



Diverticular Disease-among Myths, Paradigms and Scientific Evidence

Divertiküler Hastalık-mitler, Paradigmalar ve Bilimsel Kanıtlar Arasında

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ABSTRACT

Diverticular disease is among the most common gastrointestinal disorders affecting the Western population. Although complications arising from colonic diverticula significantly affect a patient's quality of life and the overall health sector, the scientific evidence to facilitate its better management is limited in the literature. Several recommendations and guidelines have been made, albeit based on expert opinions rather than on the outcomes of controlled clinical trials. The more recent research on the natural history of this disorder has led to a shift from the historic dogmatic recommendations to a more individualised approach.

Keywords: Diverticular disease, epidemiology, risk factors, conservative treatment, surgery

ÖZ

Divertiküler hastalık, Batı'da en sık görülen gastrointestinal bozukluklar arasındadır. Kolonik divertikülden kaynaklanan komplikasyonlar, hastaların yaşam kalitesi ve sağlık hizmetleri sektörü üzerinde önemli bir etkiye sahip olmakla birlikte, divertiküler hastalığın tedavisi için bilimsel kanıtların sınırlı olduğu kabul edilmelidir. Pek çok öneri ve kılavuz, kontrollü klinik çalışmaların sonuçlarından ziyade uzman görüşüne dayanmaktadır. Bununla birlikte, bu bozukluğun doğası ile ilgili yeni araştırmalar, tarihsel dogmatik önerilerden daha kişiselleştirilmiş bir yaklaşıma geçişe yol açmıştır.

Anahtar Kelimeler: Divertiküler hastalık, epidemiyoloji, risk faktörleri, konservatif tedavi, cerrahi

Introduction

Diverticulosis and its associated problems can be regarded as one of the most common gastrointestinal disorders affecting the Western world, and it is ranked among the top 10 diagnoses in an outpatient setting.¹

Diverticulosis was previously regarded as a rare disease that was diagnosed mainly based on the presentation of the clinical symptoms, and an increasing incidence of this disease was recorded with the beginning of the industrial revolution; however, this was long before the possibility arose to use modern diagnostic tools such as flexible endoscopy and computed tomography (CT).² This situation led to the development of "scientific assumptions" about the pathogenesis of diverticulosis and about diverticulitis

leading to therapeutic recommendations, which began to be questioned with modern ongoing research.

As an example of this development, a past publication reported a risk of up to 25% of experiencing an episode of diverticulitis for all patients with asymptomatic diverticula, which was then revised to a maximum of 5% based on more recent findings.³

Similarly, the risk of having recurrent attacks following the first event of diverticulitis has been largely overestimated.^{4,5} Back in the 90s of the last century, the recurrence rates of 45%-60% (which was associated with higher complication rates and morbidity) were considered acceptable^{4,5}, leading to therapeutic consequences (e.g. indication for surgery), which have also been completely questioned in the meanwhile.⁶



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Furthermore, it has been shown (contrary to previous, conventional perceptions) that increasing age is not associated with a higher risk for the development of diverticulitis. In this context, Strate et al.⁷ demonstrated a decrease of 24% risk for diverticulitis per every additional decade of life.

This review attempted to elucidate some of the shifts of paradigms observed in the medical literature in the last decades as well as to indicate the updated recommendations for the management of this disorder (which varies partly among different societies and are partly under critical review).⁸

Classification

Diverticula per se cannot be regarded as a disease, since most of the patients will not experience symptoms from this condition and will not need any specific medical intervention.⁹

Potential complications include those that may arise due to inflammation, haemorrhage or pain and functional issues.

Therefore, the classification for diverticular disease includes the following entities:

- a. Symptomatic Uncomplicated Diverticular Disease (SUDD)
- b. Segmental Colitis Associated with Diverticulosis (SCAD)
- c. Diverticulitis (complicated or uncomplicated)
- d. Diverticular Haemorrhage

SUDD

SUDD is characterised by gastrointestinal (unspecific) and chronic symptoms in patients with diverticula, but without any evidence of inflammation or a history of diverticulitis.¹⁰

However, patients with SUDD show microscopic inflammatory infiltrates, contrary to healthy controls and sigmoid resection has been successful in acquiring pain resolution in >80% of the patients operated for persistent symptoms associated with SUDD. It is further noteworthy that, after histological evaluation of the resected colonic specimens, a majority (>75%) of the patients revealed features of deep bowel inflammation, despite no clinical history of diverticulitis.^{11,12}

