk of diverticular bleeding (OR: 6.90, 95% CI: 3.86-12.35, p< 0.00001 and OR 2.84, 95% CI: 2.19-3.67, p < 0.00001,

respectively) or complicated diverticulitis (OR 3.13, 95% CI: 1.73-5.68, p = 0.0002, and OR 1.49, 95% CI: 1.02–2.17, p = 0.04, respectively) [22]. Similarly, the use of opioid analgesics has been associated with an increased risk of diverticular perforation (OR=2.16, 95% CI: 1.55-3.01) [23]. Thus, the use of paracetamol should be preferred.

3.2. Symptomatic uncomplicated diverticular disease (SUDD): diagnosis and treatment

PICO 2: What symptoms and signs suggest a diagnosis of SUDD?

Statement 2.1. We suggest suspecting SUDD in patients with recurrent abdominal pain mainly localised in the left lower quadrant, often associated with a change in bowel habits or bloating without evidence of diverticular inflammation.

Agreement: 82% [A+ (73%); A (9%); A- (18%); D-(0%); D(0%);D+(0%)]

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LE: very low; GR: Consensus recommendation

Summary of evidence: SUDD may be experienced as a recurrent debilitating illness that significantly affects quality of life (QoL) [24,25]. Notably, this clinical scenario may be difficult to distinguish from irritable bowel syndrome (IBS). Some features could help to distinguish these conditions: i) gender distribution (female to male ratio 1:1 in SUDD and 2:1 in IBS), ii) age (SUDD is more common in subjects over 50 years of age whereas IBS is more common in younger people), iii) characteristics of pain (localised in the lower left abdomen and lasting more than 24 hours in SUDD or typically diffuse and short-lasting in IBS) [26]. While some biomarkers, such as faecal calprotectin [27,28] or ultrasound (US) characteristics [29], have been suggested as potential elements for differentiating between SUDD from IBS, the available data remain scarce. Furthermore, as no definitive criteria for diagnosis of SUDD have been identified, the differential diagnosis with IBS remains challenging and is primarily based on clinical features. Finally, it should be noted that Asian patients may report pain in the right abdominal guadrant due to a the higher rate of rightsided diverticula.

PICO 3: In which patients with suspected SUDD should instrumental investigations be performed?

Statement 3.1. We suggest against routinely prescribing instrumental investigations in patients with suspected SUDD unless other conditions are suspected, such as inflammatory or ischaemic colitis or colorectal cancer.

Agreement: 82% [A+ (73%); A (9%); A- (18%); D-(0%); D(0%);D+(0%)]

LE: unable to assess using GRADE methodology; GR: Consensus recommendation

Summary of evidence: Imaging (e.g. virtual colonoscopy) or endoscopy (e.g. flexible sigmoidoscopy or colonoscopy) is used in clinical practice to rule out other conditions such as colorectal cancer, inflammatory or ischaemic colitis. In frail patients and/or with acute abdominal symptoms in an urgent/emergency setting, abdominal computed tomography (CT) should be preferred. Blood tests should be performed to exclude anaemia and/or acute inflammation. The role of intestinal US in differentiating SUDD in patients with abdominal symptoms has recently been proposed. Patients with SUDD showed a significantly greater muscle thickness than patients with IBS, patients with unclassified abdominal pain and healthy subjects, but comparable to patients with diverticulosis [29].

PICO 4: What is the most effective treatment for SUDD?

Statement 4.1. In SUDD patients, we suggest following dietary and behavioural recommendations described for subjects with diverticulosis.

Agreement: 91% [A+ (73%); A (18%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: unable to assess using GRADE methodology; GR: Consensus recommendation

Summary of evidence: Similar to subjects with asymptomatic diverticulosis, patients with SUDD may benefit from a high-fibre diet (if tolerated) and reduced consumption of red meat. Weight loss if overweight or obese, physical exercise, smoking cessation and avoidance of NSAIDs should be encouraged as they reduce the risk of diverticular complications (see PICO 1).

Statement 4.2. In SUDD patients, we suggest that cyclic nonabsorbable antibiotics associated with fibre supplementation may be effective in relief of abdominal symptoms.

