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Italian consensus conference for colonic diverticulosis and diverticular disease

Rosario Cuomo[1], Giovanni Barbara[2], Fabio Pace[3], Vito Annese[4], Gabrio Bassotti[5], Gian A Binda[6], Tino Casetti[7], Antonio Colecchia[2], Davide Festi[2], Roberto Fiocca[8], Andrea Laghi[9], Giovanni Maconi[10], Riccardo Nascimbeni[11], Carmelo Scarpignato[12], Vincenzo Villanacci[13] and Bruno Annibale[14]

Abstract

The statements produced by the Consensus Conference on Diverticular Disease promoted by GRIMAD (Gruppo Italiano Malattia Diverticolare, Italian Group on Diverticular Diseases) are reported. Topics such as epidemiology, risk factors, diagnosis, medical and surgical treatment of diverticular disease (DD) in patients with uncomplicated and complicated DD were reviewed by a scientific board of experts who proposed 55 statements graded according to level of evidence and strength of recommendation, and approved by an independent jury. Each topic was explored focusing on the more relevant clinical questions. Comparison and discussion of expert opinions, pertinent statements and replies to specific questions, were presented and approved based on a systematic literature search of the available evidence. Comments were added explaining the basis for grading the evidence, particularly for controversial areas.

Keywords

Diverticulosis, diverticular disease, diverticulitis, consensus, diagnosis, medical therapy, surgical therapy

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Introduction

Colonic diverticulosis has been recognized as an increasingly common clinical condition in industrialised countries, the highest rates occurring in the United States and Europe. This condition nowadays ranks as fifth most important gastrointestinal disease in terms of direct and indirect costs. Diverticular disease (DD) is a term generally used to include diverticulosis and diverticulitis.[1,2]

While most people with colonic diverticulosis remain asymptomatic, about 20% experience abdominal symptoms and, eventually, complications, episodes of diverticulitis or bleeding.[3,4] Symptoms of DD can be acute or chronic, ranging from gastrointestinal symptoms similar to those of irritable bowel syndrome (IBS) (e.g. abdominal pain and discomfort, bloating, constipation and diarrhoea) to acute symptoms resembling appendicitis (e.g. fever, acute abdominal pain and leucocytosis), chronic abdominal pain or recurrent severe attacks of abdominal pain, fever or acute abdomen.[5–7] Acute diverticulitis is characterised by

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inflammation, micro-perforation and abscess formation; about one third of affected patients may experience recurrent episodes.[8,9] In patients with gastrointestinal symptoms without overt diverticulitis, low-grade inflammation, altered intestinal microbiota, visceral hypersensitivity and abnormal colonic motility have been identified as factors leading to symptom generation.[5,10]

Although the pathogenesis and management of diverticulosis and DD remain uncertain, new hypotheses and observations are changing the pharmacological and surgical management of DD. It is currently believed that medical therapy is generally required in symptomatic DD to treat infection, improve symptoms, and prevent recurrence of symptoms or development of complications. Recommendations for the diagnosis and treatment of DD have been issued by many medical societies in various countries.[11–13] Most available guidelines, however, are dated, and no international guidelines with grades of recommendations, based on level of evidence, are yet available.

Despite the large epidemiological and economic burden of DD, there is surprisingly limited knowledge about this condition. This generates uncertainties in the clinician and dissatisfaction in patients. It has been proposed that DD should be viewed as a potentially chronic illness with implications on everyday outpatient practice, and that clinicians should be prepared to address its impact beyond acute diverticulitis.[14]

We have summarised the current Italian perspective on DD in this consensus conference report, aiming to develop guidelines for the clinical, diagnostic and therapeutic management of DD.

Methods

The primary aim of this document was to provide clinical guidelines for appropriate definition, diagnosis and management of DD. The promoter of this initiative was the Italian Study Group of Diverticular Disease (Gruppo Italiano Malattia Diverticolare (GRIMAD)) – see Appendix 1. GRIMAD identified a scientific board of experts (BA, GB, RC, FP), who defined the methodology and targets, and acted as developers and reviewers.

The methodology to process the guidelines consisted of six steps:

1. The scientific board selected four main areas of interest in DD: (a) definition and epidemiology, (b) pathophysiology, (c) diagnosis, and (d) medical and surgical therapy.
2. For each topic, a working party was created, which included a coordinator and at least two experts. The latter were chosen on the basis of their recognised scientific expertise in DD. Together with the scientific board, the working party selected a number of clinically relevant, clear, answerable questions, focusing on current practice and areas of controversy. The questions were circulated among the working parties to share relevance, improve clarity, and avoid duplication. A preliminary meeting of the working parties was held in Bologna (June 2011) to share methods, aims, timelines, and the entire guideline process.
3. The working parties independently carried out a systematic search for, and analysis of, the literature relevant to their topics during October 2012, using Medline/PubMed and the Cochrane Database. Each recommendation was graded according to the Oxford Centre for Evidence-Based Medicine, according to the level of evidence (EL) (Supplementary Material, Table 1S).
4. By November 2012 the working parties issued initial statements and attributed them a grade (strength) of recommendation (RG), from A–D, consistent with the level of evidence (Table 1). Each coordinator drafted provisional statements that were circulated within his/her group.
5. Subsequently, each coordinator (BA, GB, RC, FP) evaluated the preliminary statements produced and the related grades of evidence. A redrafted document containing the statements was then prepared and submitted to all participants for an online session, for a first round of votes and comments, using a simplified scale (agreement/disagreement); the participants voted using a modified Delphi procedure until a minimum agreement level of at least 67% was achieved for each statement. Statements were then submitted to the scientific board, who wrote an advanced version, and fed back the new statements to the working parties.
6. On 19 and 20 February 2013, a consensus meeting was held in Bologna. The consensus group included 33 participants, who were selected taking into account diverse expertise in various aspects of DD, and geographical distribution. The consensus group was led by a non-voting chairman (GG) and the non-voting members of the scientific board (BA, GB, RC, FP), and included experts of working parties and multi-disciplinary professionals/experts such as gastroenterologists, gastrointestinal (GI) endoscopists, pharmacologists, surgeons, radiologists, pathologists, and general practitioners. Overall, 76 statements were submitted to the global consensus group for an open discussion driven by the non-voting chairman and the non-voting members of the scientific board. Following a plenary discussion held before voting, 21 statements were deleted, and 45 were partially rephrased. The final 55 statements

Table 1. Main statements

N	Statements	EL (*)	RG (*)
Definition and epidemiology			
1.1.1	'Diverticulosis' is merely the presence of colonic diverticula; these may become symptomatic or complicated.	**1c**	**B**
1.1.3	Symptomatic uncomplicated diverticular disease (SUDD) is a syndrome characterized by recurrent abdominal symptoms (i.e. abdominal pain and bloating resembling or overlapping irritable bowel syndrome (IBS) symptoms) attributed to diverticula in the absence of macroscopically evident alterations other than the presence of diverticula.	**1c**	**B**
1.1.4	Acute diverticulitis is an acute episode of severe, prolonged, lower abdominal pain (usually on the left side), change in bowel movements, low-grade fever and leucocytosis. The clinical presentation has a broad spectrum ranging from mild self-limiting episodes to abscess, perforation and peritonitis.	**1c**	**B**
1.1.6	A small subset of patients with diverticulosis may develop segmental colitis associated with diverticulosis (SCAD).	**4**	**C**
1.2.1	The prevalence of diverticulosis and diverticular disease (DD) is increasing in Western countries in parallel with increased life-expectancy.	**2c**	**B**
1.3.1	DD is a relevant cause of hospitalization and not devoid of mortality, particularly in elderly patients.	**2c**	**B**
1.4.1	During the last 10–20 years there has been an increasing rate of hospital admission for diverticulitis.	**2c**	**B**
1.5.1	Mortality in perforated disease remains elevated, due to the high rate of relevant comorbidity.	**2c**	**B**
1.7.1	In general, DD has a favourable long-term outcome with a very low incidence of complications. Symptomatic disease, acute diverticulitis and complicated DD represent distinct clinical entities among groups.	**4**	**D**
1.8.1	DD does not increase the risk of colon cancer.	**4**	**C**
Diagnosis			
3.2.1	SCAD is a defined pathological entity characterized by a chronic inflammatory response involving the inter-diverticular mucosa of a colonic segment involved. The rectum and the right colon are spared from inflammation. Hence, SCAD can be considered a separate pathological entity.	**1b**	**B**
3.2.3	Limitation of mucosal lesion to the diverticular segment is the most important diagnostic criterion for SCAD (rectal sparing). Rectal and descending colon biopsies are required to distinguish SCAD from inflammatory bowel disease (IBD).	**2a**	**B**
3.5.1	A prompt colonoscopy (i.e. within 12–24 h) is mandatory for diagnosis and to direct therapy. Massive bleeding should be managed with selective angiography.	**2a**	**B**
3.6.1	US can be used as a sensitive and specific diagnostic technique to detect acute diverticulitis and its septic abdominal complications, provided that the procedure is carried out by an expert investigator.	**1b**	**A**
3.7.1	Colonoscopy and CT colonography (CTC) must be considered the first-line test to diagnose or rule out colonic diverticula. The choice for CTC or colonoscopy depends on the patient's age, risk factors, clinical status and preference.	**3b**	**C**
3.7.2	Diagnostic accuracy of double contrast barium enema (DCBE) for DD is similar to that of CTC. Use of DCBE should be considered only if CTC is unavailable.	**3a**	**B**
3.8.1	Contrast-enhanced computerized tomography (CE-CT) should be considered as the first-line colonic examination since it offers a more comprehensive evaluation of uncomplicated and complicated forms; CE-CT can also be used to guide therapeutic interventions.	**1b**	**A**
3.8.3	The use of magnetic resonance colonography (MRC) in diagnosing diverticulitis is not sustained by robust data. Feasibility seems to be limited by the difficult access to magnetic resonance (MR) scanners in emergency departments.	**4**	**D**
3.9.2	Endoscopic follow-up should be reserved only to patients with persistently severe symptoms to exclude either cancer or IBD.	**3a**	**B**
Medical and surgical treatment			
4.1.1	There is no rationale for drug treatment of asymptomatic diverticulosis, but there are limited indications to suggest an increase in dietary fibre.	**2b**	**B**
4.1.2	There is a possible relationship between low dietary fibre intake, particularly insoluble fibre, and the development of DD. A high daily fibre intake is recommended to reduce the risk of DD.	**2c**	**B**
4.1.3	There is no rationale to avoid in the diet the consumption of nut, corn and popcorn to prevent diverticular complications.	**2c**	**B**
4.1.4	Regular treatment with aspirin or Nonsteroidal anti-inflammatory drugs (NSAIDs) carries the potential risks of diverticular complications.	**2b**	**B**