Contrary to this finding of “occult, chronic inflammation”, an overlap of SCUDD with irritable bowel syndrome (IBS) has also been described with similar pathophysiological mechanisms, including visceral hypersensitivity.⁷ Although some further evidence for a similarity of SCUDD with IBS has been demonstrated (altered colonic motility due to a reduction in the colonic interstitial cells of Cajal), at this time point, the exact pathomechanisms and the correlation between both the entities remain unclear and, in fact, only speculative.^{7,13}

SCAD

SCAD is a subtype characterised by abdominal pain (mainly in the left lower quadrant), chronic diarrhoea (contrary to SUDD wherein constipation is predominant) and occasional episodes of bleeding. Endoscopic and histologic features are non-specific and can also be observed in inflammatory bowel disease (IBD).¹⁴ In a prospective study, Tursi et al.¹⁴ analysed more than 6,000 patients who underwent a colonoscopy for the above-mentioned symptoms matching IBD-like changes in 11.4% of the patients with concurrent diverticula. In their series, SCAD was mainly noted in male patients of age >60 years.

Consensus and/or recommendations regarding therapy and the outcomes are lacking due to the missing data from appropriate studies; however, there is some evidence that SCAD shows good response to medical therapy (mainly 5-ASA), but with a recurrence rate of >40%.^{15,16}

Acute Diverticulitis

With the ongoing diagnostic progress as well as the availability of therapeutic options, acute inflammation of colonic diverticula requires a more distinct classification. Historically only diagnosed based on the clinical examination and barium enema, the introduction of CT as well as laboratory tests has led to the possibility of distinguishing patients with “diverticulitis” and with “complicated diverticulitis”.

While there is a certain acceptance that a triad of left-sided lower abdominal pain, absence of vomiting and a C-reactive protein level of >5 mg/dL has a high sensitivity to define acute diverticulitis, CT is considered necessary to identify patients with complicated diverticulitis (such as abscess, perforation, fistula and stenosis).⁸

Galetin et al.⁸ reviewed 11 national and/or international guidelines for diverticular disease and noted a concordance about the necessity to apply imaging methods for the diagnosis of symptomatic patients (11 out of 11 guidelines); however, a certain discordance was noted regarding the role and time point for the use of CT or ultrasound, respectively. When CT was used, 7 of the 11 guidelines were in favour of the Hinchey score¹⁷ to classify the severity of the disease; however, other scoring systems have also been repeatedly published^{18,19,20} in the literature (Table 1).

It has been widely accepted that a distinction between patients with uncomplicated (e.g. Hinchey class I or Neff grade 0 in CT imaging) and complicated diverticulitis via a classification system may lead to the development of different therapeutic consequences (e.g. inpatient vs. outpatient treatment, antibiotic therapy vs. no antibiotic therapy).^{21,22}

Table 1. Classification systems for acute diverticulitis

Stage	Hinchey	Ambrosetti	Neff	Buckley
I	Abscess	Wall thickening (<5 mm)	Wall thickening and/or fat stranding	Wall thickening and/or fat stranding
II	Contained pelvic abscess	Pericolonic fat stranding	Locally complicated diverticulitis	Wall thickening >3 mm and/or small abscess
III	Purulent peritonitis	Abscess	Localised pneumoperitoneum	Wall thickening >5 mm and/or free air and/or abscess >5 mm
IV	Faecal peritonitis	Extraluminal air	Abscess <4 mm	
V		Extraluminal contrast	Abscess >4 mm in the pelvis	
VI			Abscess in the abdominal cavity	
VII			Significant pneumoperitoneum and/or intra-abdominal free liquid	

Diverticular Haemorrhage

Diverticular bleeding typically presents as acute-onset, painless haematochezia, but with no evidence of other colonic lesions (e.g. polyps, haemorrhoids and cancer) or bleeding sites identified on colonoscopy.

The mean incidence was recorded to be approximately 14 cases per 100,000 inhabitants per year by a recent publication from Iceland, and no change in the incidence rate has been observed over the last decade.²³ Advanced age, hypertension, coronary heart disease as well as medication associated with anti-coagulative or anti-thrombotic properties (such as aspirin, NSAID, clopidogrel, warfarin and NOAC) have been described as risk factors for colonic and/or diverticular bleeding.^{24,25}

Although the majority of these patients can be managed successfully via conservative treatment, an elective colonoscopy following haemodynamic stabilisation and appropriate bowel preparation within the first 24 h has been suggested.²⁶

An early endoscopic evaluation is recommended to establish the definitive diagnosis, albeit with the possibility to localise and eventually treat the potential bleeding source.^{26,27}

If endoscopy fails to provide an exact localisation of the origin of bleeding; angiography, CT angiography or 99 mTc erythrocyte scintigraphy can also be performed.²⁷ All of these methods are limited due to the possible institutional issues as well as due to the need for a certain intensity of bleeding.

