

**REVIEW ARTICLE**

# German guideline diverticular disease/diverticulitis

## Part II: Conservative, interventional and surgical management

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**Abstract**

Diverticulosis and diverticular disease are ranked among the most common gastroenterological diseases and conditions. While for many years diverticulitis was found to be mainly an event occurring in the elder population, more recent work in epidemiology demonstrates increasing frequency in younger subjects. In addition, there is a noticeable trend towards more complicated disease. This may explain the significant increase in hospitalisations observed in recent years. It is not a surprise that the number of scientific studies addressing the clinical and socioeconomic consequences in the field is increasing. As a result, diagnosis and conservative as well as surgical management have changed in recent years. Diverticulosis, diverticular disease and diverticulitis are a complex entity and apparently an

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interdisciplinary challenge. To meet these considerations the German Societies for Gastroenterology and Visceral Surgery decided to create joint guidelines addressing all aspects in a truly interdisciplinary fashion. The aim of the guideline is to summarise and to evaluate the current state of knowledge on diverticulosis and diverticular disease and to develop statements as well as recommendations to all physicians involved in the management of patients with diverticular disease.

#### KEYWORDS

colon, diagnosis, diverticular disease, diverticulitis, inflammation, treatment

## CHAPTER 5: PROPHYLAXIS AND CONSERVATIVE TREATMENT: PHARMACOTHERAPIES, DIET, LIFESTYLE

### Foods and stimulants: Dietary fibre

**Recommendation 5.1** Evidence level 1, recommendation grade A, strong consensus  
A high-fibre diet ( $\geq 30$  g/day) rich in fruit, vegetables and cereals, should be recommended for men and women, regardless of age, for primary prophylaxis of diverticular disease and in accordance with general dietary recommendations.

**Recommendation 5.2** Evidence level 2, recommendation grade B, strong consensus  
A recommendation to avoid nuts, grains, corn and popcorn should not be made for the primary prophylaxis of diverticular disease.

**Recommendation 5.3** Evidence level 2, recommendation grade B, strong consensus  
Limitation of red meat consumption is advisable for primary prophylaxis of diverticular disease. When consumption is greater than 105–135 g/week, the risk increases linearly by about 50%, plateauing at approx. 540 g/week.

**Statement 5.4** Evidence level 2, strong consensus  
Other than avoiding red meat and consuming plenty of fibre, there is currently insufficient evidence for other specific dietary recommendations.

**Recommendation 5.5** Evidence level 1, recommendation grade A, strong consensus  
Nicotine abstinence should be recommended for primary prophylaxis of diverticular disease

**Statement 5.6** Evidence level 2, strong consensus  
An increased risk for diverticular disease has been documented for acute alcohol intoxication, for alcohol abuse and for alcohol dependence syndrome.

(Continued)

There are currently no data indicating that low-risk or even risky alcohol consumption lead to an increased risk of developing diverticular disease.

**Recommendation 5.7** Evidence level 2, recommendation grade B, strong consensus  
There are no data that show an association of coffee consumption with the occurrence of diverticular disease. Therefore, a recommendation to this effect regarding coffee consumption should not be made.

**Recommendation 5.8** Evidence level 1, recommendation grade A, strong consensus  
Maintenance of normal weight should be recommended to prevent diverticular disease.

**Recommendation 5.9** Evidence level 1, recommendation grade A, strong consensus  
Physical activity can reduce the likelihood of developing diverticular disease or diverticulitis. The most benefit can be gained from over 50 MET-h (metabolic equivalent)/week, corresponding to about 12 h walking at 5 km/h, 6 h cycling at 24 km/h or 4.5 h jogging at 11 km/h. At a minimum, however, in accordance with the DGE, 30–60 min of moderate physical activity per day should be recommended (10 guidelines of the DGE).

**Recommendation 5.10** Evidence level 2, recommendation grade A, strong consensus  
A healthy lifestyle should be recommended for primary prophylaxis of diverticular disease. A lifestyle incorporating reduced red meat intake, increased consumption of dietary fibre and vigorous physical activity, while maintaining a normal BMI and abstaining from smoking, reduces the risk of developing diverticulitis by up to 50%.

(Continued)

**Recommendation 5.11**

Use of NSAIDs, corticosteroids, opioids, and postmenopausal hormone replacement therapy, but not aspirin or coxibs, is associated with an increased risk of developing diverticular disease, diverticulitis, and complicated diverticulitis. The risk association for paracetamol exists primarily with respect to diverticular bleeding. In view of these risks, the corresponding medications should only be administered after careful risk-benefit assessment.

Evidence level 1–2, recommendation grade A, strong consensus

All Statements and Recommendations commented in Supplemental Material.

### Pharmacological, dietary and probiotic therapies in active disease

**Recommendation 5.12**

Segmental colitis associated with diverticulosis (SCAD) can be treated with mesalazine.

Evidence level 5, recommendation grade 0, strong consensus

#### Comment—Recommendation 5.12

SCAD is characterised by differing manifestations of colitis between non-inflamed diverticula. In contrast to ulcerative colitis, the rectum is not affected. The prevalence of this clinical condition has been reported to be 0.3%–1.3% in patients with diverticula<sup>1</sup>; SCAD is therefore quite rare, not least because it is probably often overlooked or incorrectly diagnosed (differential diagnosis e.g., IBD). The prognosis seems favourable, without a need for long-term therapy. Formal therapy studies are not available. Acute therapy usually consists of medications used in IBD, with oral mesalazine as first-line therapy.<sup>2,3</sup>

### Acute diverticular disease/diverticulitis

**Recommendation 5.13**

Acute uncomplicated diverticular disease/diverticulitis (CDD types 1a and 1b) should primarily be treated conservatively.

Expert consensus, strong recommendation, strong consensus

#### Comment—Recommendation 5.13

Acute uncomplicated diverticulitis is practically always treated conservatively. There is no indication for a first-line surgical approach. Studies comparing a conservative versus a surgical approach in the acute situation are not available. In various prospective and

retrospective case series, conservative treatment of acute uncomplicated diverticulitis has shown high rates of success, and recurrence rates were also low.<sup>4</sup>

**Recommendation 5.14**

Patients with confirmed uncomplicated diverticular disease/diverticulitis (CDD1a/b) can be treated on an outpatient basis if there are no signs of serious disease and/or increased risk, and provided they can be closely medically monitored.

Evidence level 1, recommendation grade 0, strong consensus

#### Comment—Recommendation 5.14

In a systematic review with a literature search in 2011, Friend & Mills found four studies investigating whether outpatient oral antibiotic therapy is adequate for the treatment of uncomplicated diverticulitis.<sup>5</sup> Besides one randomised controlled trial (RCT) with 79 patients, there were two prospective cohort studies (each with 70 patients) and one retrospective cohort study (693 patients). On the basis of these studies, the authors concluded that outpatient treatment is possible under the following conditions: (1) oral intake (fluids, medication, etc.) is possible; (2) there are no significant comorbidities; (3) oral antibiotics are available; (4) adequate pain control is possible; (5) adequate follow-up is accessible and, if necessary, support in the social environment is available; and (6) ultrasound or CT shows diverticulitis without any significant abscess.