(continued)

Table 1. Continued

N	Statements	EL (*)	RG (*)
4.2.1	Fibre supplementation alone provides controversial results in terms of symptoms relief.	**2b**	**B**
4.2.3	Fibre plus rifaximin provide a greater prevalence of symptom-free patients compared to fibre alone.	**2b**	**B**
4.2.4	Rifaximin plus fibre is more effective than fibre alone in preventing acute diverticulitis with a low therapeutic advantage.	**2b**	**B**
4.2.5	There is no clear evidence that mesalazine alone is effective in reducing symptoms.	**2b**	**B**
4.2.6	There is no clear evidence that mesalazine reduces acute episodes of diverticulitis.	**3b**	**C**
4.2.7	There is insufficient evidence that probiotics are effective in reducing symptoms.	**4**	**C**
4.3.1	Management and treatment approaches depend on severity (uncomplicated and complicated) and complexity (i.e. abscess, fistula, etc.) of the condition.	**3b**	**C**
4.3.2	Antibiotics may not improve outcome in acute uncomplicated diverticulitis (AUD) and are used on a case-by-case basis.	**3b**	**C**
4.3.3	In severe/complicated acute diverticulitis (AD), hospitalization, bowel rest and broad-spectrum antibiotics are needed.	**3b**	**C**
4.4.1	The decision to perform elective resection after one or more episodes of AD should be undertaken on a 'case-by-case' basis.	**2b**	**B**
4.5.1	Elective surgery should be recommended in patients with symptomatic complicated diverticular disease (e.g. fistula, stenosis). Specific clinical situations should be carefully evaluated (persisting symptoms and signs, age, degree of diverticulitis, immunocompromised patients).	**3a**	**B**
4.6.1	Elective resection in a patient with an episode of AD is safer when performed in an inflammation-free interval.	**3a**	**B**
4.7.1	Laparoscopic resection is safe and provides faster recovery in uncomplicated cases; it has to be performed by well trained surgeons.	**2a**	**B**
4.8.1	Several surgical options may be appropriate, but the choice mostly depends on the severity of peritonitis. Laparoscopic peritoneal lavage should be considered as an alternative to primary resection and anastomosis in purulent peritonitis.	**2b**	**B**
4.9.1	The best treatment option for a diverticular abscess >4 cm in diameter is percutaneous guided drainage. Diverticular abscesses not responding, or not amenable, to non-operative management should be treated surgically.	**3b**	**C**
4.10.1	Though technically feasible, laparoscopic resection for perforated diverticulitis has to be restricted to selected cases and to experienced laparoscopic surgeons.	**4**	**C**
4.10.2	Current evidence is inadequate to support an urgent laparoscopic colorectal resection for perforated diverticulitis. This approach should be reserved to centres and surgeons with appropriate laparoscopic expertise.	**5**	**C**

*Evidence level (EL) and grade of recommendation (RG) were graded according to the Oxford Centre for Evidence-Based Medicine as detailed in text.

were then submitted to the global consensus group for anonymous keypad voting (Delphi process) without any explanation or justification. The Delphi process brought to a change of view from a position previously held, avoiding any uneasiness among participants or influence on individual votes. The agreement/disagreement level was scored on a six-point Likert scale as follows: A+: strongly agree; A: agree with minor reservations; A−: agree with major reservations; D−: disagree with major reservations; D: disagree with minor reservations; D+: strongly disagree. Level of agreement was expressed as percentage of each point of the scale. Immediate feedback was given to participants on a screen, who were prompted by the non-voting chairman and the non-voting members of the scientific board to discuss the statements, and suggest changes in case of controversy (<67% agreement). Consensus was defined a priori as agreement by at least 67% of respondents. The entire work and discussions were tape-recorded.

The format of the following recommendations comprises the question, the statement, its level of evidence and strength of recommendation, and the percentage agreement of the global consensus group on the final version.

In the present document the statements are accompanied by comments made by each working party and reviewed by the scientific board taking into account relevant observations and suggestions made during the plenary discussion. In some areas the

evidence level is low, reflecting the lack of randomised trials and good quality studies. For some topics only the expert opinion was considered, where appropriate.

Statements

1 Definition and epidemiology of diverticular disease

1.1 Does a finding of colonic diverticula correspond to a diagnosis of DD?

1.1.1 Statement (evidence level (EL) 1c – grade of recommendation (RG) B): 'Diverticulosis' is merely the presence of colonic diverticula; these may become symptomatic or complicated.

Consensus levels of agreement: A+ 91%; A 9%.

Colonic diverticula are usually acquired and do not involve all the wall layers, but are rather herniations of the mucosa and submucosa; hence they would be more appropriately defined as pseudo-diverticula. Their number can vary from one to literally hundreds; they can occur anywhere in the colon, although they are mainly present in the left colon, at least in Western populations.[14–16]

1.1.2 Statement (EL 1c – RG B): Colonic diverticulosis is the finding of diverticula in patients without abdominal complaints who undergo evaluation for other indications (e.g. cancer screening).

Consensus levels of agreement: A+ 69%; A1 6%; A− 3%; D+ 12%.

1.1.3 Statement (EL 1c – RG B): Symptomatic uncomplicated diverticular disease (SUDD) is a syndrome characterised by recurrent abdominal symptoms (i.e. abdominal pain and bloating resembling or overlapping IBS symptoms) attributed to diverticula in the absence of macroscopically evident alterations other than the presence of diverticula.

Consensus levels of agreement: A+ 71%; A 19%; A− 7%; D− 3%.

A significant but not yet well defined proportion of DD patients complain of symptoms – mainly abdominal pain (broadly ranging from abdominal discomfort to more prolonged painful episodes), bloating, altered bowel habits. In addition, considering the high prevalence of both IBS (10–20%) and diverticulosis (up to 65% in the elderly), the two conditions may frequently coexist by chance. Both conditions presumably also share some underlying predisposing (i.e. mild inflammation) or pathophysiological factors (i.e. visceral sensitivity). The clear differentiation between the two conditions is challenging and should mainly be based on clinical history (i.e. duration of symptoms, age at symptoms onset, documented episode of acute diverticulitis).[7,17–19]

1.1.4 Statement (EL 1c – RG B): Acute diverticulitis is an acute episode of severe, prolonged, lower abdominal pain (usually on the left side), change in bowel movements, low-grade fever and leukocytosis. The clinical presentation has a broad spectrum ranging from mild self-limiting episodes to abscess, perforation and peritonitis.

Consensus levels of agreement: A+ 78%; A 16%; A− 6%.

As many as 10–25% of patients with known DD may suffer from diverticulitis. This event may represent the first manifestation of an otherwise previously unidentified colonic diverticulosis. The clinical presentation of acute diverticulitis varies according to the extent and severity of the disease process, which encompasses a broad spectrum of manifestations from mild self-limiting episodes to acute abdomen. In classic cases, patients report constipation and abdominal pain involving the left lower abdominal quadrant. Abdominal or perirectal fullness, or 'mass effect' may be present, and low-grade fever and leucocytosis are common. Alternative diagnoses for lower abdominal pain must be considered. The severity and progression of the disease is presumably associated with the depth of the perforation. A clear-cut diagnosis and evaluation of complications requires the use of imaging techniques (see further). In this context the Hinchey, Buckley, and Ambrosetti classifications further sub-classify acute diverticulitis on the basis of computerised tomography (CT) scan findings.[20–25]

1.1.6 Statement (EL 4 – RG C): A small subset of patients with diverticulosis may develop segmental colitis associated with diverticulosis (SCAD).

Consensus levels of agreement: A+ 66%; A 25%; A− 9%.

SCAD is a recently defined clinical entity with specific macroscopic and microscopic features (see further) characterised by chronic, sometimes relapsing, mucosal inflammation in an area with presence of diverticula – usually the sigmoid-descending colon, sparing the proximal and rectal colon. In a recent meta-review the prevalence of SCAD in patients with diverticulosis ranged from 0.3–1.3%, with a male prevalence and a mean age of 63.6 years (range 26–87). The most common presenting symptoms were rectal bleeding, diarrhoea and abdominal pain. Many of these patients showed a benign course even with spontaneous resolution, or responded to 5-aminosalicylates or steroids.[26]

1.2 Is the prevalence of DD increasing in Western countries?

1.2.1 Statement (EL 2c – RG B): The prevalence of diverticulosis and DD is increasing in Western countries in parallel with increased life-expectancy.

Consensus levels of agreement: A+ 72%; A 19%; A− 9%.

DD is one of the most frequently reported findings diagnosed during colonoscopy, particularly in elderly patients.[27] Two studies carried out in Oxford on asymptomatic volunteers reported an increasing prevalence of diverticulosis with age, with a prevalence of 34.9% in those over 60 years of age.[28,29] A study conducted in Edinburgh estimated that the incidence of DD in patients referred for barium enema was 1.55 per 1000 population. There was a female predominance and increased occurrence with age, with an incidence rate of 5.74 per 1000 population in those over 75 years.[30] From these studies is possible to conclude that the prevalence of DD is increasing in the Western world largely because the population is getting older.

1.3 Does DD have any clinical and economic relevance?

1.3.1 Statement (EL 2c – RG B): DD is a relevant cause of hospitalisation and not devoid of mortality, particularly in elderly patients.

Consensus levels of agreement: A+ 56%; A 28%; A− 13%; D− 3%.

There are no studies reporting on mortality for diverticulosis. Mortality associated with DD, acute diverticulitis and complicated DD has been reported in case series, national audits and population-based data.[31] The age-standardised mortality rates associated with a death certificate diagnosis of DD using the International Classification of Diseases, Ninth Revision (ICD-9), codes for England failed to show any consistent change in rates from 1979–1999.[32] The rates were consistently higher among females than males. Data from the United States National Inpatient Sample (NIS) database reported that hospital mortality related to acute diverticulitis decreased from 1.6% to 1.0% from 1998 to 2005,[33] and surgical mortality decreased from 5.7% to 4.3% during the same time period.[30] Mortality associated with DD was substantially higher among females than males.

There is still little information in the scientific literature on the economic impact of DD. A retrospective study performed in a large UK department, aimed at reviewing costs for inpatient and outpatient investigations, treatment and hospitalisation of all patients treated for DD during one financial year in a district hospital.[34] A total of 148 patients were treated; 83 of them were admitted for more than one day, 55 of whom were emergency admissions. The study shows that DD poses a major clinical problem (for instance, inpatient mortality rate was 6%, and peri-operative mortality 26.3%) for a surgical department, showing considerable financial implications, with an impact on the global budget as high as 5.3% of the annual resources for general surgery.