Agreement: 82% [A+ (73%); A (9%); A- (18%); D-(0%); D(0%);D+(0%)]

LE: low; GR: Conditional

Summary of evidence: According to a meta-analysis including four studies (one RCT and three open studies), the administration of rifaximin (400 bid for 7 days per month) plus fibre supplementation (dietary=20 mg/day) or glucomannan (2–4 g/day) may be effective in relieving abdominal symptoms in SUDD patients (NNT = 3) compared with fibre supplementation alone at 1–2 years [30]. However, high-quality evidence based on placebocontrolled RCTs evaluating the long-term and cost-effectiveness of non-absorbable antibiotics in the treatment of SUDD is still lacking [31].

Statement 4.3. In SUDD patients, we suggest against using of mesalazine to relieve abdominal symptom.

Agreement: 82% [A+ (64%); A (18%); A- (9%); D-(9%); D(0%);D+(0%)]

LE: low; GR: Conditional

Summary of evidence: In a systematic review of 13 RCTs on the role of mesalazine in DD [32], only one study aimed to assess disease remission with mesalazine (3000 mg/day for 6 weeks) compared with placebo. However, no clinical benefit was observed for the use of mesalazine (OR 1.04; 95% CI 0.8–1.34) [33]. Studies evaluating the efficacy of mesalazine in DD have shown conflicting results due to the heterogeneity in study design [i.e. type of treatment (mesalazine plus other treatment such as probiotics), primary outcome (maintenance of remission or relief of symptoms), different dosage and posology (continuous vs. cyclic)] [32], which prevents us from making a definite recommendation.

3.3. Acute diverticulitis (AD): diagnosis and treatment

PICO 5: What symptoms and signs suggest a diagnosis of AD?

Statement 5.1. We recommend suspecting AD in patients with long-lasting and severe abdominal pain, more often localised in the left lower abdomen, associated with fever and/or change in bowel habits.

Agreement: 91% [A+ (73%); A (18%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: unable to assess using GRADE methodology; GR: strong

Summary of evidence: Patients with AD generally complain of severe and long-lasting left-sided abdominal pain and tenderness, often associated with fever and/or changes in bowel habits. Bloating, nausea, rectal passage of mucus or bleeding may be present. In right-sided diverticulitis, particularly in Asian people, the pain may be localised to the righ side of the abdomen.

PICO 6: What are the referral criteria for urgent hospital evaluation in people with suspected AD?

Statement 6.1. We recommend referring the same day for urgent hospital evaluation if the patient with suspected AD complains of severe abdominal pain and/or signs of intra-abdominal abscess, perforation/peritonitis, sepsis, bladder or vaginal fistula, and intestinal obstruction.

Agreement: 91% [A+ (91%); A (0%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: unable to assess using GRADE methodology. GR: Strong

Summary of evidence: Patients with severe abdominal pain or signs of intra-abdominal abscess (mass on abdominal or rectal examination), perforation/peritonitis (abdominal stiffness or peritonism), sepsis (changes in mental status, increased respiratory rate, decreased systolic blood pressure, increased heart rate, fever, decreased urine output, pale skin), bladder or vaginal fistula (fecaluria, pneumaturia, pyuria, passing stools from the vagina), intestinal obstruction (no passage of stools and gas, vomiting or ab-

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dominal distension) have to refer for urgent hospital evaluation for suspected complicated diverticulitis.

PICO 7: Which investigations are useful for patients with suspected AD who are referred for urgent hospital evaluation?

Statement 7.1. We recommend the assessment of vital signs (in particular body temperature), complete blood count, urea, electrolytes and C-reactive protein (CRP) in patients with suspected AD referred for urgent hospital evaluation.

Agreement: 100% [A+ (91%); A (9%); A- (0%); D-(0%); D(0%);D+(0%)] LE: low; GR: Strong

Statement 7.2. In patients with suspected AD, we recommend performing a contrast-enhanced computed tomography (CT) scan to confirm the diagnosis and guide management. If contrast is contraindicated, we recommend performing noncontrast CT, Magnetic Resonance Imaging (MRI), or ultrasound based on local expertise.

Agreement: 100% [A+ (100%); A (9%); A- (0%); D-(0%); D(0%);D+(0%)]

LE: Moderate; GR: Strong

Summary of evidence:

Complete blood count and CRP are useful blood tests to detect inflammation. Urea and electrolytes assess renal function and help determine whether a contrast-enhanced CT scan can be performed. Contrast-enhanced CT is highly accurate for the diagnosis and staging AD, with a sensitivity of over 94% and a specificity approaching 99% [34–40]. The diagnostic criteria for diverticulitis are the detection of inflamed diverticula, thickening of the intestinal wall to over 3 mm and increased contrast medium absorption. An early CT scan allows early detection of complications, exclusion of other GI and extra-GI diseases or identification of people with uncomplicated diverticulitis who can be discharged or antibiotics already started can be discontinued [41–43]. The most commonly used systems for staging AD are the Hinchey and modified Hinchey CT classification [44].