A very well-designed systematic review came to the conclusion that outpatient treatment of acute uncomplicated diverticulitis is possible in selected patients, that is, if complications, comorbidities and immunosuppression are ruled out and there is adequate oral intake and social integration. However, the authors also critically note that well-designed randomised studies are lacking, with almost all the evidence coming from observational studies and only three studies existing in which there was no use of antibiotics. Therefore, there is a need for better studies without antibiotics.<sup>6</sup>

Before outpatient treatment of diverticulitis can be considered, complicated diverticulitis must be ruled out. This requires reliable, rapid predictors that are universally available. One candidate is CRP. In a cohort study of 247 patients, only CRP was significantly correlated with perforation in the regression model. The best accuracy was found for a CRP of 150 mg/L, with a sensitivity of 44% and a specificity of 81%. A CRP value < 50 mg/L (normal value: < 5 mg/dl) was shown to have a negative predictive value of 0.79, while a CRP of >150 mg/L had a positive predictive value of 0.57.<sup>7</sup> Notably, however, perforations were also found in patients with normal CRP levels in this study. It should also be borne in mind that inflammation parameters usually take 1–2 days to develop as a distinguishing feature of complicated disease; therefore, clinical and laboratory (CRP) re-evaluation of the patient is recommended after 48 h (48-h rule).<sup>8</sup> Further studies confirm the correlation of CRP with more severe

diverticulitis<sup>9</sup> and with therapy failure.<sup>10,11</sup> In contrast, leucocytes and body temperature fail to differentiate perforating from non-perforating diverticulitis. Since clinical parameters cannot differentiate with sufficient sensitivity and specificity between uncomplicated and complicated diverticulitis, the use of imaging techniques (sonography or CT) is essential before deciding on outpatient therapy. Conversely, it may be concluded that all patients who do not meet the requirements for outpatient treatment should be treated as inpatients.

## Diet and lifestyle in symptomatic uncomplicated diverticular disease

### Recommendation 5.15

There is insufficient evidence for a recommendation to use a high-fibre diet or fibre supplements in the management of symptomatic uncomplicated diverticular disease.

Nevertheless, a high-fibre diet can be recommended on the basis of general nutritional recommendations (see 2.1.1).

Evidence level 4, recommendation grade 0, strong consensus

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### Comment—Recommendation 5.15

A systematic review examined the role of a high-fibre diet or fibre supplements in the management of symptomatic uncomplicated diverticular disease (SUDD).<sup>12</sup> The aim of the intervention was to reduce abdominal symptoms and/or prevent flares of acute diverticulitis. Nineteen studies, involving a total of 2443 patients, were included in the review, including all those discussed in Ünlu's earlier review (2012).<sup>13</sup> On the Jadad study quality scale, only one study achieved the highest score of 5 points, 12 studies scored between 1 and 3 points, and six studies zero points. Due to the low quality of the studies and their heterogeneity with regard to the quantity and quality of dietary fibre used, a meta-analysis was not possible. Consequently, although individual studies suggested a positive effect of dietary fibre, it was impossible to make a statement regarding the effectiveness of dietary fibre in the reduction of abdominal symptoms or prevention of acute diverticulitis in patients with SUDD.

## Pharmacological therapy of acute (symptomatic) uncomplicated diverticular disease (CDD 1a)

The aim of pharmacotherapy is to improve symptoms and, in particular, to reduce pain. A further aim is to prevent the development of diverticulitis, especially complicated diverticulitis.

### Recommendation 5.16

Mesalazine may be considered for the treatment of acute episodes of uncomplicated diverticular disease (CDD 1a).

Evidence level 2, recommendation grade 0, consensus

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### Comment—Recommendation 5.16

Alongside open observations of mesalazine treatment in acute (active) uncomplicated diverticular disease<sup>14</sup> that show positive results for symptomatic improvement, there are also three RCTs. In a placebo-controlled 4-week study ( $n = 123$ ), 1000 mg tid mesalazine was described to have various effects on pain.<sup>15</sup> In another randomised, 12-week study, two doses of mesalazine were compared to two doses of rifaximin ( $n = 170$ ). A significant improvement in pain was recorded in both groups, whereby mesalazine (1600 mg/d) had a significantly more pronounced effect than rifaximin.<sup>16</sup> In another randomised study ( $n = 268$ ) with a similar design (mesalazine vs. rifaximin), the effects of mesalazine on symptoms were confirmed, and here too, its significant superiority over rifaximin was shown.<sup>17</sup> All studies confirm the drug to have good tolerability, with few side effects.

Despite these various studies, it must be kept in mind that their very different and limited individual quality, very different designs and different endpoints devalue the formal evidence level and preclude a stronger recommendation.

### Recommendation 5.17

Therapy of acute uncomplicated diverticular disease with rifaximin or with probiotics cannot be recommended.

Evidence level 3, recommendation grade 0, consensus

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### Comment—Recommendation 5.17

Based on evidence suggesting that the microbiome plays an essential role in the pathogenesis of uncomplicated diverticular disease, several studies have investigated the use of antibiotics and probiotics.

The effectiveness of the poorly absorbable broad-spectrum antibiotic rifaximin in uncomplicated diverticular disease was examined in a meta-analysis.<sup>18</sup> There were 4 controlled studies, three of them with an open design (Jadad Score 2–3) and one placebo-controlled. All comparisons were made with a combination therapy consisting of rifaximin plus dietary fibre. In the only placebo-controlled trial, there was no difference in symptomatic improvement between the rifaximin plus fibre and the fibre plus placebo groups within the first 3 months.<sup>19</sup> Recently, a controlled open-label study was published that compared rifaximin 400 mg bid for 10 days per month with a fibre supplement. The randomisation was questionable, since imaging was not among the inclusion criteria. After 3 months, a global symptom score improved in both groups. However, no statistics were reported for the inter-interventional difference.<sup>20</sup> Data on the treatment of acute uncomplicated diverticular disease are therefore so few and so incongruent that it is not possible to make an evidence-based recommendation.

Several other double-blind, placebo-controlled studies of probiotics in uncomplicated diverticular disease are discussed in two systematic reviews.<sup>21,22</sup> The study protocols are characterised by a high degree of heterogeneity, for example, very diverse

combinations are tested against different controls, each with different microorganisms and dosages. The studies are mostly of a preliminary nature and of very limited quality. A meta-analysis was therefore not possible; rather, the need for further and better studies was pointed out.<sup>21</sup> Thus, a recommendation for probiotics cannot be given.

### Acute uncomplicated diverticulitis with surrounding tissue reaction (CDD 1b)

Mesalazine

#### Recommendation 5.18

Mesalazine should not be prescribed for acute uncomplicated diverticulitis (CDD 1b).

Evidence level 1, recommendation grade B, consensus

#### Comment—Recommendation 5.18

In contrast to acute symptomatic uncomplicated diverticular disease, there are hardly any therapeutic studies of mesalazine in CT-verified acute diverticulitis. A retrospective, single-centre cohort study found no significant benefits of mesalazine.<sup>23</sup> In the most recent systematic review on mesalazine in diverticular disease, one RCT in acute diverticulitis is cited.<sup>14</sup> This study also showed no significant benefit.<sup>24</sup> The negative recommendation is therefore based not only on the sparse availability of study data, but also on the negative results reported in the cited studies.

#### Recommendation 5.19

Therapy of acute uncomplicated diverticulitis with probiotics cannot be recommended.