An almost identical study has been conducted more recently in Italy,[35] taking into consideration the clinical workload and the financial impact of DD in a large university hospital over a seven-year period. A total of 738 patients were treated and 840 hospital discharge records were reviewed. As many as 193 surgical operations were performed, with a total cost of this activity equal to 0.2% of the total hospital budget.

1.4 What are the time trends of hospital admission and surgery rates for DD?

1.4.1 Statement (EL 2c – RG B): During the last 10–20 years there has been an increasing rate of hospital admission for diverticulitis.

Consensus levels of agreement: A+ 42%; A 32%; A− 10%, − 3%, D 3%; D+ 10%.

The occurrence of acute diverticulitis has been reported in three studies using data from the United States NIS database and a study from the UK.

The first of these studies reported a 26% increase in admissions coded as acute diverticulitis from 1998–2005 (120,500 to 151,000 admissions).[33] The greatest increase in admissions was in the age ranges of 15–44 and 45–64 years. A further study of NIS data from 1998–2005 reported an overall age-adjusted increase in hospital admissions from 61.8 per 100,000 to 75.5 per 100,000 hospitalisations, with equal gender and age distribution.[36] A further study of USA NIS data from 2002–2007 reported a 9.5% increase in emergency admissions over this time period but a smaller increase involving younger age groups.[37] Finally, in a study from the UK[38] relying on a database from 1996–2006, the primary outcomes examined were 30-day overall and one-year mortality, 28-day readmission rates and extended length of stay beyond the 75th percentile (median inpatient stay six days). In the time period considered, 560,281 admissions with a primary diagnosis of DD were recorded in England. The national admission rate increased from 0.56 to 1.20 per 1000 population/year. As many as 232,047 (41.4%) were inpatient admissions, of which 55,519 (23.9%) were elective and 176,528 (76.1%) were emergency. Surgery was undertaken in 37,767 (16.3%). Thirty-day mortality was 5.1% ($n = 6735$) and one-year mortality was 14.5% ($n = 11{,}567$). Increasing age, comorbidity and emergency admission were independent predictors of all primary outcomes. There are few population-based data focusing on individual complications. A study from Northern Finland reported an

increase in the prevalence of perforated diverticular disease from 2.4 per 100,000 in 1986 to 3.8 per 100,000 in 2000.[39] A further study, using UK primary care data to identify cases of perforated diverticular disease, reported a two-fold increase (incidence risk ratio (RR) 2.18, 95% confidence interval (CI) 1.79–2.95) in incidence rates from 1990–2005.[40]

1.5 What is the time trend for mortality in severe/complicated DD?

1.5.1 Statement (EL 2c – RG B): Mortality in perforated disease remains elevated, due to the high rate of relevant comorbidity.

Consensus levels of agreement: A+ 48%; A 32%; A− 10%; D+ 10%.

The excess mortality associated with perforated DD compared to the general population was reported in a study from the General Practice Research Database. This study reported a six-fold increase in the mortality (hazard ratio (HR) 5.63, 95% CI 4.68–6.77) of patients diagnosed with perforated diverticular disease in the first year of follow-up. The greatest absolute risk was in those with the highest comorbidity.[40]

A subsequent study detailing the excess mortality following a diagnosis of stricture or fistula demonstrated that patients with diverticular stricture had a 2.4-fold higher mortality rate compared to the general population and this was limited to the first year after diagnosis. In comparison, those with a fistula had a 2.6-fold higher mortality, with a 41% increase in mortality in subsequent years.[41] The authors stated that a possible reason for this could be the excess comorbidity and the increased age of patients with diverticular fistulae. As recalled above, mortality associated with DD is substantial, although it appears to be decreased for acute diverticulitis (at least in the USA); conversely, patients with perforated DD have a significant one-year mortality along with a substantial excess mortality compared to the general population.

1.6 Are there any relevant lifestyle risk factors for symptoms development?

1.6.1 Statement (EL 4 – RG C): The analysis of the literature does not provide sufficient evidence to establish a clear-cut link between the absence of physical activity, and lower fibre, nut, corn, and popcorn consumption, or smoking with increased risk of DD. Increased body mass index (BMI) is a consistent risk factor for complicated DD.

Consensus levels of agreement: A+ 58%; A 16%; A− 23%; D+ 3%.

Lifestyle factors, along with aging, are considered to be major risk factors for the development of diverticulosis and its complications, diverticulitis and diverticular bleeding. Approximately 40% of the adult population in Western countries is estimated to have diverticulosis, and diverticulitis and diverticular bleeding are among the most common gastrointestinal indications for hospital and medical visits.[27] The following lifestyle factors have been evaluated for their risk on symptoms development: physical activity, diet (including fibre content and nut, corn and popcorn consumption), smoking habit and obesity. Strate et al.[42] studied physical activity and DD during an 18-year follow-up. Men in the highest quintile of vigorous physical activity had a 25% risk reduction of diverticulitis, and a 46% risk reduction of diverticular bleeding when compared to men who exercised the least. As to diet and risk of hospitalisation for DD in the European Prospective Investigation into Cancer and Nutrition (EPIC) Oxford study, a cohort of 47,033 healthy individuals were followed-up for five years. High fibre intake (25.5 g/day in women and 26.1 g/day in men) was associated with a relative risk of 0.58 (95% CI 0.46–0.73) when compared to those with the lowest fibre intake (<14 g/day).[43]

In a retrospective study, 56 patients admitted with SUDD were later questioned regarding their fibre intake. Those with a high fibre intake (>25 g/day) were significantly less likely to have had symptoms (19% vs 44%) or diverticular complications (6.5% vs 32%).[44] In a study of 47,000 men followed for 18 years as part of the Health Professionals Follow-up Study,[45] consumption of nuts, corn or popcorn did not increase the risk of diverticulitis or diverticular bleeding. In fact, men who consumed nuts or popcorn at least twice weekly were at a lower risk of diverticulitis than those who consumed these foods less than once a month (RR 0.80; 95% CI 0.63–1.01; p for trend < 0.04 for nuts and 0.73; 95% CI, 0.56–0.92; p for trend < 0.007 for popcorn). In 36,000 women enrolled from 1997–2008 in the Swedish mammography cohort, past and current smokers had a 24% increased risk of hospitalisation for DD when compared to non-smokers, and no significant dose response was found.[46] In a male Swedish cohort of 7500 men followed for up to 28 years, current smokers had a RR 1.89 (95% CI 1.15–3.10) for perforated disease compared to non-smokers.[47] In the EPIC-Oxford cohort, individuals who smoked >15 cigarettes a day had a relative risk of 1.34 and those who smoked >15 cigarettes a day a relative risk of 1.86 of hospitalisation for DD compared to non-smokers.[43] Rosemar et al.[47] followed a cohort of 7500 men in Sweden for 28 years: men with a BMI > 30 had a four-fold increased risk of diverticulitis compared to men with a BMI of 20–22.5.

Strate et al.[48] followed 47,000 men for 18 years: men with a BMI > 30 had 78% higher risk of diverticulitis

and a threefold increased risk of diverticular bleeding compared to men with a BMI < 21.

1.7 What is the long term outcome of DD?

1.7.1 Statement (EL 4 – RG D): In general, DD has a favourable long-term outcome with a very low incidence of complications. Symptomatic disease, acute diverticulitis and complicated DD represent distinct clinical entities among groups.

Consensus levels of agreement: A+ 42%; A 42%; A− 16%.

The natural history of DD is largely unknown. Most studies are retrospective, and treatment recommendations are not based on recent literature. There is only one prospective, long-term study assessing the development of complications in patients with symptomatic diverticular disease.[18] A total of 163 patients were followed up for an average of five years. After the initial diagnosis, two patients (1.7%) presented with an episode of diverticulitis, which was treated conservatively. Only one patient (0.8%) required surgery for chronic symptoms; 97% had mild or no symptoms after a median follow-up of 66 months. The study showed that SUDD presents with a long-term benign course, and a very low incidence of subsequent complications.

1.8 Does DD predispose to colon cancer?

1.8.1 Statement (EL 4 – RG C): DD does not increase the risk of colon cancer.

Consensus levels of agreement: A+ 89%; A 7%; A− 4%.

It has been hypothesised that patients with DD – especially elderly patients – have an increased risk of colon cancer. Clear-cut evidence of this association is limited by the high prevalence of the two conditions, as the association may be just determined by a high chance of having both diseases. Data from a retrospective Swedish study[49] showed an association between diverticulosis and the risk of colon cancer with a 1.8 relative risk, 95% CI 1.1–2.7, for both genders and in all age groups. This risk was also present two or more years after the first hospital discharge, in relation to diverticulosis. Analysing the data by anatomical region, this risk seemingly existed only for the left colon. A subsequent retrospective study conducted on 288 patients treated for diverticulitis, with a mean follow-up of 12 years, showed a low prevalence of both colorectal cancer and colonic adenomas compared to expected lifetime risk.[50] Finally, a recent case-control study[51] performed in Sweden, which comprised 41,037 patients with colon cancer diagnosed between 1992–2006, reached the conclusion that the increased risk of colon cancer previously reported was most likely due to confounders related to indication and/or surveillance bias.

2. Pathophysiology of diverticular disease

2.1 Is a low fibre diet a key factor in the development of diverticulosis?

2.1.1 Statement (EL 2b – RG C): Low fibre diets play a pathogenetic role in the development of diverticulosis.

Consensus level of agreement: A+ 38%; A 22%; A− 28%; D− 6%; D+ 6%.

Lifestyle factors are considered key elements for the development of diverticulosis and its complications. Painter and Burkitt in 1971 reported for the first time that a low-fibre diet played a major role in the pathogenesis of diverticulosis.[52] Accordingly, it was observed that DD was common in Western societies where fibre intake is low, but was rare in geographical areas where fibre intake is high (i.e. in Africa and Asia). Also, it was noted that DD developed with the adoption of a Western lifestyle.[29] The low-fibre hypothesis is further supported by case-control studies in vegetarians. Accordingly, diverticulosis was less prevalent in 56 vegetarians, compared to 264 non-vegetarian controls, who on average consumed less fibre (21.4 g/day vs 41.5 g/day; $p < 0.001$).[29] In addition, in a large prospective cohort of 47,033 subjects in England, vegetarians were 31% less likely to be hospitalised for DD compared with meat eaters.[43]

Despite this evidence, the low-fibre hypothesis has been challenged.[1] In non-vegetarian subjects, fibre intake was not different between those with diverticulosis and those without (21.8 vs 22.1 g/day, respectively).[29] In addition, in a recent cross-sectional study, Song et al. found no association between fibre intake and diverticulosis.[53] However, the most surprising outcome has been reported in another recent study by Peery et al. who assessed the prevalence and risk factors of diverticulosis in 2104 subjects undergoing colonoscopy. Data analysis showed that a high fibre intake was positively associated with the presence of diverticulosis (prevalence ratio = 1.30; 95% CI, 1.13 – 1.50).[54] Although these studies seem to disprove the original fibre hypothesis, they should be taken with caution. For instance, the study by Song et al.[53] was performed in Korea. Most colonic diverticula in Asian subjects are right-sided and the pathogenesis of these forms is likely different from the left-sided diverticulosis described in Western populations. In addition, the cross-sectional design of the study by Peery et al.[54] who carried out a short term investigation of dietary habits before colonoscopy, failed to identify clear-cut pathogenetic elements.