Ultrasound (US) is a dynamic, real-time, widely available and easily accessible alternative for the diagnosis of AD, with a sensitivity and specificity of up to 98% in the hands of an experienced examiner [45]. However, US is operator dependent, inaccurate in obese patients, and less sensitive in detecting abdominal gas-free and deep abscesses. In addition, US is unreliable in distinguishing between GI and extra-GI diagnoses [46,47]. Thus, the choice of ultrasound should depend on the availability of local expertise [38]. Although CT is the most sensitive imaging test for patients with suspected AD, a step-up approach, in which CT is performed after an inconclusive or negative US, has been proposed as a safe and alternative method for patients with suspected AD [48]. Magnetic resonance imaging is highly sensitive but less specific than CT and is not generally used in the acute setting [49]. Colonoscopy is generally contraindicated in the acute phase for a slightly increased risk of perforation and should be performed at least 6-8 weeks after AD, especially if complicated, to rule out colorectal cancer [50,51].

PICO 8: Which investigations are helpful to perform in patients with suspected AD who are not referred for urgent hospital assessment?

Statement 8.1. We suggest a careful evaluation of GI symptoms, conducting a physical examination, assessing body temperature, and performing blood tests, including leukocyte count and CRP, in patients with suspected AD who are not referred for urgent hospital assessment.

Agreement: 91% [A+ (91%); A (0%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: unable to assess using GRADE methodology, GR: Conditional

Summary of evidence: We suggest a careful evaluation of GI symptoms, physical examination, assessment of body temperature and blood tests (leukocyte count, CRP). Consider referring patients to urgent hospital assessment in case of clinical suspicion of AD and increased inflammatory markers.

PICO 9: What are the most clinically effective treatments for managing AD?

Statement 9.1. We suggest a no-antibiotic prescribing strategy and a conservative approach with simple analgesia in patients with acute uncomplicated CT-proven diverticulitis without signs of systemic illness. Patients can be managed on an outpatient basis and should be advised of the need to be re-evaluated if the symptoms persist or worsen.

Agreement: 82% [A+ (64%); A (18%); A- (9%); D-(9%); D(0%);D+(0%)]

LE: Moderate GR: Conditional

Statement 9.2. We suggest an antibiotic prescribing strategy for immunocompromised patients with uncomplicated AD or those presenting with signs and/or symptoms of sepsis along with signs of systemic impairment or significant comorbidities.

Agreement: 91% [A+ (91%); A (0%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Moderate GR: Conditional

Summary of evidence: The routine use of antibiotics in uncomplicated AD has been questioned due to emerging theories suggesting that diverticulitis may have a primarily inflammatory rather than infectious basis, and concerns about antibiotic resistance and/or complications [52].

In uncomplicated AD, RCTs comparing antibiotic therapy with intravenous fluids (AVOD trial) [53], an observational strategy (DI-ABOLO trial) [54] or anti-inflammatory and symptomatic treatment in an outpatient setting (DINAMO-study) [55] have not shown a significant difference in major clinical outcomes such as hospitalisation, complication rate, risk of recurrent disease, need for surgery, and mortality. Long-term follow-up results confirmed that omitting antibiotics did not increase the risk of developing complications of AD, recurrent diverticulitis or surgery [56,57]. In a recent placebo-controlled double-blind RCT, omitting antibiotic treatment did not prolong the hospital stay or increase adverse events and readmission rates to the hospital within 1-week/30-days [58].

Accordingly, systematic Cochrane reviews and meta-analyses, including observational studies and RCTs, failed to show a clear benefit of systemic antibiotics over supportive therapy [59–61]. Thus, the treatment of uncomplicated AD without systemic antibiotics is feasible, safe, and effective [62,63]. In addition, a multicentre, randomised, open-label study showed that non-antibiotic treatment of mild AD is safe and effective even in the outpatient setting [55].

Although the available evidence supports outpatient management of uncomplicated AD, in real life early diagnostic imaging may not always be possible due to difficulties in its availability through National Health Services (other than emergency departments).