Evidence level 2, recommendation grade 0, strong consensus

#### Comment—Recommendation 5.19

There are several studies on probiotic therapy in acute uncomplicated diverticulitis. Two systematic reviews and meta-analyses<sup>21,22</sup> list 3 studies, of which one will not be considered here because diverticulitis was not confirmed by a cross-sectional imaging procedure.<sup>25</sup> A double-blind RCT showed no significant difference in a global symptom score after 12 weeks' treatment with a combination of probiotics and mesalazine compared with placebo.<sup>24</sup> Another blinded, placebo-controlled RCT compared the therapeutic effect of 10 days' treatment with *Lactobacillus reuteri* versus placebo. Both groups had additionally received antibiotic therapy with ciprofloxacin/metronidazole for 1 week.<sup>26</sup> The combination with *L. reuteri* resulted in a significant improvement in terms of pain reduction and inflammatory markers and a shorter hospital stay in comparison to placebo. Due to the sparse and inconsistent data, no recommendation can be made for the use of probiotics in acute uncomplicated diverticulitis.

#### Recommendation 5.20

In acute uncomplicated left-sided diverticulitis (CDD 1b) without risk indicators for complicated disease, antibiotic therapy need not to be prescribed, provided the patient is under close clinical monitoring.

Evidence level 1, recommendation grade 0, strong consensus

#### Comment—Recommendation 5.20

The question of whether to use antibiotic therapy in acute uncomplicated diverticulitis continues to be a topic of heated national and international debate. In addition to numerous retrospective and smaller prospective studies, two large, randomised multicentric studies have been conducted. The largest study, of 623 patients with CT-confirmed uncomplicated left-sided diverticulitis, revealed no statistically significant differences between the group treated with antibiotics and those who received no antibiotics, in respect of rates of complications (perforation, need for resection, length of hospital stay) during hospitalisation or rates of readmission for recurrence of diverticulitis after 1 year of follow-up.<sup>27</sup> Abscess formation was statistically higher in the group not receiving antibiotics (1% vs. 0%;  $p = 0.08$ ). The study has several methodological weaknesses: The antibiotic therapy (type of drug, administration route) was not standardised, and there was no blinding and no placebo control. CRP on admission was statistically higher in the antibiotics group (100 vs. 90 mg/L;  $p = 0.07$ ). Comorbidities were not classified according to a validated comorbidity index and were based on data from surgical medical records. Several exclusion criteria (e.g., sepsis) were inadequately defined.<sup>27</sup> There is now a follow-up publication with a median follow-up of 11 years that essentially confirms these results.<sup>28</sup> Another open-label study included 528 patients with Hinchey stages 1a/b.<sup>29</sup> The patients were randomised to 2 groups, one with standardised antibiotic administration (initially amoxicillin/clavulanic acid i.v. for at least 4 days with the possibility to switch to oral administration (amoxicillin/clavulanic acid or ciprofloxacin/metronidazole) thereafter, for a total of 10 days), and for comparison, a group that was only observed. The median time to clinical improvement (composite endpoint) was 12 days (7–30 days) in the antibiotic group and 14 days (6–35) in the observation group. Secondary endpoints similar to those of the AVOD study<sup>27</sup> also showed no significant differences. Only the hospital stay was shorter in the observation group. A follow-up study of these patients yielded findings similar to those of the initial study.<sup>29</sup> This study was also subjected to criticism. An up to date, very thorough and critically well-balanced systematic review<sup>30</sup> arrived at the conclusion that treatment of acute uncomplicated diverticulitis without broad-spectrum antibiotics is feasible, safe, and effective. However, as the authors point out, the subgroup analysis of only the randomised studies shows a significantly higher failure rate in patients not treated with antibiotics. The authors also note that the influence of certain risks, for example, comorbidity, on the question of the need for antibiotic therapy has not been sufficiently investigated. Indeed, this points to a crucial aspect that is often overlooked: All of these studies examine a strictly selected (inclusion criteria) patient population with generally mild disease. This

**TABLE 6** Lists risk indicators that play a role in the individual indication for antibiotic therapy in acute uncomplicated diverticulitis.<sup>31</sup>

Risk indicators		
Clinical risk indicators	Laboratory risk indicators	Drug-induced risk indicators
Patient under immunosuppression	High CRP	Immunosuppression
Comorbidity	Leucocytosis	NSAID
Poor overall condition		Corticosteroids
High fever/sepsis		
Complications: Peritonitis, abscess		

is illustrated by some of the exclusion criteria from the AVOD<sup>27</sup> and DIABOLO studies<sup>29</sup>: Poor general condition (ASA > III), high fever, clinical suspicion of bacteraemia, sepsis, peritonitis, immunosuppression. In large studies of antibiotics, in addition to the exclusion criteria mentioned here, a number of clinical and drug-related risk indicators must be taken into account that are associated with more severe diverticulitis and possibly with the risk of a worse course of disease. Overall, comorbidity (Charlson Index  $\geq 3$ ) and immunosuppression play a particularly important role in the disease course.

The results of a recently-published randomised, placebo-controlled, double-blind comparative study with 201 patients, which has yet to be included in any meta-analysis, underline that the jury is still out on whether antibiotic therapy should be given in acute uncomplicated diverticulitis.<sup>32</sup> The therapeutic efficacy of rifamycin SV, a barely absorbable, topically acting antibiotic, was investigated. While antibiotic therapy showed only a statistically marginal ( $p = 0.06$ ) effect after 10 days, the effect was seen much earlier in the antibiotic group than in the placebo group. After 3 days, a significant improvement was observed. In the group of patients with prolonged clinical symptoms, the antibiotic was significantly superior after 10 days. It has also been shown previously that a short, 4-day course of antibiotics (ertapenem) is not inferior to a therapy of longer duration.<sup>33</sup>

In summary, treatment of acute uncomplicated diverticulitis is frequently possible without the use of antibiotics. The limited assessability not only of risk factors, but also of clinical disease severity in the acute situation, indicate that there is scope for individual case-based decision-making, leading to a “can” recommendation (Table 6). This level is corroborated by the fact that while there is good evidence against 10 days of antibiotic therapy, there is strong evidence that a shorter course of treatment with antibiotics may have clinical benefits.

#### Recommendation 5.21

When diagnosing acute diverticulitis, the patient's general health status and risk indicators should be evaluated and the prognosis assessed.

Evidence level 1, recommendation grade A, strong consensus

#### Comment—Recommendation 5.21

Since there are various options for the therapy of acute uncomplicated diverticulitis, it is necessary to assess the severity and risks of

each specific case. This also allows a prognosis to be made about the possible disease course. Algorithms can assist in estimating the future course of acute diverticulitis that

### Supportive therapy in acute, uncomplicated diverticulitis

#### Recommendation 5.22

Adult patients hospitalised due to acute uncomplicated diverticulitis require no special dietary restrictions.