Incontrovertible evidence in favour of a high fibre diet in the treatment of diverticular disease is still lacking, although guidelines and position papers[12,13,55] recommend a high-fibre intake for the prevention of diverticulosis and diverticulitis, and in the treatment of symptomatic DD.

2.2 Do changes in colonic motility play a role in the pathogenesis of diverticulosis?

2.2.1 Statement(EL 3a – RG C): Changes in colonic motility represent a relevant pathogenetic factor in intestinal diverticulosis.

Consensus levels of agreement: A+ 45%; A 24%; A− 21%; D 7%; D+ 3%.

Increased resting and stimulated (meal, anti-cholinesterase agents) colonic intraluminal pressures and abnormal segmental and propagated motor activity have been detected in patients with diverticular disease, and are thought to contribute to the development of diverticula.[56–58] Indeed, intraluminal pressure is low in the right colon, and other factors, including a genetic component and structural wall alterations may be more strongly involved in the pathogenesis of diverticulosis in Asian populations.[59] The mechanisms underlying motor dysfunction in patients with diverticulosis remain poorly investigated. Neurotransmitter abnormalities in colonic specimens obtained from surgical resections have been described in patients with DD.[60–62] Bassotti et al.[63] found a marked decrease in the number of interstitial cells of Cajal and glial cells in full thickness colonic specimens of 39 patients with diverticulosis compared to control colonic specimens. These changes occurred in the absence of significant quantitative abnormalities in the neurons of the submucous or myentric plexuses. More recently, an altered pattern of factors involved in colonic smooth muscle contractility has been reported in patients with DD.[64] Taken together, these findings support a role for colonic neuromuscular dysfunction in the pathogenesis of left-sided diverticulosis and suggest the involvement of neuroanatomical changes at the neuromuscular gut wall level.[65]

2.3 Do changes in the connective tissue of the colonic wall play a role in the pathogenesis of diverticulosis?

2.3.1 Statement. (EL 3b – RG C): Changes in the connective tissue of the colonic wall contribute to the pathogenesis of colonic diverticulosis.

Consensus levels of agreement: A+ 47%; A 22%; A− 13%; D− 6%; D 6%; D+ 6%.

The concept that colonic wall abnormalities lead to increased rigidity and reduced resistance of the colon with subsequent diverticula formation has been introduced a long time ago.[66] The involvement of connective tissue is supported by indirect evidence from earlier literature showing a high prevalence of diverticulosis in the Ehlers-Danlos[67] and Marfan syndromes.[68] In diverticulosis, attention has been directed to two major extracellular matrix components, elastin and collagen. Elastin is increased only in the longitudinal muscle layer, with subsequent thickening of the colonic wall.[69] Collagen fibrils are smaller and more densely packed and show higher cross-linking, leading to increased rigidity of the wall.[70,71] It has been hypothesised that the progressive elastosis of the taenie is at least partly attributable to the increased amino acid proline largely found in Western diets and used as additive by food industries.[69]

2.4 Do changes in colonic motility and sensitivity play a role in the development of abdominal pain in SUDD?

2.4.1 Statement (EL 4 – RG C): Changes in colonic motility and sensitivity play a potential role in the development of abdominal pain in SUDD.

Consensus levels of agreement: A+ 53%; A 17%; A− 13%; D− 3%; D 7%; D+ 7%.

Although colonic diverticulosis has been defined as a painless change due to aging,[72] up to 20% of subjects with diverticula experience abdominal pain.[73] As diverticulosis and IBS are both highly incident conditions, patients with symptomatic DD could well be patients with IBS in whom diverticulosis overlaps. Nonetheless, there are some clinical-epidemiological features that may help distinguish those with 'true' IBS from those with diverticula associated with 'IBS-like' symptoms. First, IBS incidence peaks in the second and third decades of life and declines thereafter, whereas diverticulosis increases with age, particularly after 60 years of age.[74] As a consequence, the overlapping conditions are predominantly present in middle-aged or older patients. Second, IBS is more frequent in females while diverticulosis affects equally males and females.[17] Third, differently from IBS, pain is more often localised in the lower left quadrant, and patients suffer more frequently from long-lasting (>24 h) pain, sometimes for weeks, with longer periods of symptomatic quiescence.[6,73] Fourth, only 15% of patients with DD fulfil the Rome I criteria for IBS.[73] This is mainly due to the fact that, differently from IBS, abdominal pain caused by DD is less frequently relieved by the passage of air or stool.[73]

Although IBS and symptomatic DD could be different disorders, they share some of the mechanisms believed to be important for symptom generation. These include abnormal motor function and reduced threshold for perception of visceral sensitivity (referred to as visceral hypersensitivity). Patients with SUDD

displayed increased duration of rhythmic, low-frequency, contractile activity, particularly in the segments bearing diverticula.[58] Colonic visceral pain perception in response to luminal distension was evaluated in patients with SUDD or asymptomatic diverticulosis, compared to healthy controls.[75] Only SUDD patients displayed an increased pain perception not only in the sigmoid colon with diverticula, but also in the unaffected rectum.[75]

2.5 Are changes in environmental factors (e.g. microbiota) and low-grade inflammation important in the development of abdominal pain in SUDD?

2.5.1 Statement (EL 4 – RG D): Changes in environmental factors (e.g. intestinal microbiota) and low-grade inflammation partly play a role in the development of abdominal pain in subsets of patients with SUDD.

Consensus levels of agreement: A+ 29%; A 13%; A− 26%; D− 10%; D 6%; D+ 16%.

Although dysbiosis and low-grade immune activation are known to play a role in the pathophysiology and development of pain in patients with IBS,[76,77] a similar paradigm for symptomatic DD has yet to be demonstrated; there is nevertheless recent evidence that these patients present increased colonic mast cells in all the layers of the colonic wall, which may contribute to pain development (78). Colonic diverticula are pouches of the colonic wall, which may predispose to faecal entrapment and faecolith formation. The putative involvement of intestinal microbiota and low-grade inflammation in symptomatic DD is based on the hypothesis that trauma caused by faecoliths on the thin diverticular wall leads to epithelial breakdown and bacterial translocation which may eventually lead to diverticulitis. In this context, pain is an alarm response to the activity of immune cell reaction to the bacterial translocation evoked by a number of different mediators, which are released by inflammatory cells acting on sensory receptors located on sensory fibres conveying information to the brain. Examination of mucosal biopsies from symptomatic DD showed low-grade inflammation (i.e. lymphocytes and neutrophils) despite a normal mucosa, apart from diverticula, at colonoscopy.[79,80] Post-inflammatory gut dysfunction following acute infectious gastroenteritis (post-infectious IBS) or in patients during periods of remission of ulcerative colitis is a well characterised phenomenon.[81] Similarly to these conditions, a recent study showed that patients with diverticulitis were 4.6 times more likely to develop IBS-like symptoms over the observation period compared to matched controls.[82]

3. Diagnosis of DD

3.1 Is diverticular disease normally associated with histological changes in the mucosa surrounding diverticula?

3.1.1 Statement (EL 1b – RG A): The vast majority of patients with DD have no evidence of histological changes in the mucosa surrounding diverticula (excluding diverticular lesions and their complications).

Consensus levels of agreement: A+ 88%; A 6%; A− 6%.

The histopathological diagnosis of lesions associated with DD is a difficult field, due to the presence of alterations still needing a precise definition. While on surgical specimens the diagnosis (and also the differentiation from Crohn's disease or ulcerative colitis) is relatively simple, there are still numerous controversies on diagnostic and classification criteria to be used on biopsy material.[83,84]

3.2 Is SCAD a defined pathological entity?

3.2.1 Statement (EL 1b – RG B): SCAD is a defined pathological entity characterised by a chronic inflammatory response involving the inter-diverticular mucosa of a colonic segment involved. The rectum and the right colon are spared from inflammation. Hence, SCAD can be considered a separate pathological entity.

Consensus levels of agreement: A+ 75%; A 13%; A− 6%; D− 3%; D+ 3%.

Based on this definition it is also possible to suggest a correct terminology. Different synonyms are used in the literature to refer to this disease, such as segmental colitis, sigmoid colitis, crescentic colitis, diverticulosis-associated colitis, diverticular disease-associated segmental colitis, focal active colitis. However, none of these definitions clearly identifies this condition nor is any one definition accepted worldwide. DD associated with SCAD is a condition of chronic colitis localised in the colonic segment presenting diverticula. SCAD involves the interdiverticular mucosa.[83–85]

3.2.2 Statement (EL 1b – RG B): The spectrum of histological lesions associated with SCAD is variable. It includes mild non-specific inflammation and inflammatory bowel disease (IBD)-like changes, making differential diagnosis difficult.

Consensus levels of agreement: A+ 88%; A 8%; A− 3%.

3.2.3 Statement (EL 2a – RG B): Limitation of mucosal lesion to the diverticular segment is the most important diagnostic criterion for SCAD (rectal sparing). Rectal and descending colon biopsies are required to distinguish SCAD from IBD.

Consensus levels of agreement: A+ 91%; A 6%; A− 3%.

A correct approach to biopsies in terms of sampling and number of specimens taken is of paramount importance. As a first step, it is important to take biopsies (minimum four samples) on the borders of the diverticula and in the apparently normal adjacent mucosa as well as biopsies in both the colon proximal to the diverticular area and the rectum. The second step is the evaluation of different morphological aspects, among which the most important is the differential diagnosis with IBD; two elements are fundamental for the diagnosis: (a) crypt architecture, because the internationally accepted guidelines stress crypt architectural distortion as one of the most important features in the differential diagnosis between IBD and non-IBD colitis. However, crypt distortion can be observed also in the context of diverticular disease where it may be associated with cystic dilatation of the crypts; (b) lamina propria cellularity: this morphological change is extremely variable, from a substantially nonspecific inflammation composed of plasma cells, lymphocytes, rare eosinophils, to an active inflammation with crypt aggression and complete crypt abscesses. On the basis of the above morphological changes it is possible to consider two different categories. The first category comprises the majority of cases in which the discovery of diverticula represents an incidental finding, in the absence of specific symptoms; in such cases the fundamental element – provided that a correct biopsy sampling is made – is the presence of cystically dilated crypts with mild inflammatory infiltrate in the lamina propria and no cryptitis. Another important feature is the absence of basal plasmocytosis, a critical finding in the differential diagnosis with IBD. The second category includes, as a rule, symptomatic cases in which the histological lesions may resemble or even be indistinguishable from those of ulcerative colitis. For these cases, the correct sampling is the main tool for the differential diagnosis (i.e. rectal sparing).