Barium enema has been historically used as the main diagnostic tool for diverticular diseases until the introduction of CT. For haemorrhage resulting from diverticula, some authors see a certain role for barium enema as a potential

therapy for frail patients who are not fit for surgery or in whom other therapeutic measures have failed.^{28,29} In collective reports, barium enemas have been described as being beneficial either due to its tamponade effect or due to the direct haemostasis resulting from barium. However, there does not exist any sufficient evidence for a strong recommendation for this approach.

The role of surgery is limited to the rare situation when bleeding cannot be controlled by conservative and/or endoscopic/radiological measures and rather consists of total colectomy or segmental colectomy, when the localisation of the bleeding source has been established.²⁷

Risk Factors

Fibres

The common belief that diverticulosis is strongly associated to the Western lifestyle based on dietary factors dates back to the publication of Burkitt et al.³⁰ of >4 decades ago.

Their hypothesis about the decrease in colonic transit time due to the low-fibre diet (which is associated with high pressure in the sigmoid colon) has been questioned based on the outcomes of colonic motility studies as well as epidemiological evidence.^{31,32}

Recently, diet has been challenged as the main risk factor responsible for diverticulosis and diverticular disease following recent epidemiological and genetic studies.^{33,34,35,36} Based on anatomic studies showing the prevalence of diverticulosis in the right colon in the Asian population, the role of the “high pressure problem” in the sigmoid colon had to be revised. In addition, several studies dealing with population migration have failed to demonstrate an increase of diverticular disease and/or its related complication as well as a shift from the right sided to sigmoid localisation due to

a change to the Western lifestyle, thus proposing a genetic impact.^{33,34,35,36}

Analysis of the Swedish twin registry by Granlund et al.³⁷ revealed an odds ratio of 7.15 to develop diverticular problems in monozygotic twins compared to only 3.2 for dizygotic twins. These results were partly confirmed by another study from Denmark that calculated a 40%-50% risk of developing diverticular disease based on the genetic factors.³⁸

Furthermore, genome-wide studies conducted in Iceland and Denmark have identified variants in genes that were associated with diverticular disease (namely, ARHGAP15, COLQ, FAM155A) as well as variants in FAM155A, which were detected specifically in diverticulitis.³⁹

Furthermore, the role of a fibre-poor diet as the only and the main causative factor has also been questioned by studies that could not determine any association between the fibre intake and the risk for the development of diverticulosis.^{40,41} However, these results have been mainly based on one single study with a certain methodological limitation.

Despite these concerns about the “low fibre/high pressure hypothesis”, a correlation of fibre intake and the risk for diverticular disease has been supported by two prospective studies which suggested that a low-fibre diet is associated with increased symptoms in patients with diverticular disease as well as with increased rates of hospital admission and deaths.^{42,43}

There is strong evidence that different sources of dietary fibre may have different effects on the disease risk, which may explain the previous conflicting results on this topic.⁴³ In the “Million Women Study” by Crowe et al.⁴⁴, the type of fibre (i.e. from fruit or vegetables) played a key role on the effect observed from diverticular disease. A total of 690,075 women with known diverticular disease and with a consistent diet since >5 years were followed for 6 years and assessed by using a standardised (40-item) food questionnaire. The survey results revealed that 17,325 women were admitted to the hospital or died from a diverticular disease. Data analysis revealed a strong association between the risk of diverticular disease and the source of fibre, the reduced risk being strongest for cereal and fruit fibres.⁴⁴

In summary, the assumption of a high-fibre diet as a prevention against the development of colonic diverticula (as suggested in the past) has rather shifted to a strong recommendation for fibre-rich diet as a preventive measure against the development of complications associated with diverticula.^{8,45}

Nuts, Seeds and Corn

Historically, physicians have advised that individuals with diverticular disease should avoid nuts, seeds, popcorn, corn

and other high-residue foods.^{46,47} The recommendation that individuals with this condition should avoid them has evolved merely based from a theoretical assumption that a luminal, mechanical trauma could serve as a causal mechanism triggering inflammatory processes with subsequent diverticulitis, perforation or bleeding.