Evidence level 2, recommendation grade 0, strong consensus

#### Comment—Recommendation 5.22

Supportive therapy in acute, uncomplicated diverticulitis with low-fibre diet or starvation is often recommended for a short period of time, in the assumption that a less active or “resting” bowel has a beneficial effect with regard to irritation or inflammation of the bowel. Data from studies comparing a liberal versus a restricted diet in acute, uncomplicated diverticulitis in the outpatient and inpatient setting, with or without the use of antibiotic treatment, were assessed in a systematic review.<sup>34</sup> Five studies investigating the effect of dietary fibre were included in the analysis—three randomised controlled studies and two observational studies. Overall, the study quality was very low and meta-analyses could not be conducted due to the inconsistent and divergent data. Patients on a liberal diet had a shorter hospital stay; no differences were found with regard to symptoms, treatment failure or disease recurrence.<sup>34</sup>

### Secondary prophylaxis of acute, uncomplicated diverticulitis

#### Recommendation 5.23

There is insufficient evidence for a recommendation to use a high-fibre diet or fibre supplements as secondary prophylaxis following a flare of acute, uncomplicated diverticulitis. Nevertheless, a high-fibre diet should be recommended on the basis of general nutritional recommendations

Expert consensus, strong recommendation, strong consensus

## Comment—Recommendation 5.23

A systematic review identified three studies examining the effect of altered dietary fibre intake on prevention of a further episode of diverticulitis or GI symptoms after an episode of acute uncomplicated diverticulitis.<sup>34</sup> Two of the three studies lacked control groups with a low fibre intake. The authors concluded that the evidence that a high-fibre diet or fibre supplementation has a protective effect against diverticulitis recurrence or improves GI symptoms is very limited. On the other hand, there is also no evidence that a low-fibre diet is superior.<sup>34</sup> Although evidence to support fibre intervention as a secondary prophylaxis after acute, uncomplicated diverticulitis is lacking, the authors recommend long-term consumption of a fibre-rich diet in accordance with generally accepted nutritional recommendations.<sup>34</sup>

A dietary fibre intake of 25–32 g/day for adult women and 30–35 g/day for adult men is recommended throughout Europe. In Germany,  $\geq 30$  g/day is recommended for adults, regardless of age and gender. In some countries, recommendations for dietary fibre intake are lowered in older adults to reflect their reduced calorie requirement (e.g., in the USA; for men aged 19–50 years 38 g/day, and for men aged  $>51$  years 30 g/day). In large meta-analyses of prospective cohort studies, a beneficial effect of a high-fibre diet has been documented for for example, mortality regardless of cause, coronary heart disease, arterial hypertension, stroke, hyperlipidaemia, type 2 diabetes, obesity, constipation, diverticular disease and various cancers inside and outside the GI tract.<sup>35</sup>

The American Gastroenterological Association Institute Technical Review on the Management of Acute Diverticulitis addresses, amongst other things, whether a high-fibre diet should be recommended for secondary prophylaxis of acute diverticulitis, whether corn, nuts and popcorn should be avoided, and whether aspirin or non-aspirin NSAIDs should be avoided. In all four instances, the authors are unsure whether the corresponding measure reduces the risk of recurrence of diverticulitis, a related complication, the need for surgery, or abdominal pain.<sup>36</sup> Only with regard to the high-fibre diet were studies found that investigated the question in a population previously affected by acute diverticulitis (included in Carabotti's 2017 systematic review<sup>12</sup>). The very low data quality allowed no firm conclusions to be drawn. Data from prospective cohort studies in collectives without previous diverticulitis (see 2.1.1 and 2.4.1) were considered of insufficient value to solve the question of secondary prophylaxis.<sup>36</sup>

## Treatment of acute complicated diverticulitis (CDD 2a)

### Recommendation 5.24

Patients with complicated diverticulitis should be hospitalised and monitored.

Evidence level 2, recommendation grade A, strong consensus

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## Comment—Recommendation 5.24

Acute complicated diverticulitis (CDD 2a, b, c) is a serious illness associated with relevant morbidity and mortality.<sup>37,38</sup> In a multicentric study, 743 patients with acute left-sided diverticulitis were hospitalised. In 67.4% of the patients, the primary treatment was conservative, while 32.6% initially underwent surgery. Post-operatively, complicated diverticulitis of Hinchey grade 0–1 was confirmed in 60.7% of patients, Hinchey 2 in 11.6%, and the most severe complications, Hinchey 3 and 4, in 27.7%.<sup>39</sup>

Of 528 patients with acute diverticulitis initially diagnosed as uncomplicated, 16 (3.0%) went on to develop complicated disease forms with perforations, abscesses and obstructions.<sup>40</sup> This percentage is very probably an underestimate, since the patients comprised a study population rather than a “real world situation”, and were thus recruited and initially diagnosed at specialised centres. The American PRACTICE Guidelines assume that 15%–30% of patients hospitalised with acute diverticulitis develop complications requiring an operation shortly after admission.<sup>41</sup>

The prospective DIABOLO substudy identified pericolic fluid accumulation and an inflamed colon segment  $>8.6$  cm in length in the initial CT as prognostic parameters for the progression of diverticulitis initially assessed as uncomplicated. On the other hand, detection of pericolic extraluminal air had no prognostic value.<sup>40</sup>

In summary, complicated diverticulitis is a serious illness with an uncertain course that requires permanent, interdisciplinary monitoring and differentiated (conservative/interventional/surgical) therapeutic strategies. The corresponding diagnostic procedures must therefore be immediately available. Constant monitoring, including the review of risk indicators for complicated disease, is a prerequisite for rapid intervention in the event of deterioration (see also Statements and Comments 4.2.0 and 4.2.1).<sup>42–44</sup>

### Recommendation 5.25

If oral fluid intake is insufficient, parenteral fluid substitution should be administered.

Evidence level 3, recommendation grade B, strong consensus

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## Comment—Recommendation 5.25

Complicated diverticulitis is a severe intraabdominal infectious event. There are no specific studies on the value of intravenous fluid replacement; however, general recommendations apply in this situation and clearly call for fluid substitution.<sup>45</sup>

### Recommendation 5.26

Oral feeding can be adapted individually depending on the clinical situation.

Evidence level 5, recommendation grade 0, strong consensus

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There is no evidence for a negative effect of situatively adapted enteral nutrition in complicated diverticular disease. A smaller prospective study of 25 patients showed no disadvantage of a careful stepwise liquid diet during the course of treatment.<sup>46</sup>

#### Recommendation 5.27

In patients with complicated diverticulitis, antibiotic therapy should be administered.

Evidence level 3, recommendation grade B, strong consensus

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#### Comment—Recommendation 5.27

The evidence on this topic is weak, probably because there is a broad clinical consensus. For this reason, the recommendation for antibiotic therapy is not evidenced by targeted studies in this patient group, but must be extrapolated for example, from older studies<sup>47–49</sup> which, however, only sought to compare different antibiotic regimens with one another. Additional pertinent data can be found in a subgroup analysis of the DIABOLO study.<sup>29</sup> Due to the small numbers of cases, the authors are unable to draw any firm conclusions. They do, however, make the recommendation that antibiotic therapy should not be withheld in patients with complicated diverticulitis (in this case Hinchey 1b, no information on comorbidity).

From two study cohorts (including the prospective DIABOLO study), all patients with Hinchey 1a diverticulitis (thickening of the colonic wall >4 mm with limited pericolic inflammation) and free extraluminal, pericolic air were retrospectively selected. The median volume of free air detected in the 109 selected patients was 1.5 cm<sup>3</sup>. 92% of the cases were treated conservatively. 48% of the patients received antibiotic therapy. In the antibiotics group, the median CRP tended to be higher, at 142 versus 115 mg/L, and the median free air volume was significantly greater than in patients who received no antibiotics, at 2.0 versus 1.5 cm<sup>3</sup>. Treatment failure was observed in 7/52 (13%) in the antibiotics group versus 2/57 (4%) in the non-antibiotics group. In the multivariate analysis, antibiotic therapy had no influence on treatment failure; an effect was identified only for increased CRP, with an OR of 1.01 for each mg/L.<sup>10</sup>

The antibiotics recommended for the treatment of complicated diverticulitis are those that cover the expected polymicrobial spectrum of pathogens. There are currently no data indicating a combination therapy to be superior to monotherapy. There is also insufficient evidence as regards the route of administration (intravenous or oral). However, smaller studies have demonstrated the possibility of success with a sequential intravenous/oral therapy.<sup>50,51</sup> The selection and administration route of antibiotic therapy require an individual decision, taking into consideration the patient's overall condition and risk profile as well as any local resistance. Drugs used in clinical routine are cefuroxime, ceftriaxone and ciprofloxacin, as well as metronidazole, ampicillin/sulbactam, piperacillin/tazobactam and moxifloxacin. When making this selection, it should be noted that there is an official warning for fluoroquinolones.