Another challenging point is represented by the differential diagnosis with Crohn's disease. A Crohn-like reaction may be a localised reaction to diverticulitis alone. Pathologists should be cautious before making a diagnosis of sigmoid colonic Crohn's disease in the context of diverticulosis. Caution is required before making the diagnosis of coexistent conditions, in the absence of collateral evidence to support a diagnosis of Crohn's disease.[85–89]

3.4 Is a standardised classification of colonoscopic findings useful in DD?

3.4.1 Statement (EL 5 – RG D): In the attempt to standardise colonoscopy findings, the following parameters may be considered:

a. extent: the extent of diverticular disease (limited to or prevalent in the sigmoid colon or extended to the proximal colon)
b. grading of wall rigidity: a three-grade scale for the evaluation of wall rigidity (absent, present, inability to pass strictures of the colonic segment bearing diverticula)
c. mucosal abnormalities: presence/absence of mucosal abnormalities.

Consensus levels of agreement: A+ 33%; A 13%; A− 30%; D− 7%; D+ 17%.

In clinical practice the endoscopic findings related to DD are not standardised nor is specific literature available to this regard.

3.5 Is colonoscopy necessary in acute lower GI bleeding of suspected diverticular origin?

3.5.1 Statement (EL 2a – RG B): A prompt colonoscopy (i.e. within 12–24 h) is mandatory for diagnosis and to direct therapy. Massive bleeding should be managed with selective angiography.

Consensus levels of agreement: A+ 25%; A 44%; A− 28%; D− 3%

Patients with severe lower gastrointestinal bleeding (LGIB) should undergo clinical evaluation and stabilisation as done with upper-GI bleeding. Colonoscopy is useful in the diagnosis and treatment of diverticular bleeding. Colonoscopy is recommended in the early evaluation of LGIB. The procedure should be performed after preparation of the colon by using polyethylene glycol-based solutions.

Colonic preparation facilitates endoscopic visualisation, improves diagnostic yield, and may improve the safety of the procedure by decreasing the risk of perforation. The diagnostic yield of a colonoscopy ranges from 48–90%. The timing of colonoscopy after initial presentation varies among studies and ranges from 12–48 h. Early colonoscopy has been associated with shorter hospital stay. Several endoscopic treatment modalities can be used to achieve haemostasis when a source of LGIB is identified at the time of colonoscopy. In a large prospective study of urgent colonoscopies for diverticular haemorrhage, treatment of bleeding and non-bleeding visible vessels and adherent clots achieved haemostasis without recurrences. Endoscopic metallic-clip placement also serves as an alternative treatment for diverticular haemorrhage. Angiographic or surgical therapy may be necessary in cases of massive bleeding from a diverticulum not amenable to endoscopic treatment.[90–95]

3.6 Can abdominal ultrasonography (US) be performed as first line imaging when suspecting acute diverticulitis (AD) and abdominal septic complications?

3.6.1 Statement (EL 1b – RG A): US can be used as a sensitive and specific diagnostic technique to detect acute diverticulitis and its septic abdominal complications, provided that the procedure is carried out by an expert investigator.

Consensus levels of agreement: A+ 9%; A 41%; A− 22%; D− 9%; D 6%; D+ 13%

US can identify the five layers that make up the intestine, assess bowel wall thickening, and its relationship with mesenteric fat, vessels and other adjacent organs. Moreover perintestinal fluid and collections or abscesses can be also visualised.

Although US is able to identify colonic diverticula[96,97] it cannot be considered the first line technique in diagnosing or ruling out diverticulosis because of the lack of appropriate studies on its performance.[98]

AD can be detected by ultrasound[97,99–103] and so can its complications (i.e. abscesses and fistulae),[98,99] provided that the procedure is carried out by an expert investigator.

Although a systematic review[102] showed that US provides the best evidence for the diagnosis of diverticulitis, recent evidence from a multicentre Dutch study (Optima Study)[104] comparing US and CT scan accuracy of unselected patients, referred for acute abdominal pain to the emergency department, shows that CT is more sensitive than US (81% vs 61%) in detecting AD. Thus a conditional strategy with US as first-line method immediately followed by CT, whenever inconclusive or doubtful, seems to represent probably the most effective approach.

3.7 Which imaging test should be considered as the best method for colonic examination when the clinical question is to confirm or rule out DD?

3.7.1 Statement (EL 3b – RG C): Colonoscopy and CT colonography (CTC) must be considered the first-line test to diagnose or rule out colonic diverticula. The choice for CTC or colonoscopy depends on the patient's age, risk factors, clinical status and preference.

Consensus levels of agreement: A+ 35%; A 23%; A− 26%; D− 3%; D 13%.

3.7.2 Statement (EL 3a – RG B): Diagnostic accuracy of double contrast barium enema (DCBE) for DD is similar to that of CTC. Use of DCBE should be considered only if CTC is unavailable.

Consensus levels of agreement: A+ 41%; A 22%; A− 34%; D+ 3%

A correct diagnosis of DD is challenging for clinicians. Patients' symptoms and laboratory findings are unspecific and overlap with other gastroenterological conditions (e.g. IBS) and, in young women (<40 years), also with gynaecological disorders.[11]

Thus, imaging tests, and particularly CTC and/or colonoscopy represent the best diagnostic methods. The choice of the first-line imaging examination depends mostly on the patient's age, risk factors, clinical status and preference, but also on imaging availability and local expertise.[105] In elderly individuals, especially if frail and with potential contraindication to colonoscopy and sedation (e.g. patients with concurrent severe chronic cardiopulmonary disease, in anticoagulant therapy, etc.), a less invasive approach using CTC might be preferred. On the other hand, in younger patients where symptoms might be related also to colonic inflammatory changes, colonoscopy should be the first-choice test.

DCBE can effectively diagnose diverticulosis,[106,107] similarly to CTC,[108] the latter being preferred because of higher patient compliance,[109] shorter examination time, fewer complications,[110] and lower radiation exposure.[111] It is noteworthy that a 3–5 mSv exposure, which is still considered a quality standard in CTC,[112] will soon become obsolete with the advent of new technologies (i.e. first- and second-generation iterative algorithms). Iterative algorithms will reduce overall exposure to less than 1 mSv.[113,114] Sub-mSv exposure should be compared with DCBE, which usually delivers a rough average of 7–9 mSv.[111] CTC also reveals therapeutically significant extra-colonic findings 'so that it is beginning to seem rather irresponsible to continue to offer routine DCBE examinations'.[115] The only true limitation of CTC is still the limited access in small centres and peripheral hospitals. This is the reason why today DCBE is still considered applicable, but only when CTC is unavailable.

US does not play a major role in the first diagnostics approach, since it has many limitations in detecting (and conversely, in excluding) colonic diverticula, not only in the right colon (as expected), but also in the sigmoid colon, particularly when the lumen is filled with stools.[103]

Magnetic resonance colonography (MRC) is an exciting potential alternative, particularly interesting because of the lack of ionising radiations.[116] Preliminary results, based on a limited number of studies, are promising.[117] However, MRC needs further technical refinements, since the examination is much longer than CTC, and MRC is more prone to motion artefacts, which is relevant in elderly patients. Thus, at present, MRC cannot be considered readily feasible for widespread use within the radiological community.

3.8 Which imaging test should be considered as the best method for colonic examination in case of patients presenting with acute abdominal symptoms and clinical suspicion of diverticulitis?

3.8.1 Statement (EL 1b – RG A): Contrast-enhanced computerised tomography (CE-CT) should be considered as the first-line colonic examination since it offers a more comprehensive evaluation of uncomplicated and complicated forms; CE-CT can also be used to guide therapeutic interventions.

Consensus levels of agreement: A+ 58%; A 23%; A− 13%; D− 3%; D 3%.

3.8.2 Statement (EL 4 – RG C): The use of DBCE using water-soluble iodinated contrast agent should be strongly discouraged because of its poor diagnostic performance.

Consensus levels of agreement: A+ 69%; A 13%; A− 9%; D− 3%; D 3%; D+ 3%.

3.8.3 Statement (EL 4 – RG D): The use of MRC in diagnosing diverticulitis is not sustained by robust data. Feasibility seems to be limited by the difficult access to MR scanners in emergency departments.

Consensus levels of agreement: A+ 67%; A 15%; A− 9%; D− 3%; D 3%; D+ 3%.

In case of a patient presenting in an acute setting, with clinical signs and symptoms highly suspicious for an acute inflammatory process (fever, leucocytosis), CE-CT should be considered as the first-line colonic examination.[23,102–118] CE-CT examination, obtained with multi-detector technology,[120] offers a more comprehensive evaluation of uncomplicated and complicated forms, particularly in case of perforations with free peritoneal air.[121] The severity of diverticulitis on CT scan is also statistically predictive of the risk of medical treatment failure during the acute phase and of the chances of bad secondary outcome after a successful medical treatment of the first episode.[122] Additional benefits of CT imaging include guiding therapeutic interventions, and providing an alternative diagnosis in patients without diverticulitis.[123,124]

US has a similarly high (around 90%) diagnostic accuracy, but only in SUDD.[23,118] A conditional strategy where CT scan follows a preliminary negative or inconclusive US might be advantageous, because the number of CT exams can be reduced by about 50%.[125,126]

The role of MRC in diagnosing acute diverticulitis is questionable since no robust data have been published in the literature.[127,128] Practical feasibility seems also to be limited by the difficult access to MR scanners in emergency departments.

4. Medical and surgical treatment of diverticular disease

4.1 What are the measures and treatments to prevent the progression of diverticulosis to DD?

4.1.1. Statement (EL 2b – RG B): There is no rationale for drug treatment of asymptomatic diverticulosis, but there are limited indications to suggest an increase in dietary fibre.

Consensus levels of agreement: A+ 55%; A 36%; A− 9%.

4.1.2 Statement (EL 2c – RG B): There is a possible relationship between low dietary fibre intake, particularly insoluble fibre, and the development of DD. A high daily fibre intake is recommended to reduce the risk of DD.

Consensus levels of agreement: A+ 29%; A 26%; A− 29%; D− 10%; D 0%; D+ 6%.

There is no evidence that pharmacological treatment is useful in asymptomatic diverticulosis.