However, all these studies included a strictly selected patient population with mild, uncomplicated diverticulitis, excluding those who were immunocompromised or had any signs or symptoms of sepsis/systemic inflammation or significant comorbidities. In patients with CT-confirmed uncomplicated AD, the risk of progression to complicated disease is approximately 5%. Risk factors for progression include systemic comorbidities, concurrent ASA score

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III or IV, symptoms lasting more than 5 days, vomiting, and elevated CRP levels (>140 mg/L) [64]. Similarly, fluid accumulation and, to a lesser extent, the length of the inflamed bowel on the initial CT scan may indicate a complicated course of the disease [65]. Therefore, patients with any of these features are at high risk of progressing to complicated disease and should be considered for antibiotic treatment.

Immunocompromised patients are at increased risk of complications and diverticulitis mortality compared with immunocompetent patients [66,67]. Therefore, in immunocompromised patients with uncomplicated AD or signs and/or symptoms of sepsis and signs of systemic impairment or significant comorbidities, a prescribing strategy of antibiotics covering gram-negative and anaerobic bacteria, intravenous fluids, and nothing by mouth is recommended. Results from RCTs have not shown important clinical differences in terms of route of administration (oral vs intravenous) [68,69] or duration (short vs long) [61,70] of antibiotic treatment.

Few data support dietary recommendations for uncomplicated AD. A small prospective, uncontrolled study including 86 patients with uncomplicated diverticulitis concluded that an unrestricted diet was well tolerated, although 8% had severe adverse events and 20% had persistent symptoms [71]. We advise bowel rest (clear liquid or low-residue diet) during the acute phase of uncomplicated diverticulitis, as many patients have reported greater abdominal comfort.

Symptoms usually improve within 2–3 days with conservative therapy, after which a solid diet can be resumed. Finally, we suggest against the use of NSAIDs for symptomatic relief, preferring treatment with paracetamol for pain control.

Statement 9.3. We suggest an intravenous antibiotics prescribing strategy in patients admitted to secondary care with complicated AD. Re-evaluate therapy with intravenous antibiotics within 48 hours or after re-scanning and shift to oral antibiotics where possible.

Agreement: 100% [A+ (100%); A (0%); A- (0%); D-(0%); D(0%);D+(0%)]

LE: Low GR: Strong

Summary of evidence: Due to a broad clinical agreement on the use of antibiotic therapy for complicated AD, the evidence on this topic is weak. Antibiotics that cover the expected polymicrobial spectrum of pathogens are recommended for the treatment of complicated diverticulitis [72,73]. Oral feeding should be individually considered depending on the clinical picture. For guidance on antibiotic therapy, see Table 2.

Statement 9.4. We recommend urgent surgical evaluation of patients with AD complicated by sepsis, overt perforation, diffuse peritonitis or those who fail to improve despite medical therapy and/or percutaneous drainage.

Agreement: 100% [A+ (100%); A (0%); A- (0%); D-(0%); D(0%);D+(0%)]

LE: Very low, GR: Strong

Summary of evidence: Urgent surgical evaluation is required in patients with AD complicated by sepsis, diffuse peritonitis or non-response to medical therapy and/or percutaneous drainage [41,74].

3.4. Management of diverticular disease complications

PICO 10: What are the most effective treatments for intraabdominal diverticular abscess?

Statement 10.1. We recommend contrast-enhanced CT results to guide abscess management according to its location and size. If contrast is contraindicated, we suggest performing non-contrast CT, MRI, or ultrasound based on local expertise.

Agreement: 91% [A+ (91%); A (0%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Very low, GR: Conditional

Statement 10.2. We suggest considering an initial trial of antibiotics alone for abscesses < 3 cm in size. There is no indication for elective surgery after successful conservative therapy.

Agreement: 91% [A+ (82%); A (9%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Low, GR: Conditional

Statement 10.3. We suggest considering percutaneous drainage (if anatomically feasible and local expertise available) or surgery for abscesses \geq 3 cm not responsive to antibiotics alone. The choice of treatment should consider factors such as the patient's age, comorbidity, and performance status. If percutaneous drainage is performed, a pus sample should be sent to a microbiology laboratory to guide antibiotic treatment.

Agreement: 91% [A+ (82%); A (9%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Low; GR: Conditional

Statement 10.4. We suggest re-imaging if the clinical condition does not improve or worsens, in patients with CT-confirmed abscesses to guide the therapeutic strategy.