Overall, these statements are derived from general recommendations of guidelines for antibiotic administration in complicated intraabdominal infections,<sup>45</sup> which also offer guidance on the administration route—intravenous or oral—(no preference) and therapy duration. In this case, 4–7 days are recommended, at least in those patients who respond to therapy.

### Chronic uncomplicated diverticular disease (CDD 3a)

#### Mesalazine

#### Recommendation 5.28

Intermittent mesalazine therapy can be given to improve symptoms and prevent symptomatic episodes in chronic uncomplicated diverticular disease.

Evidence level 2, recommendation grade 0, consensus

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#### Comment—Recommendation 5.28

Patients with persistent symptoms (over months to years), often after initial episodes of acute diverticulitis, are classified as having chronic uncomplicated diverticular disease, also known as symptomatic uncomplicated diverticular disease (SUDD). The disease is characterised by typical symptoms (persistent pain of undulating intensity, flatulence, irregular stools), but not by clear inflammatory changes (fever, CRP, tomographic imaging). The therapeutic goal is therefore to improve symptoms or prevent their exacerbation. Two recently published systematic reviews discuss a number of RCTs, some of them placebo-controlled, according to the PRISMA standard.<sup>14,52</sup>

In,<sup>52</sup> the authors analyse 7 publications that describe the symptomatic effects seen in 6 RCTs, of which 4 had a duration of between 12 and 48 months.<sup>52</sup> One placebo-controlled trial is available.<sup>53</sup> In this 4-armed study, patients received intermittent (10 days/month) treatment with either mesalazine 1.6 g/d or *Lactobacillus casei* subsp. DG 24 billion/d or *Lactobacillus casei* subsp. DG 24 billion/d plus mesalazine or placebo, for 12 months. Several interesting findings emerged. Following treatment, 93.3% of patients on mesalazine were symptom-free, compared with 54.0% in the placebo group. A total of 7 (3.1%) patients developed acute diverticulitis, of whom 6 were in the placebo group. A further symptomatic episode of diverticular disease occurred in 8 patients (14.5%) on mesalazine therapy compared with 23 (46.0%) of those on placebo. The effect for maintenance of remission of symptoms after 12 months, as primary endpoint, was thus significant and an NNT of 3 was given by the authors. The review<sup>52</sup> concludes that mesalazine is superior to placebo and other therapies in achieving remission of symptoms in SUDD. However, the quality of the data, especially with regard to the inclusion criteria used in the studies, is criticised.

The most recent systematic review, by Iannone, which also applies the PRISMA methodology, comes to very similar conclusions.<sup>14</sup> After a rigorous selection process, 13 RCTs were included in the



analysis. Six RCTs explicitly concerned patients with uncomplicated diverticular disease, while 7 focussed on uncomplicated diverticulitis (not considered here). Four of the 6 RCTs on SUDD demonstrated a significantly greater reduction in a global symptom score after treatment with mesalazine compared with the control groups. The authors<sup>14</sup> conclude that mesalazine might reduce the frequency of symptomatic episodes and improve quality of life in patients with SUDD.

### Non-absorbable antibiotics (rifaximin)

#### Recommendation 5.29

Rifaximin cannot be recommended for the treatment of chronic uncomplicated diverticular disease.  
Evidence level 2, recommendation grade 0, strong consensus

#### Comment—Recommendation 5.29

Rifaximin is a practically non-absorbable antibiotic approved for a variety of indications including hepatic encephalopathy and travellers' diarrhoea, and has been prescribed off-label for diverticular disease for almost 20 years. It has a broad antimicrobial spectrum of action against gram-positive and -negative as well as aerobic and anaerobic pathogens. The available systematic reviews and meta-analyses date back several years.<sup>18,54</sup> National recommendations on the use of rifaximin in uncomplicated diverticular disease vary widely.<sup>55</sup> Whereas in Italy, Poland and Denmark, there are clear recommendations for a combination therapy consisting of rifaximin and dietary fibre, in other guidelines, rifaximin is either not mentioned or not recommended.

The only existing meta-analysis examined the results of 4 RCTs, all of which investigated a combination therapy with rifaximin/fibre.<sup>18</sup> With regard to the goal of preventing new symptomatic episodes, there was a pooled difference of -2% (95% CI: -3.4 to -0.6;  $p = 0.0057$ ; NNT = 50) versus controls. In the only double-blind study (rifaximin 2x400 mg/d for 7 days/month plus glucomannan 2 g/d compared to glucomannan only), there was no difference in effectiveness.<sup>19</sup>

In the same study,<sup>19</sup> a global symptom score showed significant improvement in both therapy arms; however, after 12 months, the effect was significantly greater in the group treated with rifaximin plus glucomannan. This difference was also found in three open-label studies with a similar design.<sup>18</sup>

A large retrospective study presents findings from an observation of patients with chronic uncomplicated diverticular disease who received intermittent therapy with rifaximin or rifaximin-free treatment. The two groups showed no significant differences in terms of recurrence of a symptomatic episode, need for surgery, or mortality. Likewise, no difference was seen in the intensity of abdominal pain; however, the results for bowel habits and bloating were significantly

better in the rifaximin group. No adverse effects were reported in the rifaximin group.<sup>56</sup>

#### Recommendation 5.30

Probiotics cannot be recommended for maintenance of remission in chronic uncomplicated diverticular disease.  
Evidence level 2, recommendation grade 0, strong consensus

#### Comment—Recommendation 5.30

The role of the intestinal microbiome in diverticular disease is increasingly the subject of interest in the scientific literature, and as a result, a growing focus of scientific research. The therapeutic use of probiotics is based on data describing dysbiosis in diverticular disease.<sup>56</sup>

A current systematic review identified 13 studies of probiotics in all types of diverticular disease that met the PRISMA standard.<sup>22</sup> Four of the 13 studies were uncontrolled. Six of the 9 controlled trials tested a combination of a probiotic and (mostly) mesalazine. The remaining 3 studies compared a probiotic monotherapy twice versus placebo.

In a small study, while *Lactobacillus casei* achieved a similar proportion of symptom-free patients compared with mesalazine after 12 months, the combination of both treatments was significantly superior.<sup>57</sup>

In another RCT,<sup>25</sup> 14.3% of patients in the *Lactobacillus casei* group remained free of symptoms (pain) throughout the 12-month study period, compared to 4.0% in the placebo group. Episodic symptom recurrence occurred in 14.5% on probiotics compared to 46.0% on placebo ( $p = 0.0$ ). During the study, a total of 7/210 patients developed acute diverticulitis, one in the probiotic group and six on placebo.

The most recent RCT is a double-blind study ( $n = 143$ ) from England that compares a multispecies preparation versus placebo in patients with a confirmed diagnosis of uncomplicated diverticular disease (SUDD) and pain that had persisted for at least 3 months.<sup>58</sup> The primary outcome of the study, pain intensity over 3 months of therapy, did not differ significantly between the probiotic and placebo groups. Also, the study yielded unconvincing results for the investigational product versus placebo in 8 different, typical symptoms of SUDD.