Contrary to this report, a histological study on bleeding colonic diverticula noted the absence of mucosal inflammation.⁴⁸ In fact, abnormalities were only recorded at the vasa rectum and involved intimal thickening near the site of bleeding as well as an asymmetric rupture toward the lumen.

Nuts and seeds do not appear to increase the risk, and in a large, prospective cohort (the Health Professionals Follow-up Study), nuts and popcorn were associated with a reduced risk of diverticulitis.⁴⁹ In fact, 47,228 US men (aged: 40-75 years) who were free of diverticular disease were evaluated by using a food-frequency questionnaire. During a follow-up of 18 years, 801 cases of diverticulitis and 383 cases of diverticular bleeding were identified. Multivariate analysis did not reveal any associations between corn consumption and diverticulitis or between nut, corn or popcorn consumption and diverticular bleeding or uncomplicated diverticulosis. Contrary to this report, an evidence has been provided for a protective effect of these food items.^{49,50}

This observation is also supported by the findings for patients with cardiac disorders showing that nuts are rich in nutrients with anti-inflammatory properties, such as vitamin E, α -linoleic acid and other unsaturated fatty acids and phytochemicals.^{51,52} Nut consumption has been reported to have a protective action against certain inflammatory disease states.^{51,52}

In addition to some of these contradictions against historical believes, the so-called “typical” Western lifestyle is associated with an increased risk for the development of complicated diverticular disease. The lack of physical activity, obesity (with a special emphasis on central obesity), greater consumption of red meat and fat as well smoking has been shown to lead to a higher incidence of diverticulitis.^{50,53,54}

Microbiome and the Role of Probiotics

In general, the role of colonic microbiome can be considered as a basis for an intact mucosal barrier protecting against intraluminal inflammatory factors as well for providing an intact defence system against inflammation. Short-chain fatty acids (SCFAs) are regarded as one of the “key players” that support this function as they are responsible for an increased production of mucus and antimicrobial peptides, thus mediating an unimpaired colonic barrier function and homeostasis, respectively.

Past studies on the microbiome in patients with diverticular disease have provided evidence of a decrease in bacterial population, which are the main producers of SCFAs.⁵⁵

Furthermore, a depletion of Clostridium Cluster IV-usually a group of bacteria with anti-inflammatory properties has been described during the inflammatory processes of the colon, which suggest that a decrease in the population of anti-inflammatory gut bacteria together with an increase in mucosal inflammation may play a role in the development of diverticulitis.⁵⁶

Apart from the impairment of the protective system that should be supported by an intact colonic microbiome, dysbiosis of the microbiota is supposed to be associated with inflammation.⁵⁷ In this context, Barabara et al.⁵⁷ showed a 70% increase in colonic macrophages during the study of the microbiome as well as the metabolome in patients with diverticulitis.

This observation as well as other research provide a strong evidence that several mechanisms per se or together, including pathogenic bacterial overgrowth (due to an impairment of the competitive bacterial inhibition), or a decrease in the tight junction integrity lead to the deterioration of the mucosal defence as a step toward development of inflammation in the colon.⁵⁷

Therefore, the idea to use probiotics in order to promote adequate bacterial colonisation so as to restore the healthy colonic microenvironment appears to be an attractive therapeutic approach.

Although single-controlled trials using probiotics for diverticular diseases have occasionally shown a trend toward a positive clinical response on the abdominal symptoms or their recurrence, most of them have failed to present an effect in preventing complications and/or recurrence in the future.^{58,59,60}

Accordingly, the AGA (as well as most other guidelines of Western associations) does not recommend probiotics as a standard therapy for diverticular diseases.⁴⁵

Treatment

Historically, patients with diverticulitis had to be admitted to hospital, followed by conducting a treatment involving restriction to a fluid diet and intravenous antibiotics therapy; these therapeutic recommendations were not based on modern scientific evidence.⁶¹

In addition, strong criteria for elective surgery were considered appropriate to prevent the recurrence of diverticulitis and/or the risk for perforation, but the modern research strongly contradicted against these older dogmas. However, recently, newer concepts with a tendency toward a less aggressive treatment approach have evolved in surgery as well as in conservative therapy.

