# Diverticulitis : new insights on the traditional point of view

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### Abstract

Diverticulosis of the colon is a common disease with an increasing incidence in Western countries. Recent literature has shown some changes in the traditional approach of this disease. The theory that diverticulosis is caused by a reduced intake of dietary fibre, is doubtful.

There might be some chemical and histological overlap between diverticulitis, inflammatory bowel disease and irritable bowel disease. High quality clinical study found no effect for antibiotics in acute, uncomplicated diverticulitis. Cyclic administration of mesalazine and rifaximin result in reduced symptoms of diverticular disease. For the treatment of diverticular abscesses, percutaneous drainage shows promising results.

Recurrence of acute diverticulitis is rare and most serious complications are linked to the first episode. Recent evidence does not support the traditional recommendation for elective surgery after two episodes of acute diverticulitis any more.

This review summarizes the last evidence in diverticular disease and diverticulitis. (Acta gastroenterol. belg., **2015**, 78, **38-48**).

Keywords : Diverticulitis, Diverticular disease, fibre, Antibiotics, percutaneous drainage, and elective surgery/

## Introduction

Diverticulosis was widely believed to be rare until the beginning of the 1900s, which prompted some authors to describe it as a "20<sup>th</sup>-century problem" and a "disease of Western civilization". The supposed explanation for the increase in incidence of diverticular disease was the decline in dietary fibre intake.

Most diverticula are acquired pseudo diverticula in which only the mucosa and submucosa herniates through the muscular layer of the colonic wall, whereas true congenital diverticula contain all layers of the bowel wall. The sigmoid colon is most commonly affected. More than 90% of diverticula occur in the left hemicolon, whereas congenital diverticula are usually located in the right hemicolon (1).

There are some long-accepted dogma about diverticular disease :

- First : diverticulosis is the result of a low-fibre diet.
- Second : diverticulitis is an infection and must be treated with antibiotics.
- Third : elective surgical resection of the affected colon has been recommended after a second attack of diverticulitis and after a first attack in young patients. However recent advances in the understanding of the pathophysiology and natural history have led to substantial changes in diverticulitis treatment guidelines. Complicated diverticulitis is now reliably diagnosed

by using computed tomography (CT). Similarities exist between the physiology and inflammatory processes for diverticulitis, irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) (2).

This led to new insights in the prevention and management of diverticulitis.

# **Terminology and classification**

The terminology used to describe the manifestations of diverticulosis or diverticular disease is not uniform. Figure 1 shows an overview of current terminology.

Chronic recurrent diverticulitis may begin early after the initial episode, and may be consistent with failure of the index episode to 'settle'. Segmental colitis associated with diverticulosis is defined as peridiverticular colitis that spares the rectum (3).

Another category of chronic disease has been termed uncomplicated, symptomatic diverticular disease and is defined as diverticulosis associated with chronic gastrointestinal symptoms in the absence of diverticulitis or overt colitis. The criteria for a diagnosis of symptomatic uncomplicated diverticular disease do not include a history of acute diverticulitis (3).

# Epidemiology

# Diverticulosis

The incidence of diverticulosis coli in Western industrialized countries is increasing with age. Uncommon in populations under 40 years of age, it affects 5-10% of the population in the fifth decade of life, 30% at age 60 and over 60% of people over the age of 80, without sex differences (4). In a consecutive series of 2000 barium enemas, approximately two thirds of adults older than the age of 85 were found to have colonic diverticula (5). Diverticulosis was found in 71% of colonoscopies in individuals older than 80 years (6). Of patients with diverticula, about 80 to 85% are believed to remain asymptomatic (7).

The prevalence of patients that require medical or surgical treatment has increased 16% in the last 20 years (4).

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Submission date : 01/02/2015 Acceptance date : 02/02/2015



Fig. 1 : Potential evolution and terminology of patients with diverticula (8-10)

### From diverticulosis to diverticulitis

It is traditionally reported that 10-25% of patients with diverticulosis will develop diverticulitis during their lifetime (8). This estimate is based on a widely cited review of the natural history of diverticular disease published by Parks (1975) (9).

Technology such as CT has improved the diagnosis of acute diverticulitis and population-based data have provided more accurate estimates of the true incidence of diverticulitis which is lower than previously thought (8). A recent publication mentioned that up to 5% of the patients with diverticulosis developed acute diverticulitis (10).

# Risk of recurrence

There are two studies with adequate reference testing that give information on the natural disease history, and they reported an estimated risk of recurrence of 9 and 23% respectively (11). The highest risk of recurrence seems to be in the first year (10%) and drops to approximately 3% in the years thereafter, in patients with symptoms severe enough for hospital admittance (11).

## **Complications**

Only a small number of patients will develop complications of diverticulitis such as abscess formation, fistulae, obstruction, or haemorrhage (7).

# **Pathophysiology : old hypothesis**

The hypothesis that diverticular disease is a deficiency disease of Western civilization was based on the

observation that diverticulosis was rare in rural Africa, but increasingly common in economically developed countries. The difference was attributed to differences in dietary fibre (12). Potentially confounding variables such as age and sex were not taken into account (13).

Decreased dietary fibre intake results in decreased intestinal contents and smaller size of the lumen which in turn results in muscular contractions of the colon rather than the contents. This results in the formation of diverticula at the weakest point in the wall, namely the sites of penetration by blood vessels (14).

However, motility studies of the colon have not consistently shown that patients with diverticulosis have increased colonic pressures (8). A population consuming a Western diet had longer mean colonic transit times and lower mean stool weights compared with an African population (8).