### Recurrent diverticulitis without complications (CDD 3b)

#### Recommendation 5.31

Mesalazine should not be used for secondary prophylaxis of recurrent diverticulitis.  
Evidence level 1, recommendation grade A, strong consensus

## Comment—Recommendation 5.31

There are four prospective, randomised, double-blind, placebo-controlled phase 3 studies on the use of mesalazine to prevent relapse of recurrent diverticulitis. The Prevent 1 and Prevent 2 studies, which included 590 and 592 subjects, respectively, had identical study protocols and were published together.<sup>59</sup> The studies included patients who had experienced at least one episode of diverticulitis that had responded to conservative treatment, without surgery, during the last 24 months. The patients were randomised into 4 arms to receive therapy with 1.2 g/day, 2.4 g/day or 4.8 g multimatrix mesalazine or placebo for 104 weeks. The primary endpoint was CT-confirmed recurrence of diverticulitis. In the Prevent 1 study, 53%–63% of patients on mesalazine had no recurrence of diverticulitis, compared with 65% on placebo; in the Prevent 2 study, 59%–69% of patients on mesalazine versus 68% on placebo had no relapse. There was no statistical difference between the 1.2 and 2.4 g groups, respectively, and placebo ( $p = 0.159$ – $0.780$ ), in either study. In the 4.8 g group of Prevent 1, however, there was a statistical difference (52.7% vs. 64%,  $p = 0.047$ ), which was not confirmed in Prevent 2 (67% vs. 64%,  $p = 0.778$ ). In the Prevent 2 study, the time until relapse was statistically even shorter under mesalazine 1.2 and 2.4 g (but not 4.8 g) therapy than under placebo ( $p = 0.013$ ,  $p = 0.044$ ,  $p = 0.179$ ). In Prevent 1, no differences were observed in the time until relapse.

Two jointly published studies, SAG-37, which randomised 345 subjects to 3 g mesalazine granules or placebo for 48 weeks, and SAG-51, which randomised 330 subjects to 1.5 g, 3 g or placebo for 96 weeks, also showed no effect in preventing relapse.<sup>60</sup> The study populations consisted of patients who had experienced at least one episode of uncomplicated diverticulitis confirmed by CT or sonography. The primary endpoint was disease relapse confirmed by clinical and laboratory evaluation within 48 and 96 weeks, respectively. In the SAG-37 study, 67.9% of patients receiving mesalazine were relapse-free, that is, the proportion was not significantly higher than under placebo (74.4%). In the SAG-51 study, the proportion of relapse-free patients on 1.5 g mesalazine (46%) or 3 g mesalazine (52%) after 96 weeks was also not higher than in the placebo group (58%).

In the DIVA trial, a 12-week study of 117 subjects with acute uncomplicated diverticulitis who received placebo, mesalazine (2400 mg) or a combination of mesalazine and Bifidobacterium infantis in three arms, there was no difference in a global symptom score after 12 weeks; a significant difference in favour of mesalazine was seen only in the analysis at 52 weeks. The therapy had no significant influence on the number of recurrences during the follow-up period.<sup>24</sup>

In a placebo-controlled study, intermittent intake of mesalazine for 10 days/month for 1 year also failed to produce any recurrence-preventing effect.<sup>61</sup>

Two meta-analyses confirm the lack of effect of mesalazine in the secondary prevention of uncomplicated diverticulitis.<sup>62,63</sup>

## Recommendation 5.32

Rifaximin should not be used for secondary prophylaxis of recurrent diverticulitis.

Evidence level 5, recommendation grade B, strong consensus

## Comment—Recommendation 5.32

The use of rifaximin to prevent recurrent flares of acute diverticulitis is another topic of intense debate. However, the effect of rifaximin monotherapy on remission maintenance has yet to be examined in a controlled study. There is evidence to suggest that the combination of rifaximin and dietary fibre may have a positive effect with regard to remission maintenance.<sup>64</sup> Most of the trials with rifaximin were conducted in Italy. A position paper of the Italian Society for Gastroenterology concludes that the concept of a therapy with rifaximin is promising, but that its effectiveness still requires investigation.<sup>65</sup>

Probiotics are the subject of much debate. However, there are no reliable studies on the intake of probiotics in stage 3b. (See also review<sup>22</sup>).

It might be speculated that dietary fibre intake could be effective not only in primary prophylaxis but also in secondary prophylaxis, in stage 3b. Unfortunately, there are not enough data to verify this. There is only one study, a small retrospective analysis of 72 subjects, that shows an effect.<sup>66</sup>

There are also no studies investigating the effectiveness of physical exercise, a low-meat diet, or the avoidance of overweight. However, in view of the general health benefits and the high plausibility of a positive effect with regard to chronic diverticular disease, these measures should not be discouraged.

## CHAPTER 6: CHOICE OF OPERATIVE INTERVENTIONS

### Conservative versus operative approach

#### Recommendation 6.1

After acute uncomplicated diverticulitis (CDD 1b), elective sigmoid resection should not be performed in symptom-free patients, regardless of their medical history.

Evidence level 2, recommendation grade B, strong consensus

#### Recommendation 6.2

In patients with acute uncomplicated diverticulitis CDD 1b with persistent symptoms ("smouldering diverticulitis"), elective sigmoid resection can lead to an improvement in quality of life.

Evidence level 2, recommendation grade 0, strong consensus

#### Statement 6.3

To distinguish between micro and macro abscesses, a threshold value of approximately 3 cm can be applied, since this reflects the

Evidence level 3, recommendation grade 0, consensus

(Continues)

(Continued)

possibility of interventional drainage and the risk of recurrence correlates with the size of the abscess.

**Recommendation 6.4** Evidence level 3, recommendation grade B, strong consensus  
 Patients with acute diverticulitis with microabscess (CDD type 2a) should be hospitalised and treated with antibiotics. There is no indication for elective surgery after successful conservative therapy.

**Recommendation 6.5** Evidence level 3, recommendation grade O, strong consensus  
 Larger retroperitoneal or paracolic abscesses (>3 cm) can be interventionally drained (sonography, CT).

All recommendations and statements commented in Supplemental Material.

Complicated acute diverticulitis 6.

## Complicated acute diverticulitis

### Statement 6.6

Patients with acute diverticulitis with macroabscess (CDD 2b) should be hospitalised for antibiotic therapy and referred to a surgeon for examination/co-evaluation.

Evidence level 2, recommendation grade A, strong consensus

### Comment—Statement 6.6

Complicated acute diverticulitis with macroabscess is a potentially life-threatening condition. A Danish registry analysis of 3148 patients reported a 30-day mortality rate of 8.7%. Only a small proportion, 6%, of patients was reported to have undergone surgery during the initial inpatient stay.<sup>67</sup>

The proportion of patients who fail to show adequate clinical improvement, or even deteriorate, under first-line non-surgical therapy and go on to require surgery during the initial inpatient stay, varies greatly in the available literature, ranging from 5%<sup>68</sup> to 33%.<sup>69</sup>

A current multi-centric retrospective study from the Netherlands reports that 8.9% of patients require urgent emergency surgery after initial conservative therapy.<sup>70</sup> The only prospective randomised study available on complicated acute diverticulitis found that 11% of patients with treatment failure required emergency surgery.<sup>71</sup>

The risk increases with the size of the abscess and the need for percutaneous drainage. A meta-analysis of 22 studies including 1051 patients, 50% of whom had percutaneous drainage, showed a 30% failure rate of primary conservative therapy.<sup>72</sup> The risk of failure of primary conservative therapy is higher in patients with abscesses than in patients with evidence of extraluminal air (15.6%).<sup>73</sup> A large American registry study showed that twice as many patients required surgery during the first hospital stay due to

failure of initial conservative therapy of an abscess compared with an overt perforation, since the latter occurs correspondingly less frequently.<sup>74</sup>