Agreement: 91% [A+ (91%); A (0%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Very low, GR: Conditional

Summary of evidence: Currently, no high quality research is available on the best treatment of AD intra-abdominal abscesses; thus, existing recommendations are mainly based on retrospective observational cohort studies, providing outcome data for comparisons between antibiotics, percutaneous drainage (PCD) and surgery, or their various combinations. Antibiotic therapy is always required in the treatment of a diverticular abscess. For smallsize (<3 cm) abscesses, initial treatment with systemic antibiotics alone is considered safe and effective, whereas the best treatment for larger abscesses remains uncertain because antibiotics may not reach the therapeutic concentrations, resulting in an increased failure rate [75]. For larger abscesses, percutaneous drainage combined with intravenous antibiotics should be considered, but the evidence is of low quality [36]. Indications for PCD are heterogeneous, and depend on abscess size (failure of medical management alone is more likely in patients with abscesses >5 cm) and location (larger retroperitoneal or paracolic abscesses). as well as the response to antibiotics as sole therapy [41,76–78]. Gregersen retrospectively stratified a nationwide cohort of 3148 patients with Hinchey Ib and II diverticulitis into 3 groups according to treatment (surgery, percutaneous drainage, or antibiotics) to investigate short-term mortality, readmission, and abscess recurrence rates [79]. Although a reliable comparison between the treatment groups could not be made due to lack of data on abscess size and location, the feasibility of drainage, suitability for surgery, and the patient clinical condition, survival was similar between treatment groups. However, patients treated with PCD had a significantly higher risk of recurrence, as reported by Buchwald et al, who found a higher recurrence rate of diverticular abscess after initial conservative treatment (antibiotics +/- percutaneous drainage) compared to surgery [80].

Furthermore, PCD as a treatment for large abscesses does not affect outcomes such as failure rate, 30-day mortality, need for emergency surgery, permanent stoma, recurrence, or length of hospital stay compared to antibiotics alone [63,81], which may still be a safe and feasible alternative to PCD as the initial therapy for larger abscesses, followed by surgery [82]. Overall, there is still no

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Table 2

Systemic antibiotics for adults with acute diverticulitis.

Antibiotic ^a	Dosage and course length ^b		
First-choice oral antibiotic for suspected or confirmed uncomplicated	acute diverticulitis		
Amoxicillin-clavulanic acid	875 mg/125 mg two-three times a day for 5 days		
Alternative first-choice oral antibiotics if penicillin allergy or amoxicil	llin-clavulanic acid is unsuitable		
Cefalexin (caution in penicillin allergy) with metronidazole	Cefalexin: 500 mg twice or three times a day (up to 1 to 1.5 g three or four		
	times a day for severe infection) for 5 days		
	Metronidazole: 500 mg three times a day for 5 days		
Ciprofloxacin (only if switching from IV	Ciprofloxacin: 500 mg twice a day for 5 days		
ciprofloxacin with specialist advice; consider safety issues ^c) with metronidazole	Metronidazole: 500 mg three times a day for 5 days		
First-choice intravenous antibiotics ^d for suspected or confirmed comp	licated acute diverticulitis		
Amoxicillin-clavulanic acid	1000 mg/200 mg two-three times a day		
Cefuroxime with metronidazole	Cefuroxime: 750 mg three or four times a day (increased to 1.5 g three or fou		
	times a day if severe infection)		
	Metronidazole: 500 mg three times a day		
Amoxicillin with gentamicin and metronidazole	Amoxicillin: 500 mg three times a day		
	(Increased to 1 g four times a day if severe		
	infection)		
	Gentamicin: Initially 5 to 7 mg/kg once a day,		
	subsequent doses adjusted according to serum		
	gentamicin concentration ^e		
	Metronidazole: 500 mg three times a day		
Ciprofloxacin ^f (consider safety issues ^c) with	Ciprofloxacin: 400 mg twice or three times a		
metronidazole	day		
	Metronidazole: 500 mg three times a day		
Alternative intravenous antibiotics			
Consult local microbiologist			

^a Consider appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy, breastfeeding, and administering intravenous (or, where appropriate, intramuscular) antibiotics.

^b A more prolonged course may be needed based on clinical assessment. Continue antibiotics for up to 14 days in patients with CT-confirmed diverticular abscess.