Crowe et al.[43] documented, instead, that vegetarian and high fibre diets are associated with a lower risk of admission to hospital or death from DD. Similar results have been obtained by Aldoori et al.[129] who showed a protective effect of a high fibre diet on the occurrence of symptomatic DD. Evidence indicates that insoluble fibre is strongly associated with lower risk of DD; this association was particularly strong for cellulose.[129,130]

4.1.3 Statement (EL 2c – RG B): There is no rationale to avoid in the diet the consumption of nut, corn and popcorn to prevent diverticular complications.

Consensus levels of agreement: A+ 73%; A 12%; A− 9%; D− 3%; D 3%; D+ 0%.

In a large, prospective study, nut, corn, and popcorn consumption did not increase the risk of diverticulosis or diverticular complications. The exclusion from the diet of these foods to prevent diverticular complications should not be recommended.[45]

4.1.4. Statement (EL 2b – RG B): Regular treatment with aspirin or NSAIDs carries the potential risks of diverticular complications.

Consensus levels of agreement: A+ 28%; A 31%; A− 25%; D− 0%; D 0%; D+ 16%.

Several controlled studies have examined the adverse effects of NSAIDs and aspirin in DD. These studies showed that these drugs represent a significant risk factor for the development of symptoms, acute diverticulitis, perforation and diverticular bleeding.[131]

A 10-day prospective randomised control trial (RCT) reported the development of AD in one subject

taking ibuprofen vs none in the placebo group.[132] A large prospective cohort study found that NSAID users were significantly more likely than non-users to develop symptomatic diverticular disease (RR: 1.5; 95% CI: 1.1–2.1);[133] in addition, seven case–control studies found that among patients with complicated diverticular disease (i.e. perforation, fistula formation, pericolic abscess, peritonitis) there was a larger use of NSAIDs compared to controls with no disease, with odds ratios (ORs) ranging from 1.8–11.2.[134–140]

The role of aspirin in acute diverticulitis is more controversial. Three case-control studies showed that its use was not significantly different in patients with perforated colonic DD vs patients with no disease[139–141] whilst a large prospective cohort study showed that its regular use (≥2 times/week) was associated with an increased risk for AD.[138]

The role of aspirin and NSAIDs in diverticular bleeding has been largely investigated. Two prospective population-based studies have shown that regular use of aspirin, even at low doses, and NSAIDs are significant risk factor for diverticular bleeding.[138,142] Several case-control studies, have consistently shown that the use of low-dose aspirin, NSAIDs and antiplatelet drugs, along with hypertension, are significant risk factors for diverticular bleeding.[143–147]

4.1.5 Statement (EL 2b – RG B): There is limited evidence that opiate analgesics and oral corticosteroid use is associated with an increased risk of diverticular perforation.

Consensus levels of agreement: A+ 29%; A 39%; A− 16%; D− 3%; D 0%; D+ 13%.

The role of opiate analgesics in diverticular perforation has been assessed in four different case-control studies. The first study involved 899 cases of incident diverticular perforation and 8980 control subjects taken from the UK General Practice Research Database, and showed that the use of opiate analgesics (OR = 2.16; 95% CI 1.55–3.01) and oral corticosteroids (OR = 2.74; 95% CI 1.63–4.61) was associated with increased risk of diverticular perforation.[141] In the second study carried out in 54 patients with diverticular perforation – as case group – and 183 matched patients with diverticular disease – as control group – the use of opioids (OR 4.51; 95% CI 1.67–12.18) and corticosteroids (OR 28.28; 95% CI 4.83–165.7) was significantly associated with perforated DD.[139] The third case-control study included two different control groups and showed that opioids (ORs: 1.8 and 3.1, respectively) and corticosteroids (ORs: 5.7 and 7.8) were significantly associated with diverticular perforation.[140] The last study, carried out in rheumatic patients, showed that, independently of rheumatic diagnosis, corticosteroid treatment was strongly associated with sigmoid diverticular abscess perforation (OR 31.9; 95% CI 6.4–159.2).[148] The effect of immunosuppression and corticosteroid treatment on the development and course of AD has been investigated in a systematic review.[149] This study showed that transplanted patients or those on chronic corticosteroid therapy had a higher rate of AD than the general population and a high mortality rate associated with AD. The outcome of AD in immunosuppressed patients has been also investigated in a recent retrospective cohort study,[150] showing that after successful medical treatment for AD, immunosuppressed patients had similar recurrence rate and emergency surgery rate for AD as non-immunosuppressed ones, but a significantly higher mortality rate (33.3% vs 15.9%) after emergency surgery.

4.2 Should symptomatic uncomplicated DD be medically treated?

4.2.1 Statement (EL 2b – RG B): Fibre supplementation alone provides controversial results in terms of symptoms relief.

Consensus levels of agreement: A+ 45%; A 36%; A− 16%; D− 3%; D 0%; D+ 0%.

The therapeutic effect of fibre supplements was evaluated in several studies, although most of them were of poor quality and affected by major biases, as documented by a recent systematic review.[151] This review identified only three randomised clinical studies and one case-control study: one RCT[152] documented a significant reduction in pain and an improvement in overall clinical symptoms, another[153] was unable to document a positive effect of fibre supplement on symptoms, but only a reduction of constipation. The third study[154] showed a significant positive effect on symptoms by the administration of methylcellulose. The case-control study[44] evaluated the effect of a high-fibre diet on the development of disease complications and the need for surgery, showing a positive effect of fibre supplementation in reducing disease complications, need for surgery and the occurrence of abdominal symptoms.[155,156]

4.2.2. Statement (EL 2b – RG B): Methylcellulose and lactulose are not effective in reducing symptoms.

Consensus levels of agreement: A+ 45%; A 25%; A− 18%; D− 6%; D+ 6%.

As to the type of fibre supplement to relieve symptoms, 16 weeks of bran or ispaghula husk[153] or three months of methylcellulose[154] were no more effective than placebo in relieving symptoms, nor were 12 weeks of lactulose supplement more effective than a high fibre.[157]

4.2.3 Statement (EL 2b – RG B): Fibre plus rifaximin provide a greater prevalence of symptom-free patients compared to fibre alone.

Consensus levels of agreement: A+ 30%; A 24%; A− 24%; D− 13%; D 3%; D+ 6%.

Antimicrobial drugs have been shown to reduce H2 production and gas-related symptoms. Antibiotic therapy increases mean stool weight in subjects taking fibre, most likely for a reduced fibre degradation.[158,159] All the above findings represent a rationale for antibiotic use in DD. Both the reduction in gas production and the increase in faecal mass reduce intraluminal pressure thus improving symptoms and decreasing the enlargement and stretching of diverticula as well as the generation of new diverticula.

Conversely, among the different systemic antimicrobial drugs available, rifaximin displays all the characteristics of the ideal antibiotic.[160] It is a non-systemic agent with a broad spectrum of antibacterial action, covering gram-positive, gram-negative, aerobe and anaerobe organisms. Being virtually non-absorbed, its bioavailability within the GI tract is rather high, with intraluminal and faecal drug concentrations that largely exceed the minimum inhibitory concentration values observed in vitro against a wide range of pathogenic organisms.[161]

Rifaximin (in addition to fibre treatment) has been studied in three open[161–163] and two double-blind[164,165] RCTs, which have been analysed in detail in a systematic review[166] and have been the object of two meta-analyses.[167,168] When four prospective RCTs, including 1660 patients were included in the meta-analysis, the pooled risk difference (RD) for symptom relief was 29.0% (rifaximin versus control; 95% CI 24.5–33.6%; $p < 0.0001$) and the number needed to treat (NNT) was three. The results of these RCTs have recently been confirmed in a non-interventional study performed in a private practice outpatient setting,[169] whose results were not available at the time of the consensus conference.

4.2.4 Statement (EL 2b – RG B): Rifaximin plus fibre is more effective than fibre alone in preventing acute diverticulitis with a low therapeutic advantage.

Consensus levels of agreement: A+ 19%; A 28%; A− 31%; D− 3%; D 6%; D+ 13%

Four RCTs[161–164] only one of which double-blind, have studied the ability of rifaximin (added to fibre treatment) to prevent acute diverticulitis in patients with colonic diverticular disease. When the four prospective RCTs, for a total of 1660 patients, were included in the meta-analysis, the pooled RD in the treatment group was −2% (95% CI −3.4 to −0.6%; $p = 0.0057$) and the NNT was 50.

A more recent, multicenter, randomised, open trial[170] studied the efficacy of rifaximin (in addition to high fibre regimen) in the secondary prevention of acute diverticulitis. Recurrences occurred in 10.4% of patients given rifaximin plus fibre versus 19.3% of patients receiving fibre alone ($p = 0.033$). Despite the methodological limitations,[171] this proof-of-concept study suggests that cyclic rifaximin treatment has the potential to prevent diverticulitis recurrence in patients with colonic diverticular disease. It must be underlined, however, that further studies are needed since – at the present time – no recommendation for any non-surgical relapse preventive therapy can be made.[172]

4.2.5 Statement (EL 2b – RG B): There is no clear evidence that mesalazine alone is effective in reducing symptoms.

Consensus levels of agreement: A+ 68%; A 19%; A− 10%; D+ 3%.

The efficacy of mesalazine in reducing symptoms of diverticular disease has been investigated in two RCT multicentre, placebo-controlled and in several randomised uncontrolled studies, most of which of suboptimal methodological quality for the lack of detailed description of patient history, symptoms assessment and inclusion and exclusion criteria.[173]

The controlled studies, which included <120 patients treated with mesalazine, showed a consistent trend ($p > 0.05$) in reducing symptoms in patients treated with mesalazine, and only some secondary end-points – such as the reduction of rectosigmoid symptoms or symptoms at specific time-points – were statistically significant.[174,175]

As to the prospective randomised open studies, one of these compared different doses of rifaximin and mesalazine for 10 days/month showing that high dose mesalazine was significantly more effective than rifaximin in relieving symptoms,[176] whilst others that included patients with recent attacks of acute diverticulitis showed that mesalazine plus rifaximin for one week/month was more effective than rifaximin alone in reducing symptoms, and that mesalazine significantly prevented relapse of symptoms and major complications compared with no treatment over a five-year follow up.[177–179]

Moreover, four open long-term RCT assessed the maintenance of symptom-free remission in asymptomatic patients with previously symptomatic diverticular disease. These studies showed a comparable efficacy of the combination of mesalazine or balsalazide plus probiotics, mesalazine or probiotics alone, but only patients with recent AD episodes, in whom high dose mesalazine (800 mg twice daily, for 10 days or their combination with *Lactobacillus casei*) resulted significantly more effective than comparator drugs.[180–183] A study recently published showed that mesalazine and *Lactobacillus casei* DG treatments, particularly when given in combination, are more effective than placebo in maintaining remission of SUDD.[184]

4.2.6 Statement (EL 3b – RG C): There is no clear evidence that mesalazine reduces acute episodes of diverticulitis.

Consensus levels of agreement: A+ 53%; A 28%; A− 13%; D 3%; D+ 3%

The efficacy of mesalazine in preventing acute diverticulitis recurrence was the primary end point of two recently published RCT placebo studies. These studies included an average of 40 patients per therapeutic arm and failed to show a significant efficacy of mesalazine alone or combined with probiotics over placebo in a follow up of 12 and 24 months.[174,185]

Three open randomised studies assessed the effectiveness of mesalazine in preventing attacks and/or recurrence of AD. Except for one study, which failed to show any effectiveness of medical therapy in preventing acute diverticulitis in patients with uncomplicated DD,[176] the others, carried out in patients with recent attacks of AD, showed that seven days/month therapy with either mesalazine alone or combined with rifaximin was significantly more effective than rifaximin alone in preventing recurrences of AD in 12- and 24-month follow up, respectively.[179,186]

Currently, two additional unpublished large multicentre double-blind, placebo-controlled studies, have assessed the effectiveness of various doses of multimatrix release (MMX) mesalazine (1.2, 2.4, or 4.8 g/day) in patients with a history of AD. Both these studies failed to show a significant difference between MMX mesalazine vs placebo (except for higher doses of mesalazine in one of these) in preventing recurrent attacks of AD (primary end point of both studies), and failed to show any effectiveness of mesalazine at whatever dose in preventing surgery for AD (secondary aim) over a 24 month follow up period.[187,188]

4.2.7 Statement (EL 4 – RG C): There is insufficient evidence that probiotics are effective in reducing symptoms.

Consensus levels of agreement: A+ 53%; A 31%; A− 13%; D− 3%.