It is not possible to predict the success of primary non-surgical therapy based on the radiological criteria of the initial CT.<sup>75</sup>

In patients who fail primary conservative therapy, urgent surgery has a relevant mortality risk (5.8%); however, antibiotic therapy alone was reported to have a 30-day mortality rate of 10.1%.<sup>76</sup> It is therefore vitally important that failure of primary conservative therapy is recognised in good time, so that the indication for surgery can be quickly made and the procedure performed without delay, in order to avoid subsequent complications. An American registry-based cohort study with 2119 patients reported a significant increase in postoperative morbidity depending on the timing of surgery within the first week after admission (from 38% within the first 24 h to 61.8% after more than one week; 0.001) and an increase in the postoperative length of stay (from 10.72 ± 9.35 days to 22.73 ± 12.06 days;  $p < 0.001$ ).<sup>77</sup>

As yet, however, there are no evidence-based and clearly defined criteria to define the failure of conservative therapy. There are also no reliable predictors for the failure of conservative therapy. Close monitoring with interdisciplinary follow-up, including the involvement of a surgeon, is therefore recommended.

### Statement 6.7

About a third of patients with acute complicated diverticulitis are readmitted due to a recurrence of diverticulitis, usually within a year.

Evidence level 2, strong consensus

### Comment—Statement 6.7

A systematic review on the frequency of recurrence after acute diverticulitis, including 35 studies with 396,676 patients, described an abscess to be the main risk factor for relapse, with a risk approximately double that observed after uncomplicated diverticulitis. Furthermore, >50% of relapses were again complicated, while 88% of recurrences after uncomplicated diverticulitis were also uncomplicated. Abscess size ( $\geq 5$  cm), drainage placement and a retroperitoneal localisation have been described as risk factors for a recurrence of diverticulitis.<sup>78</sup>

A systematic review from 2016 specifically focussing on complicated acute diverticulitis with abscess reported an overall recurrence rate of 25.5% (7653 patients) from 23 evaluated studies with 1206 patients. In this collective, the risk of relapse in patients who had had additional percutaneous drainage was lower than after antibiotic therapy alone (15.9% vs. 22.2%, 560 vs. 126 patients).<sup>79</sup>

Another systematic review from 2014, also specifically examining complicated acute diverticulitis with abscess, evaluated comparatively more patients with additional percutaneous drainage (49%). The

authors found a recurrence rate of 28% in this collective; ultimately, only 28% of the patients were able to avoid surgery in the long term.<sup>72</sup>

In the first published, prospective, randomised study on complicated acute diverticulitis with abscess (or extraluminal air), the reported rate of recurrence within 3 years of conservative therapy was 32%, whereby all relapses were complicated.<sup>71</sup>

However, a few cohort studies have reported considerably lower (10%<sup>80</sup>) or higher (60%<sup>81</sup>) recurrence rates.

In addition, large-scale registry-based cohort studies with a large number of cases are available from Denmark, Canada and the USA. The Danish study, with 3148 patients, reports relapse rates of 15.5% after antibiotic therapy alone and 23.6% in patients with additional percutaneous drainage,<sup>67</sup> while the Canadian study of 14,124 patients reports a 12% relapse rate.<sup>82</sup> In the American study, which analysed the records of 237,879 patients, abscesses were identified as the main influencing factor for relapse (OR 1.67, risk 14.0%–18.2%) and poor outcome (OR 3.84, risk 10.2%–13.7%).<sup>83</sup> Across all studies, >50% of recurrences were reported within 1 year of complicated diverticulitis.

In summary, despite the heterogeneity of the data, it can be concluded that the risk for complicated relapse after successful antibiotic or interventional therapy of acute complicated diverticulitis with macroabscess is significantly higher than after uncomplicated diverticulitis. The absolute risk of recurrence was reported in the systematic reviews and the one available randomised study to be between 25% and 28%.

#### Recommendation 6.8

Patients who have been successfully treated conservatively or inter-  
ventionally for complicated acute diverticulitis with macroabscess  
(CDD 2b) can be offered surgery in the inflammation-free interval.  
Evidence level 2, recommendation grade 0, strong consensus

### Comment—Recommendation 6.8

Numerous cohort studies report that in the long term, the majority (56%–83%) of patients with initial complicated acute diverticulitis with macroabscess underwent surgery.<sup>71,80,84</sup> However, the indication for elective surgery is often not described in detail. Whether surgery was indicated because of recurrent inflammatory flares, persistent symptoms or primarily as a result of the initial flare is unclear.

Larger registry-based cohort studies report a significantly lower rate of elective surgery in the longer term (e.g., 16% of 3148 patients<sup>76,79</sup>; 18.6% of 10,342 patients<sup>85</sup>). In the past, the indication for elective surgery after complicated diverticulitis was based, among other things, on the presumed risk of overt perforation in the event of relapse. However, newer studies have shown that the risk of perforation is at its highest during the initial flare.<sup>86</sup>

The only available prospective, randomised study on complicated acute diverticulitis shows that long-term conservative therapy is also possible without the risk of perforation or urgent surgery; on the other hand, the risk of recurrence is considerably increased

(32% vs. 9%; all relapses complicated<sup>71</sup>). However, this study has important limitations: in addition to its monocentric design and the low number of cases, only 49/107 (45%) randomised patients had an abscess, whereas in the majority of cases, only extraluminal air beads without abscess formation were described. Neither the symptoms, nor the quality of life of the patients were analysed in this study.

An American registry study with 10,342 patients found that the 5-year mortality risk for a recurrence of diverticulitis was 1.9% for patients treated conservatively and 0.6% for patients who underwent surgery. In this study, the postoperative 30-day mortality rate was 0.2%.<sup>85</sup>

A US registry analysis with 210,268 patients reported a mortality risk of 2.2% for recurrent diverticulitis with repeated conservative therapy, compared to 4.6% with urgent surgical therapy. In contrast, postoperative in-hospital mortality after elective surgery was 0.3%.<sup>86</sup> Results of the Danish registry analysis, with 1248 patients, indicate a 5-year mortality risk from recurrent diverticulitis of 2.0% after conservative therapy with percutaneous drainage, compared with 1.1% after antibiotic therapy alone and 0.6% after surgery ( $p = 0.24$ ).

Overall, these data show that elective surgery can significantly reduce the risk of death due to recurrence of diverticulitis, provided that patients with a low surgical risk are operated on by surgeons with the appropriate expertise.

Galentin's review summarises the 11 internationally available guidelines on diverticulitis<sup>87</sup>: Five of the guidelines recommend elective surgery after complicated diverticulitis, four give qualified recommendations for elective surgery after complicated diverticulitis, and two make no statement on this issue. The most recent NICE Guideline, from the UK National Institute for Health and Care Excellence, recommends considering surgery if symptoms of diverticular disease persist after successful conservative therapy.

In addition to further investigating the risks of relapse, perforation or emergency surgery, more recent studies focus increasingly on patient quality of life.<sup>88,89</sup> In a German cohort study with 290 patients, albeit with a low follow-up rate (47.6%) and a correspondingly high selection bias, patients who had undergone elective sigmoid resection for complicated diverticulitis with macroabscess had a significantly better quality of life than patients treated conservatively.<sup>89</sup> The first prospective randomised study on the effectiveness of elective resection for persistent symptoms after diverticulitis also includes a high proportion of patients with primary abscess formation.<sup>88</sup>

In summary, due to the relevant risks of relapse and mortality and the frequent improvement in quality of life, patients whose overall condition is good can be offered elective surgery. The advantages and disadvantages of surgery, as well as the risks of a wait-and-see tactic, should be discussed with the patient, based on the individual risks of surgery, recurrence and complications. This particularly applies to patients whose symptoms persist after conservative therapy.