^c Consider restrictions and precautions for fluoroquinolones due to rare reports of disabling and potentially long-lasting or irreversible side effects affecting the musculoskeletal and nervous systems. Warnings include stopping treatment at the first signs of a severe adverse reaction (such as tendonitis), prescribing with particular caution for people over 60 years, and avoiding coadministration with a corticosteroid.

^d Re-evaluate therapy with intravenous antibiotics within 48 hours or after scanning if earlier and shift to oral antibiotics where possible.

^e Therapeutic drug monitoring and assessment of renal function are required.

^f Only in people with allergy to penicillin and cephalosporins.

conclusive evidence that PCD is effective as a reinforcement of antibiotic therapy and can prevent urgent surgery.

PICO 11: What is the most effective treatment for patients with generalised peritonitis due to diverticular perforation?

Statement 11.1. We suggest considering colon resection with primary anastomosis (with or without a diverting ileostomy) in haemodynamically stable/immunocompetent patients with generalised peritonitis due to diverticular perforation. A potential alternative therapeutic strategy in selected patients (Hinchey III) is laparoscopic peritoneal lavage and drainage. However, if faecal peritonitis is identified intraoperatively, proceed to resectional surgery.

Agreement: 91% [A+ (82%); A (9%); A- (9%); D-(0%); D(0%);D+(0%)] LE: Low, GR: Conditional

Statement 11.2. We suggest considering Hartmann's procedure in haemodynamically unstable patients with multiple comorbidities or immunodepression and diffuse peritonitis due to diverticular perforation.

Agreement: 91% [A+ (82%); A (9%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Low, GR: Conditional

Summary of evidence: Surgical RCTs have compared Hartmann's procedure (HP) (which involves the creation of a stoma at the initial operation and a subsequent secondary anastomosis at a stoma reversal operation if possible) with colon resection with primary anastomosis (PRA) for the treatment of perforated diverticulitis [83–86]. Postoperative mortality was generally similar between HP and PRA. However, patients who underwent PRA were more likely to be stoma-free and had lower rates of organ/space surgical site infection and postoperative morbidity for the stoma reversal surgery, as well as lower rates of pooled ostomy non-reversal [87]. Analysis of observational studies suggests that PRA may be associated with lower overall mortality, although RCTs have not shown such a difference [88].

Long-term outcomes of the DIVERTI trial confirmed that PRA significantly reduced the incisional hernia rates and the need for reoperation, and was associated with fewer long-term complications and better QoL than HP [89]. However, due to the complexities of applying precise RCT principles in the acute setting, no clear indications for a non-restorative versus a restorative surgery have been formulated. Therefore, surgeon expertise and patient-related factors such as ASA score or the severity of intraoperative findings, should primarily support the choice of treatment.

Recently, laparoscopic lavage, consisting of laparoscopic aspiration of pus followed by abdominal lavage and placement of abdominal drains, has been proposed as an alternative approach to colon resection in AD complicated by diverticular perforation. However, prospective RCTs comparing laparoscopic lavage with colonic resection with PRA (LOLA-arm of LADIEs trial and SCANDIV trial) or HR (DILALA trial) have shown conflicting results [90–92].

The data and safety monitoring board terminated the LOLAarm of the LADIEs trial because of the increased complication rate and the need for unplanned urgent surgery in the lavage group. In the SCANDIV trial, laparoscopic lavage did not reduce severe postoperative complications, leading to worse outcomes in secondary endpoints [91], deep surgical site infections and unplanned reoperations at 1-year follow-up [93]. Long-term follow-up (5 years) showed no differences in severe complications, while recurrence

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of diverticulitis was more common after laparoscopic lavage, often leading to sigmoid resection. This has to be weighed against the lower prevalence of stoma in this group [94]. In a prospective observational multicentre study comparing peritoneal lavage and laparoscopic sigmoidectomy in patients with pelvic abscess and generalised purulent peritonitis, lavage was associated with failure to achieve source control of the peritoneal infection, more frequent need for return to the operating room and diverticular recurrence [95]. These findings do not support laparoscopic lavage for the treatment of perforated diverticulitis.