The rationale for the use of probiotics in DD relies on the hypothesis that, as a consequence of the altered colonic motility and other pathogenetic mechanisms, an intestinal bacterial overgrowth occurs, with a qualitative and quantitative change in gut microbiota. Bacterial overgrowth can impair mucosal barrier function and induce inflammatory cytokine release with localised low-grade inflammation.[14,80] These events can trigger both symptom development and disease progression towards microperforation and AD.[61,191] Restoring a normal gut microbiota by the use of probiotics could consequently influence the natural history of the disease.[190]

Although several studies have been performed aimed at evaluating the clinical efficacy of probiotics, no definitive results have yet been achieved, mainly due to the heterogeneity of the available studies.[191] Most of the studies have used probiotics in combination with topical antibiotic[192] or anti-inflammatory drugs, mainly 5-aminosalicylates (5ASAs).[184] Only two studies have tested a probiotic (*Lactobacillus paracasei*)[193] and a symbiotic mixture (containing *Lactobacillus acidophilus*[143] and *Bifidobacterium spp. 420*)[194] in patients with SUDD, documenting that the active drug was effective in reducing clinical symptoms. A different approach was used by Fric et al. who administered a non-pathogenic *Escherichia coli strain Nissle* to patients with SUDD after the third relapse of the disease, showing that the interval to the next relapse was significantly longer after probiotic treatment.[195]

4.3 Which is the best medical therapeutic strategy for AD?

4.3.1 Statement (EL 3b – RG C): Management and treatment approaches depend on severity (uncomplicated and complicated) and complexity (i.e. abscess, fistula, etc.) of the condition.

Consensus levels of agreement: A+ 30%; A 40%; A− 23%; D− 7%.

No specific RCTs evaluating this approach have been performed. With the exception of the Danish trials,[13] the available guidelines from the American College of Gastroenterology (ACG),[11] the European Association of Endoscopic Surgery (EAES)[13] and the World Gastroenterology Organisation[156] are relatively dated, but all suggest a step-wise approach. However, as emphasised by a recent systematic review,[173] treatments for DD rely mainly on data from uncontrolled studies.

Because anaerobes (like *E. coli* and *B. fragilis*) outnumber aerobes in the colon by 100:1, anaerobes must always be considered as potential pathogens in diverticulitis. Polymicrobial infections are the rule rather than the exception, and reports suggest that – on average – up to five different species of bacteria may be present, any of which may anaerobic, facultative, or aerobic. Again, recommended combination regimens are based more on clinical consensus than on RCTs.[16,196]

4.3.2 Statement (EL 3b – RG C): Antibiotics may not improve outcome in acute uncomplicated diverticulitis (AUD) and are used on a case-by-case basis.

Consensus levels of agreement: A+ 61%; A 29%; A− 10%.

In a retrospective audit of 311 patients hospitalised for AD, Hjern et al.[197] observed that antibiotic or conservative treatment yielded the same clinical outcome,

with an overlapping rate of recurrence. In a retrospective analysis, among a cohort of 693 patients referred for outpatient treatment, it was observed that treatment was effective for the vast majority (94%) of patients.[198] A prospective, multicenter RCT (the DIVER Trial) performed in 132 patients with AUD[199] has just shown that, in selected patients, outpatient treatment is safe and effective. Outpatient treatment allows important cost saving to the health systems without negative influence on the patient's quality of life. In a recent RCT, 623 patients with computed tomography-verified acute uncomplicated left-sided diverticulitis were recruited. Patients were randomised to treatment with or without antibiotics, and antibiotic use neither accelerated recovery nor prevented complications. Recurrent diverticulitis needing readmission to hospital at a one-year follow-up was similar in the two groups.[200] This new evidence needs, however, further confirmations before it can be safely adopted in clinical practice.[201] A large (more than 500 patients, stage 1a or 1b, according to Hinchey) randomised multicenter pragmatic clinical trial (the so-called DIABOLO trial) comparing two treatment strategies for AD is ongoing.[202] Patients will be randomised to a conservative strategy (antibiotics for 10 days, hospital admission, supportive measures) or to a liberal strategy (no antibiotics, supportive measures and admission only if needed on clinical grounds). The study should be completed by the end of 2014 and will surely provide objective evidence for clinical decisions. At the present time, however, there is no evidence mandating the routine use of antibiotics in AD, despite the several guidelines recommending their use.[203]

4.3.3 Statement (EL 3b – RG C): In severe/complicated acute diverticulitis, hospitalisation, bowel rest and broad-spectrum antibiotics are needed.

Consensus levels of agreement: A+ 74%; A 16%; A− 7%; D− 3%.

Although no specific RCTs evaluating this approach have been performed, hospitalisation, bowel rest and broad-spectrum antibiotics are recommended by all the available guidelines.[11–13,156] A systematic review,[204] evaluating 92 papers on the treatment of AD, concluded that patients with severe AD who do not need emergency surgery, should be treated with hospitalisation, parenteral fluids and a single intravenous antibiotic active against aerobic and anaerobic bacteria. In cases of mild AD, criteria for inpatient treatment include the presence of significant inflammation, intolerance to oral fluids, age over 80–85 years, and presence of immunosuppression or comorbidities (diabetes, chronic renal failure, malignant haematological diseases, HIV infection, chemotherapy, steroid therapy, transplant). Since the vast majority of patients with AD respond to initial medical treatment, a short hospital stay is a safe option.

In a recent Cochrane review[201] only a qualitative approach (with no meta-analysis) was possible given the variety of interventions between the studies included. Interventions compared antibiotics to no antibiotics, single to double compound antibiotic therapy and short to long intravenous (i.v.) administration. None of the studies found significant difference between the interventions tested. Recommended regimens are therefore based on clinical consensus. In this connection, a survey performed by the American Society of Colon and Rectal Surgeons (ASCRS)[205] revealed ample variations in the management of uncomplicated sigmoid diverticulitis amongst colon and rectal surgeons, especially in terms of antibiotic choice. Second generation cephalosporins were the first choice for intravenous antibiotic therapy, followed by metronidazole and metronidazole-ciprofloxacin combination. This combined antimicrobial regimen was, on the contrary, the most prescribed oral treatment, followed by ciprofloxacin and amoxicillin-clavulanic acid combination.

4.4 Is there a role for prophylactic interval colectomy after one or more episodes of acute diverticulitis?

4.4.1 Statement (EL 2b – RG B): No, the decision to perform elective resection after one or more episodes of AD should be undertaken on a 'case-by-case' basis.

Consensus levels of agreement: A+ 77%; A 20%; D− 3%.

In recent studies the natural history of diverticulitis appears much more benign than in the historical studies.[206,207] on which previous statements from three scientific associations,[11,13,208] founded their conclusions. The ASCRS, EAES and ACG agreed on the need for a prophylactic interval sigmoidectomy after two previous episodes of AD, or even in patients aged below 50 years. This statement was mainly based on the studies by Parks, and Farmakis et al.[206,207] A review by Janes in 2005 showed how these studies gave an 'inadequate evidence' to support such an aggressive surgical policy.[9] In 2006, the ASCRS already changed its policy toward a more prudent statement, considering the indication for elective surgery on a 'case-by-case' basis.[155]

The long term risk of relapse is more limited than previously believed, it usually shows a good response to medical therapy[209–212] and, above all, the long-term risks of subsequent emergency surgery (3–7%), death (<1%) and stoma formation (0–4%) are quite low.[209,210,213–216] The risk of severe complications, such as perforation, is usually with a first episode of AD.[9,41,217–219] The lower rates of surgical treatment of AD does not increase the rate of complicated diverticulitis.[220] Surgery for AD does not fully protect against

recurrence (with a rate variable from 5.8–15%)[207,210,221] or further surgery (up to 3%).[9,212,222–224] The indication for an elective sigmoid resection should not be based on the number of previous episodes of AD.[9,155,225]

4.5 Which are the indications for elective surgery?

4.5.1 Statement (EL 3a – RG B): Elective surgery should be recommended in patients with symptomatic complicated diverticular disease (e.g. fistula, stenosis). Specific clinical situations should be carefully evaluated (persisting symptoms and signs, age, degree of diverticulitis, immunocompromised patients).

Consensus levels of agreement: A+ 46%; A 36%; A− 14%; D− 4%; D 0%; D+ 0%.

Indications to elective surgery have to be evaluated balancing severity of symptoms, risks of severe recurrences, and morbidity due to surgery.

It is still controversial whether young age, generally defined as below 50 years, represents an independent risk factor of AD recurrence. It has been reported that younger patients are more prone to recurrent disease and more frequently require surgery for complicated diverticulitis, which supports the recommendation for elective surgery after their first episode of uncomplicated diverticulitis.[226–230] In a recent study no differences in the rate of successful conservative treatment were observed between patients at the first episode and those with recurrence with regard to age, suggesting that age is not a predictive factor of poor outcome.[231] Four retrospective studies failed to find any difference between younger and older patients in terms of outcome after conservative treatment of AD;[209,232–236] the authors reported that recurrent diverticulitis was significantly more frequent in younger patients (<50 years) with a shorter mean time to recurrence, although none required emergency surgery. They concluded that diverticulitis management should be based on the severity of the disease rather than on the patient's age. Similarly, the cut-off age (40 or 50 years) to identify patients at increased risk of relapse is also controversial. Some studies[210,229–232] evidenced that patients aged less than 40 years had a significantly increased risk of AD recurrence.[237] However, patients younger than 40 years had an increased risk of AD recurrence but did not show a higher risk of subsequent emergency surgery during follow-up, as previously suggested.[238]

Age does not seem to be related to a severe course of the disease after a medically treated episode of AD and should not be considered an indication for a more aggressive surgical policy after conservatively treated episodes of AD; considering the increasing incidence of AD in younger age.