**Statement 6.9**

An elective operation after successful initial conservative therapy of acute complicated diverticulitis with macroabscess should be performed ca. 6 weeks after completion of the conservative therapy. Evidence level 2, recommendation grade B, strong consensus

**Comment—Statement 6.9**

All of the studies mentioned above show that the highest incidence of relapse is within the first year after index diverticulitis. The available Kaplan-Meier curves for recurrence of diverticulitis also clearly show that the risk of relapse is significantly higher during the first 6 months than in months 7–12.<sup>67,82,86</sup> In a cohort study with 210 patients, the median time interval until recurrence was 3.5 months.

Accordingly, on the basis of their retrospective registry study, Gregersen et al. recommend that elective surgery should be performed as soon as possible after the acute symptoms of inflammation have subsided.<sup>67</sup>

Regarding the optimal timing of elective surgery, a systematic review compared patients who underwent surgery within 6 weeks with those operated after a longer interval, on the basis of 4 cohort studies. No differences were found with regard to the risks of anastomotic insufficiency or postoperative mortality. However, based on moderately heterogeneous study data, the authors found both a longer duration of operation and a higher risk of conversion to open surgery in patients who underwent early elective surgery.<sup>90</sup>

In summary, elective surgery should be performed early to minimise the risk of a recurrence of diverticulitis. However, since (too) early operation can be associated with difficult operating conditions, an interval of 6 weeks should be allowed after the infection has entirely cleared, with a corresponding convalescence period.

**Conservative versus operative approach—Complicated (recurrent) Diverticulitis**

**Recommendation 6.10** Evidence level 3, recommendation grade B, consensus  
Patients with overt perforation and peritonitis in acute complicated diverticulitis should be operated on within 6 h after diagnosis (emergency surgery).

**Recommendation 6.11** Evidence level 4, recommendation grade B, strong consensus  
Symptomatic uncomplicated diverticular disease (CDD 3a) should not be treated surgically.

**Recommendation 6.12** Evidence level 2, recommendation grade B, strong consensus  
The risk of recurrence in chronic recurrent diverticulitis CDD 3b increases with each flare. The risk of perforation is highest during the first episode and decreases with each subsequent relapse. Therefore, the indication for surgery should not be determined by the number of previous flares.

(Continued)

**Recommendation 6.13** Evidence level 2, recommendation grade B, strong consensus  
Elective sigmoid resection can significantly improve quality of life in patients with chronic recurrent diverticulitis CDD 3b. Impairment of quality of life due to recurrent disease should be an important determinant in decision-making when considering elective surgery in these patients.

**Statement 6.14** Evidence level 1, strong consensus  
The risk factors for a complicated postoperative course in patients with chronic recurrent sigmoid diverticulitis CDD 3b correspond to the general risk factors for elective colon resection.

**Statement 6.15** Evidence level 3, recommendation grade B, strong consensus  
Chronic recurrent diverticulitis CDD 3c with evidence of fistulas should be treated surgically.

**Recommendation 6.16** Evidence level 3, recommendation grade B, strong consensus  
Chronic recurrent diverticulitis CDD 3c with evidence of symptomatic colonic stenosis should be treated surgically.

All statements and recommendations commented in Supplemental Material.

**CHAPTER 7: CHOICE OF OPERATIVE INTERVENTIONS**

**Recommendation 7.1**  
If technically possible, minimally invasive sigmoid resection should be favoured over open surgery. Evidence level 2, recommendation grade B, strong consensus

**Comment—Recommendation 7.1**

The minimally invasive approach has been shown to be superior with respect to minor complications. In addition, the patients' quality of life is postoperatively better in the short-term after minimally invasive surgery.<sup>91</sup> Other outcomes of the open and laparoscopic procedures (major complications, long-term quality of life) are considered comparable.<sup>92</sup> Minimally invasive sigmoid resection is also technically feasible in patients with colovesical fistula<sup>93,94</sup> or right-sided diverticulitis.<sup>95</sup>

**Statement 7.2**  
The total laparoscopic operation, the laparoscopy-assisted operation, the robot-assisted operation, and hand port procedures are all proven, safe, and effective. Evidence level 3, strong consensus

## Comment—Statement 7.2

Comparative studies on different minimally invasive procedures are available only with a low level of evidence and show no relevant differences.<sup>96</sup> It is therefore not possible to make a relative assessment of the individual procedures.

**Recommendation 7.3** Evidence level 2, recommendation grade B, strong consensus  
In perforated sigmoid diverticulitis with generalised peritonitis (CDD 2c1/2), sigmoid resection with primary restoration of continuity, with anastomosis and protective ileostomy, should preferentially be performed as the standard surgical procedure. In patients who are unstable or have sepsis, the Hartmann procedure should be performed.

**Recommendation 7.4** Evidence level 2, recommendation grade B, strong consensus  
In patients with perforated diverticulitis with purulent peritonitis (CDD 2c1), primary sigmoid resection should be performed. A potential alternative therapeutic strategy is laparoscopic peritoneal lavage and drainage, without resection.

**Recommendation 7.5** Evidence level 3, recommendation grade O, strong consensus  
The “damage control” procedure, with sigmoid resection and blind closure of the ends of the bowel, and abdominal vacuum therapy with two-stage anastomosis max. 72 h after successful treatment of the abdominal infection, can be used as a treatment strategy for diverticulitis CDD 2c1/2.

**Recommendation 7.6** Evidence level 3, recommendation grade B, strong consensus  
The oral resection margin for sigmoid resection should be chosen directly proximal to the acutely or chronically inflamed bowel segments. Additional diverticulum-bearing bowel segments without inflammatory or post-inflammatory changes should not be resected.

**Recommendation 7.7** Evidence level 3, recommendation grade B, strong consensus  
The aboral resection margin should be situated in the upper rectum.

**Recommendation 7.8** Expert consensus, strong recommendation, strong consensus  
A tension-free, well-perfused and leak-tight anastomosis should be created. If this requires mobilisation of the left flexure, this should be performed.

**Recommendation 7.9** Evidence level 3, recommendation grade B, strong consensus  
Ligation of the inferior mesenteric artery central to the origin of the left colic artery should not be performed.

(Continued)

**Statement 7.10** Evidence level 1, strong consensus  
Provided the anastomosis is technically correctly performed, stapler and hand sutures are to be regarded as equivalent.

**Recommendation 7.11** Evidence level 4, recommendation grade B, strong consensus  
Anastomotic insufficiency after sigmoid resection should be treated using a step-by-step approach, depending on clinical severity. If diffuse peritonitis occurs, reoperation with (protective or terminal) stoma creation should be performed.

All recommendations and statements commented in Supplemental Material.

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## CONFLICT OF INTEREST

Honoraria for talks AllergoSan, Graz, Austria. Falk, Freiburg, Germany. Ferring Arzneimittel, Kiel, Germany. Nikkiso, Langenhagen, Germany. Consultation and studies Falk Pharma, Freiburg, Germany. Ferring Arzneimittel, Kiel, Germany. No other conflict of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in [repository name for example, “figshare”] at [http://doi.org/\[doi\]](http://doi.org/[doi]), reference number [reference number].

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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