On the other hand, in the DILALA trial, morbidity and mortality 12 weeks after laparoscopic lavage did not differ from HP. Laparoscopic peritoneal lavage was associated with shorter operative time, hospital stay and shorter time in the recovery unit [92] and a reduced risk of needing one or more operations within 24 months [96]. A multicentre international trial (LLO Study) found that laparoscopic lavage in selected patients with perforated Hinchey III acute diverticulitis affected by peritonitis had a high rate of successful control of sepsis, with low rates of operative mortality, reoperation and stoma formation [97]. Based on these findings, an Italian position paper stated that laparoscopy may be effective in the management of purulent peritonitis, reducing the rate of ostomy in selected patients (stable patients with diffuse purulent peritonitis, with low ASA and Mannheim Peritonitis Index scores and no visible free perforation) [98].

A systematic review and meta-analysis investigating the therapeutic role of laparoscopic lavage in the management of diverticular peritonitis found no significant difference in postoperative mortality and early reoperation rates. However, despite a lower rate of stoma formation, laparoscopic lavage was associated with a significantly higher rate of postoperative intra-abdominal abscess [99].

Thus, several controversies remain regarding laparoscopic lavage and drainage, and decision making should consider both the short and long term consequences.

PICO 12: What is the most appropriate surgical approach for patients with generalised peritonitis due to diverticular perforation?

Statement 12.1. We suggest a laparoscopic approach in haemodynamically stable patients with generalised peritonitis due to diverticular perforation.

Agreement: 82% [A+ (64%); A (18%); A- (9%); D-(9%); D(0%);D+(0%)]

LE: Very low, GR: Consensus

Statement 12.2. We suggest an open approach in haemodynamically unstable patients with generalised peritonitis due to diverticular perforation. When adequate expertise is available, the laparoscopic approach may be considered in selected patients (responders to fluid resuscitation).

Agreement: 91% [A+ (82%); A (9%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Very low, GR: consensus

Summary of evidence: A laparoscopic approach with PRA or HP is preferred in the emergency setting and in haemodynamically stable patients. A systematic review, including 4 case series and one cohort study, suggested that laparoscopic sigmoidectomy as a feasible alternative to open surgery in selected patients, when performed by experienced hands [100]. In a more recent systematic review and meta-analysis, that included four observational studies with 436 patients, the laparoscopic approach was associated with improved overall postoperative complication rates and hospital stay. However, no differences were found for other clinical outcomes, such as the rate of Hartmann's vs anastomosis, operative time, reoperation rate and 30-day postoperative mortality. Furthermore, the lack of haemodynamic data and reasons for the operative approach partially hampered the results [101]. A large retrospective analysis found that emergency laparoscopic sigmoid resection without diversion was feasible and safe in patients with perforated diverticulitis, with mortality and morbidity (including leakage) rates similar to those of elective sigmoidectomy [102]. However, given the considerable uncertainty and the low quality of the evidence, laparoscopic sigmoidectomy in the emergency setting should be performed by qualified laparoscopic surgeons.

An open approach with HP or damage control surgery is recommended for haemodynamic instability that responds transiently to fluid administration. On the other hand, for haemodynamically unstable patients who do not respond to fluid administration or require vasopressors, an open approach with damage control surgery is mandatory [98].

3.5. Prevention of recurrent AD

PICO 13: What is the most clinically effective pharmacological strategy to prevent recurrent AD?

Statement 13.1. We recommend against the use of amino salicylate to prevent recurrent AD.

Agreement: 91% [A+ (82%); A (9%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Moderate; GR: Strong

Summary of evidence: Randomised, double-blind, placebocontrolled studies have been conducted to investigate the role of mesalazine in the prevention of recurrent AD. The Prevent studies (Prevent 1 and Prevent 2) showed no statistical difference in CT-confirmed AD recurrence between patients taking mesalamine (irrespective of dose) and the placebo group [103]. A multicentre trial (SAG-37 and SAG-51) evaluating different doses of mesalazine in patients with previous episodes of uncomplicated diverticulitis found that mesalazine did not increase the proportion of patients free of recurrence over 48 or 96 weeks compared with placebo. [33] Furthermore, in a placebo-controlled study, intermittent use of mesalazine for 10 days/month for one year also failed to prevent recurrence [104]. Finally, two meta-analyses confirmed the lack of the effect of mesalazine in preventing recurrent AD [105,106].

Statement 13.2. We recommend against the routine use of nonabsorbable antibiotics to prevent recurrent AD.