Conservative Treatment

Antibiotics

Beside several observational studies, two randomised trials compared patients with uncomplicated diverticulitis (Hinchey 1) who received either antibiotics (intravenously, followed by oral administration) versus a control group with intravenous fluids only or intravenous antibiotics versus observation alone, respectively.^{62,63}

Both studies (one conducted in Sweden and Iceland and the other in the Netherlands) could not find any benefit for antibiotic treatment with regard to the time of recovery and/or the rate of development of subsequent complications.^{62,63}

Although several societies have subsequently stopped recommending antibiotics for patients with uncomplicated diverticulitis.^{64,65}, this approach must be regarded more critically based on the recent data from longer follow-up studies.⁶⁶ In a Dutch analysis conducted after 2-year follow-up, the evidence showed that a higher number of patients in the placebo group (7.7%) went for elective surgery due to recurrent symptoms when compared to the antibiotic group (4.2%).⁶⁶ Furthermore, this rate could have markedly increased as some patients were rated as censored owing to the fact that they were included into another trial (elective surgery versus conservative management), which prevented a much higher rate of patients who required surgery in the longer follow-up study.⁶⁷ Therefore, we believe that a final recommendation for the need of antibiotics (as well as dietary management) in the treatment of uncomplicated diverticulitis will require further well-designed trials in the future.

In or Outpatient Treatment

Back in 1998, oral hydration and oral antibiotics were proposed for patients with uncomplicated diverticulitis, but recommendations for outpatient management of this population were vague.^{61,68}

More recently, a Spanish study (DIVER trial) attempted to evaluate the role of outpatient treatment. They randomised 132 patients and found that four patients in group 1 (inpatient treatment) and three patients in group 2 (outpatient treatment) showed no significant difference with regard to treatment failure ($p=0.619$), recommending the management of patients with uncomplicated diverticulitis in an outpatient setting.⁶⁹

The results of the present study and those of other clinically controlled trials suggest a high concordance among societies proposing the possibility for outpatient treatment in uncomplicated diverticulitis; however, certain individual factors (e.g. the lack of compliance and/or care at home and immunocompromised patients) still need to be considered.^{8,69,70}

Rifaximin and Mesalamine

Rifaximin is a non-absorbable oral antibiotic with good effectivity in the intestinal tract. Based on the belief that rifaximin can reduce the bacterial overgrowth and improve the microbiota, it was primarily used as a treatment for SUDD.⁷¹ Four prospective randomised trials (totally 1,660 patients) noted an improvement in symptoms within one year (64% with rifaximin versus 34% in the control arm); however, the effect of rifaximin on the reduction of recurrence episodes of diverticulitis has not been proven until date.⁷² Therefore, there exists no uniform concordance regarding the recommendation for its use. On the other hand, the Italian Society of Gastroenterology (SIGE) regards the cyclic use of rifaximin, in association with high-fibre intake, as safe and useful for the treatment of SUDD.⁷³ Contrary to this recommendation, the American Gastroenterological Association (AGA) disapproves the use of rifaximin as an agent preventive against the recurrence of diverticulitis.⁴⁵

Due to the chronic inflammation during the pathogenesis of patients suffering from SUDD a possible beneficial effect of mesalamine has been postulated based on the outcomes of a randomised trial conducted over 12 weeks after an episode of acute diverticulitis.⁷⁴ Although the symptoms scores suggested some improvement, no effect on recurrence could be evaluated. Moreover, a larger randomised, double-blinded placebo-controlled trial (1,182 patients) did not find any beneficial effect of mesalamine in preventing the recurrence of diverticulitis as well as for the necessity of surgery.⁷⁵ These findings are in accordance with those of a meta-analysis describing no evidence for the reduction of recurrent episodes of diverticulitis by using mesalamine.^{76,77} However, its role in the treatment of patients with SUDD remains debatable.⁷⁸

Surgery

Elective Surgery

Historically, diverticulitis was regarded as a progressive disease in which the possibility of developing complications was strongly related to the number of recurrent episodes.⁷⁹ This perspective led to the recommendation for a more aggressive surgical approach in order to prevent the chance for perforation. However, complications, with the exception

of fistula formation, occurred more commonly during the first episode of diverticulitis than after its subsequent episodes.⁸⁰

Ritz et al.⁸¹ described, in a prospective study of 900 patients, the risk of free perforation with 25% at the first episode, which decreased to zero with ongoing episodes.

This report was in accordance with the findings of others observing an episode of complicated diverticulitis in only 4% of all patients within 2 years of the presentation of primary uncomplicated diverticulitis.⁸²

This knowledge led to a shift from the dogma of “the second episode of diverticulitis as indication for elective surgery”⁷⁹ to an individual “case to case” decision.⁸³ This finding was also associated with a marked decrease in the number of elective resections without an increase in the number of patients experiencing diverticular perforations.