Immunocompromised patients or those on immunosuppressive therapy, patients with chronic renal failure or collagen-vascular disease show a five-fold greater risk of perforation in a recurrent episode of AD[217,225,239] and therefore may benefit from early elective resection after a conservatively treated episode of diverticulitis. This statement has been challenged by the results of Biondo et al.'s study, in which patients with immunosuppression had a significantly higher mortality rate than non-immunosuppressed patients, but only during the first episode of the disease; also, patients who required emergency surgery for AD had no previous history of DD.[150]

Therefore it is still unclear whether immunocompromised patients are at higher risk of severe complication in case of AD recurrence.

After successful medical treatment of an acute episode, patients with severe diverticulitis at CT scan had a statistically greater incidence of unsatisfactory outcome than patients with moderate diverticulitis (36 vs 17%)[122,240] A retrospective study on 672 patients followed up for five years after a first episode of AD diagnosed by CT scan, found at a multivariate analysis that left sided AD, length of colon involved >5 cm and a retroperitoneal abscess were predictors of recurrence.[241]

4.6 Which is the optimal timing for an elective resection after an episode of AD?

4.6.1 Statement (EL 3a – RG B): Elective resection in a patient with an episode of AD is safer when performed in an inflammation-free interval.

Consensus levels of agreement: A+ 85%; A 11%; A− 4%.

Surgery for diverticulitis could be very demanding if a parietal or mesocolic inflammation is still present. This could lead to difficulties in bowel mobilisation, identification of the right planes and ureter, and in performing the anastomosis, because of inflamed colonic stumps. A prospective study[242] comparing early and late laparoscopic resection after an episode of AD showed a significantly higher rate of overall minor and major morbidity, anastomotic leak, abdominal wall abscess and conversion during early elective surgery. In another retrospective study, early elective laparoscopic surgery led to a higher conversion rate with higher related morbidity.[243] Elective surgery performed in an inflammation-free interval leads to better surgical results, and consequently should be postponed until antibiotic therapy is begun in order to achieve remission of the acute inflammation.

4.7 Can elective colonic resection for AD be performed laparoscopically?

4.7.1 Statement (EL 2a – RG B): Laparoscopic resection is safe and provides faster recovery in

uncomplicated cases; it has to be performed by well trained surgeons.

Consensus levels of agreement: A+ 83%; A 14%; A− 3%.

Two randomised trials comparing laparoscopic vs open resections for uncomplicated AD[244–247] showed significantly reduced hospital stay in the laparoscopic group, with a reduction of blood loss, morbidity and post operative pain in one of the trials: conversion rates were 9% and 19% respectively. No clear long term advantages were demonstrated. Similar result emerged from a meta-analysis on non randomised studies conducted until 2006[248] and from a systematic review recently published on this subject.[249] A 0.2% mortality with 11% morbidity and 2.8% conversion rate was achieved in a series of 500 consecutive patients operated in one single centre.[250] This study shows the extremely good results with laparoscopy, which was performed by well trained surgeons in a high volume centre. There is a limited number of studies on laparoscopic surgery in complicated AD: a study by Reissfelder et al.[251] on 112 patients showed an higher morbidity and conversion rate compared to resections for uncomplicated disease in term of conversion rate, wound infection and hospital stay; overall morbidity was 26.4% vs 16.1% ($p = 0.10$).

Laparoscopic versus open colonic resection for uncomplicated diverticulitis offers some advantages in term of blood loss, postoperative ileus, morbidity, hospital stay and overall costs; it could be the gold standard in elective surgical treatment of uncomplicated disease if performed by experienced, well trained surgeons, although no clear long term advantages have been demonstrated.

There are insufficient data on the safety of laparoscopic resection in complicated diverticulitis.

4.8 What is the appropriate surgical approach to an overt diverticular perforation with diffuse peritonitis?

4.8.1 Statement (EL 2b – RG B): Several surgical options may be appropriate, but the choice mostly depends on the severity of peritonitis. Laparoscopic peritoneal lavage should be considered as an alternative to primary resection and anastomosis in purulent peritonitis.

Consensus levels of agreement: A+ 64%; A 25%; A− 11%.

As far as purulent peritonitis is considered, two recent, prematurely interrupted, RCTs,[252,253] along with data from previous studies with weaker designs[254–263] and from systematic reviews,[264–266] have indicated that resection and primary anastomosis with or without proximal faecal diversion is not inferior to non-restorative resection, namely Hartmann's procedure, in terms of surgical efficacy and safety.

Moreover, when compared with the reversal of an ileostomy, the reversal of a colostomy after Hartmann's procedure adds a more challenging operation, being associated with relevant morbidity and mortality; as such, it will never be performed in a wide proportion of patients who would be left with a permanent stoma.[252,259] Accordingly, resection with primary anastomosis has to be considered a preferable approach in most patients with purulent peritonitis.

Laparoscopic lavage and drainage may be an alternative to resective procedures in diverticular perforation with purulent peritonitis. While waiting for the results of the ongoing RCTs,[267,268] several small prospective[269,270] and retrospective[271–274] case-control studies and three systematic reviews[275–277] have reported that laparoscopic lavage is not inferior to either primary resection/anastomosis or Hartmann's procedure in terms of feasibility, safety and efficacy. Criteria to opt for laparoscopic peritoneal lavage instead of resective surgery remain unsettled. Several papers suggest that patients who have faecal peritonitis, or a large perforation site, and those who fail to improve after lavage should undergo prompt resection.

Limited data are available sustaining a specific surgical strategy in diffuse faecal peritonitis. In most retrospective series faecal peritonitis and patients who are hemodynamically unstable, or have high-risk comorbidities were generally considered for a Hartmann procedure.[264–266] However, precise criteria to opt for Hartmann's procedure remain elusive, and the surgeon's experience and preference still appear to be important determinants.

4.9 What is the appropriate surgical approach to a diverticular abscess not amenable to medical management (>4 cm in diameter)?

4.9.1 Statement (EL 3b – RG C): The best treatment option for a diverticular abscess >4 cm in diameter is percutaneous guided drainage. Diverticular abscesses not responding, or not amenable, to non-operative management should be treated surgically.

Consensus levels of agreement: A+ 82%; A 14%; A− 4%.

Pericolic, intrabdominal, retrocolic and pelvic diverticular abscesses are associated with an acute mortality ranging from 5–10%. Several retrospective and small studies have shown that percutaneous CT-guided (or US-guided) drainage of this specific type of abscess is safe and effective in treating intrabdominal sepsis, eventually bridging patients to elective single-stage resection.[124,279] The size of the abscess is an important determinant of successful treatment: those ≥4 cm in

Table 2. Rejected statements

N	Statements	EL(*)	RG(*)
1.1.5	Complicated diverticular disease includes a large variety of clinical situations occurring in patients with diverticular disease, characterized by single or recurrent episodes of acute diverticulitis, bleeding, stricture, and fistula. *Consensus levels of agreement:* A+ 20%; A 27%; A− 13%; D− 17%; D+ 23%.	**1c**	**B**
3.3.1	Colonoscopy should not be considered the first-line diagnostic procedure to diagnose DD. *Consensus levels of agreement:* A+ 26%; A 16%; A− 19%; D− 13%; D 7%; D+ 19%.	**5**	**D**
3.9.1	Colonic evaluation, after non-invasive imaging diagnosis of acute diverticulitis treated conservatively, does not provide significant benefit. *Consensus levels of agreement:* A+ 15%; A 15%; A− 34%; D− 6%; D 3%; D+ 27%.	**3a**	**B**
3.9.2	Endoscopic follow-up should be reserved only to patients with persistently severe symptoms to exclude either cancer or an IBD. *Consensus levels of agreement:* A+ 38%; A 19%; A− 6%; D− 3%; D 9%; D+ 25%.	**3a**	**B**

DD: diverticular disease; IBD: inflammatory bowel disease.

diameter are less likely to be associated with successful antibiotic treatment alone, and more likely to be amenable to percutaneous guided drainage.[278,280,281]

However, only 20–30% of all diverticular abscesses are amenable to percutaneous guided drainage and 15–30% of those treated by this approach do not respond to treatment and require resective surgery.[124,282,283]

4.10 Is a laparoscopic colon resection appropriate when an urgent operation for perforated diverticulitis is required?

4.10.1 Statement (EL 4 – RG C): Though technically feasible, laparoscopic resection for perforated diverticulitis has to be restricted to selected cases and to experienced laparoscopic surgeons.

Consensus levels of agreement: A+ 52%; A 28%; A− 17%; D 3%.

4.10.2 Statement (EL 5 – RG C): Current evidence is inadequate to support an urgent laparoscopic colorectal resection for perforated diverticulitis. This approach should be reserved to centres and surgeons with appropriate laparoscopic expertise.

Consensus levels of agreement: A− 100%.

The evidence on laparoscopic resective surgery for perforated DD with peritonitis is limited to retrospective case series[251,284–287] and rare case-control studies[250,288] prevalently including confined perforations. When compared to elective colorectal resection, the emergency laparoscopic colectomy for diverticular disease appears to be a challenging procedure associated with a consistent increase in conversion rate.[289]

Though most studies did not show any significant increase in postoperative mortality after urgent laparoscopic resection, the quality of currently available evidence is inadequate to support a liberal use of this approach. Its use should be reserved to experienced laparoscopic centres and surgeons, possibly within the frame of a clinical trial.

Final note

These guidelines represent a consensus of best practice based on the available evidence at the time they were issued (Table 2). They may not apply to all situations and should be interpreted in the light of specific clinical situations and resource availability. Further controlled clinical studies may be needed to clarify some aspects of these statements, and revision may be necessary as new data become available. Clinical considerations may justify a course of action at variance with these recommendations. These guidelines are intended to be an educational tool to provide information that may assist gastroenterologist and surgeons in providing care to patients. They are not rules and should not be constructed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.

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Conflict of interest

All participants were asked to disclose any conflicts of interest. In particular, the non-voting chairman and the non-voting members of the scientific board declared that they

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Appendix 1

Promoter: Italian Study Group of Diverticular Disease (Gruppo Italiano Malattia Diverticolare - GRIMAD).
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