Agreement: 82% [A+ (64%); A (18%); A- (9%); D-(9%); D(0%);D+(0%)]

LE: Very low, GR: Conditional

Summary of evidence: Cumulative data from placebocontrolled [107] unblinded trials and meta-analyses suggest that the addition of rifaximin to fibre supplementation may be effective in the prevention of recurrent AD compared to fibre alone [30,108]. In an open trial by Lanas et al., adding rifaximin to a high fibre regimen was associated with a lower rate of recurrence compared to fibre alone (10.4% vs 19.3%, p= 0.033) [109]. However, the number needed to treat with rifaximin (NNT=50) to prevent one episode of acute diverticulitis remains high [30].

In conclusion, although these data suggest a promising role for cyclic therapy with rifaximin in preventing the recurrence of AD, the methodological limitations of the studies, such as the small number of patients and the open-label design, mean that further RCTs are needed before definitive recommendations can be made [31].

In addition, there is little evidence on the role of dietary fibre and lifestyle interventions in preventing recurrence of diverticulitis. It is reasonable to assume that the beneficial effects of dietary fibre and lifestyle interventions reported in observational studies in patients without previous diverticulitis [increased physical activity, weight loss in overweight or obese patients, smoking cessation,

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avoidance of NSAIDs] can be successfully applied in patients who have had acute diverticulitis to reduce the recurrence of diverticulitis.

3.6. Interventional management of diverticular disease

PICO 14: What are the indications for elective surgery in patients with AD, complicated or not?

Statement 14.1. We recommend against elective sigmoid resection in asymptomatic patients who have recovered from an episode of uncomplicated AD.

Agreement: 100% [A+ (91%); A (9%); A- (0%); D-(0%); D(0%);D+(0%)]

LE: Very low, GR: Strong

Summary of evidence: In uncomplicated AD treated with a conservative approach, the complication rate is generally low, regardless of initial or recurrent diverticulitis, gender, inflammatory parameters and prior comorbidity [110]. The risk of subsequent complicated disease after an episode of uncomplicated AD is less than 5% [111], and the recurrence rate after the first episode ranges from 10% to 36%, indicating that most patients never have another episode of AD and would not have the opportunity to benefit from surgery [112].

Statement 14.2. We suggest that elective sigmoid resection should be considered on a case-by-case basis in patients who have recovered from AD with persistent symptoms or recurrent diverticulitis, residual fistula or chronic obstruction due to stricture.

Agreement: 91% [A+ (82%); A (9%); A- (9%); D-(0%); D(0%);D+(0%)]

LE: Very low, GR: Conditional

Summary of evidence: Some patients (4–10%) may experience atypical chronic abdominal symptoms after AD, configuring the socalled "smouldering diverticulitis" [113]. Although a systematic review and meta-analysis found better QoL and fewer symptoms after laparoscopic surgery in patients with recurrent diverticulitis and persistent symptoms after AD, the underlying studies were of low guality [114]. In the Dutch DIRECT trial, an open-label, randomised, prospective multicentre study, elective sigmoid resection (*n*=53) in patients with recurrent diverticulitis or persistent symptoms after AD was associated with a significant improvement in QoL at six months [115] and at five-year follow-up [116] compared with the conservative approach (n=56). Similarly, a recent RCT of recurrent, complicated, or persistent painful diverticulitis (n=85)randomised to elective sigmoid resection or conservative management found that surgery effectively prevented recurrent diverticulitis and improved QoL within two years [117].

A lower threshold for elective sigmoid resection may be considered in patients with previous complicated diverticulitis or recurrent episodes of AD and clinical factors (family history, retroperitoneal abscess, and length of the colonic segment involved) [111] or comorbidities [118] carrying a higher intrinsic potential risk of recurrence and complications [119].

However, the decision to perform elective surgery for chronic or recurrent diverticulitis should be made on a case-by-case basis, taking into account factors such as the severity of symptoms, the impact on the patient's QoL, and the likelihood of improvement versus the short-term morbidity and long-term consequences of colonic resection [120].

Patients with a history of diverticulitis may develop other chronic manifestations such as fistula and stricture. Fistula formation [colovesical (65 %), colovaginal (25%), coloenteric (6.5%), colouterine (3%) and enterocutaneous (1%)] accounts for 17–27 % of surgically treated cases of DD [121]. Colonic stenosis resulting

from AD is considered clinically relevant if it obstructs fecal transit and requires surgical treatment [122,123].

Declaration of competing interest

No conflict of interest to declare.

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