Although there is a wide concordance among most societies that individual patient factors (e.g. comorbidities) as well as the quality of life (QoL) should have the strongest impact on the decision process (Table 2) considering the lack of scientific evidence and the controversies about more specific issues (e.g. time point for surgery, decision after concealed perforation, the role of age, immunosuppression and suspicion for cancer).⁸

Although some epidemiological data indicate that younger patients are at a higher risk of experiencing recurrent episodes of diverticulitis, it has not been sufficiently proven that this collective will have a worse outcome compared to older patients.^{84,85}

Therefore, an aggressive approach in younger patients cannot be absolutely recommended, albeit a more conservative management of older patients has been proposed owing to the potential risks for morbidity and mortality associated with surgery.⁸⁶

Acute Surgery

There remains an overall agreement about the role of surgery in the acute and emergency situations, such as in controlling the source of infection and achieving an acceptable QoL.

However, recommendations about the exact surgical approach have continuously evolved with time. Starting

Table 2. Indications for elective surgical therapy (“!” accepted, “?” under discussion)

Failure of conservative treatment and/or interventional drainage in acute diverticulitis!

Deterioration of quality of life due to recurrent attacks!

Possibility of cancer without further diagnostic options!

Presence of fistula!

Immunocompromised patients?

Young patients?

with a (historic) 3-stage strategy (Hartmann resection and reconstruction with rectal anastomosis plus protective stoma, followed by stoma closure), surgical strategies have continuously evolved in the last two decades. The most important negative impact for QoL is associated with the construction of a long-term or even permanent stoma.⁸⁷

Therefore, the necessity of a policy for delayed reconstruction that is based on expert opinion rather than on scientific evidence has been more and more questioned.^{88,89}

Recent randomised trials have attempted to compare the surgical approach with resection and primary anastomosis (with/without loop ileostomy) against the Hartmann procedure in patients with Hinchey III-IV diverticulitis.⁸⁸ The DIVERTI-trial showed no statistical difference between both the groups for morbidity and mortality; however, a significantly higher rate for long-term stoma in patients following a Hartmann approach (35% of patients after Hartmann procedure had a stoma after 18-month follow-up when compared to 4% after primary anastomosis).⁸⁸

Similar to these findings, the LADIES trial noted a significantly better 12-month stoma-free survival outcome in patients with primary anastomosis (65 patients with/without protective loop ileostomy) when compared with that in patients who underwent a Hartmann procedure (68 patients).⁸⁹

Although the authors concluded that, in haemodynamically stable, immunocompetent patients aged <85 years, primary anastomosis was preferable to Hartmann's procedure as a treatment for perforated diverticulitis (Hinchey III or Hinchey IV disease), these findings have been questioned by others.⁹⁰

While Cauley et al.⁹⁰ observed a higher rate for morbidity and mortality after primary anastomosis, Goldstone et al.⁹¹ described a correlation in the complication rate (7.4% mortality after Hartmann surgery versus 15% after primary anastomosis) and the training of the surgeon. In the later study, patients treated by the colorectal board certified surgeons demonstrated a significantly lower mortality rate when compared with patients operated by general surgeons.⁹¹

Another strategy to avoid the formation of a colostomy during acute diverticulitis is to employ laparoscopic lavage in order to control infection, which has shown promising results by first cohort studies.^{92,93,94}

However, long-term follow-up of randomised trials comparing lavage with primary resection showed a greater number of deep-site infection and unplanned operations in the lavage group as well as the risk for overlooking cancer.^{95,96}

A possible explanation for the controversial results could be found in the different strategy for using laparoscopic

lavage, such as, was the lavage approach applied in order to overcome the acute infectious situation, which could have been followed by an elective resection or was lavage regarded as a definitive treatment for acute, purulent diverticulitis (i.e. without any plan for sigmoid resection)?

At this time point, thus, laparoscopic lavage cannot be recommended as a standard procedure outside of clinical trials.

In conclusion, it must be accepted that, although research dealing with the management of diverticular diseases has increased in the past two decades, recommendations for the relevant diagnosis and treatment still relies mainly on expert opinions (which have replaced older, historic expert opinions themselves).⁸ Randomised trials producing valid scientific evidence have recently evolved; however, planning and performing protocols for such studies have been often hampered by various factors, such as the heterogeneity of patients and the lack of blinding (especially in acute settings), among others. Since diverticular diseases have a strong impact on the patient's QoL as well as on the health care system, further efforts to further elucidate the appropriate diagnostic and therapeutic approach are warranted.

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