There are 4 key aspects that support the old hypothesis (13) :

- Epidemiologic features of diverticular disease support a strong association with dietary fibre intake. Vegetarians have half the risk of asymptomatic diverticular disease than non-vegetarians (13).
- Colonic physiological studies have indicated that higher colonic pressures are found in patients with diverticulosis than in healthy individuals.
- Studies in animal models have strongly supported the hypothesis.
- Several interventional studies provided evidence in symptomatic (but not asymptomatic) diverticular disease for fewer episodes of diverticulitis, decreased rates of surgery and improvement in global symptoms with administration of fibre.

Three lines of argument have challenged the Painter hypothesis :

- A pathogenic role of constipation is not well supported (12).
- Recent studies suggested alternative pathogenic hypotheses suggesting a neuropathic or myopathic process (13).
- The inverse association of dietary fibre intake with diverticulosis has been questioned in recent epidemiologic studies (13). In a colonoscopy-based study, the investigators found that a high-fibre diet was associated with a higher prevalence of diverticula (8).

## **Pathophysiology : new insights**

The mechanism by which asymptomatic diverticula become inflamed and perforate (diverticulitis) is still under investigation but is plausibly associated with altered gut motility and increased pressure combined with a deranged colonic microenvironment.

In recent series, when ex vivo colonic tissue from patients with diverticulitis was exposed to chemicals that contract or relax smooth muscle, there was increased hypercontractility and lower maximum relaxation responses (10). These findings are consistent with neuropeptide abnormalities and altered histologic appearance of muscles and nerves in the bowel wall of patients with diverticulitis compared with healthy patients (10).

The natural history and interrelationships among these diverticular syndromes and the degree of overlap with conditions such as IBD and IBS are unclear (11).

Recurrent or chronic diverticulitis displays chemical and histological similarities to IBD and IBS (2).

Because an episode of severe inflammation due to infectious enteritis can trigger chronic IBS, it is plausible that diverticulitis might represent a similar trigger. Patients recovering from diverticulitis were found to be 4.7 times more likely to have a subsequent new diagnosis of IBS (15).

## **Risk factors and prevention**

# Fibre

Many investigators stated that, on the basis of low risk and theoretical benefit, a high-fibre diet and/or fibre supplementation should be considered for the prevention of diverticulosis (2). However, recent investigation using colonoscopy found that those who reported the highest fibre intake were at highest risk of diverticulosis (8). So at this moment it is absolutely not clear if fibres must be recommended for the prevention of diverticulosis and diverticular disease.

Not only the amount of fibre might be a determinant for the risk of diverticulosis, the specific type of fibre may also play a role (16-18). For example fruit and vegetable intake were inversely associated with the risk of symptomatic diverticular disease, while cereal fibre was not (16-18).

### Red meat

A study showed that the risk of developing diverticular disease was almost 50-fold higher for meat eaters as compared with people who frequently consumed vegetables (16). Another study comparing vegetarians to nonvegetarians found that the incidence of diverticular disease was higher in non-vegetarians than in vegetarians (19).

Consumption of red meat is positively associated with risk of diverticular disease (19), perhaps via an interaction with bacteria that could result in production of a "toxic metabolite", maybe a spasm inductor, creating conditions for formation of diverticula (16).

## Fat

The association of diverticular disease with total fat and various types of fat is no longer significant (20).

### Alcohol and caffeine

No association is observed between alcohol, caffeine and decaffeinated coffee and risk of symptomatic diverticular disease (21).

### Nuts, corn and seeds

There seems to be no arguments in the literature to avoid this kind of food (18).

## Lifestyle factors

Current smokers were not appreciably at risk for symptomatic diverticular disease compared with nonsmokers (16). Physical activity affects colonic function, particularly by reducing intestinal transit time (16). Overall physical activity was inversely associated with risk of symptomatic diverticular disease.

## Medication

Nonsteroidal anti-inflammatory drugs, opioids and corticosteroids have been convincingly associated with increased risk of perforated diverticulitis (2,8).

### In summary

Although some literature suggests a protective effect of healthy lifestyle and certain types of food, their preventive role diverticular disease remains to be defined.

## Clinical diagnosis and radiological imaging

# Clinical diagnosis

The accuracy of clinical and biological assessment for establishing a diagnosis of diverticulitis of the left colon, is correct in 43-68% of patients (22). This was demonstrated by 2 prospective studies evaluating the use of CT in this setting (22).

# Radiological imaging

Radiological imaging actually used for the diagnosis of acute diverticulitis are actually ultrasound (US) and computed tomography (CT).

There are not enough evident advantages of magnetic resonance imaging (MRI) (4). MRI requires a prolonged examination time potentially making cooperation of acutely ill patients difficult. MRI is not as sensitive as CT for identification of free air.

The use of CT has become the most appropriate initial imaging modality (8). CT has the advantage of delineating the extent of extraluminal disease process, and can also direct therapeutic intervention in case of complicated disease, e.g. percutaneous drainage of intra-abdominal abscesses. The most used criteria to diagnose acute diverticulitis with US and CT are increased thickness of the colonic wall, pericolic fat stranding and presence of inflamed diverticula (11). The use of intravenous contrast agents is advised.

In large prospective series a lower sensitivity (61%) was found for US, whereas the sensitivity of CT for the diagnosis of acute diverticulitis was 81% (11).

Immunocompromised patients, who may not develop a significant inflammatory response, may have only extraluminal gas on CT without other typical radiographic findings of diverticulitis (8).

The grade of severity on CT correlates with the risk of failure of non-operative management in the short-term and with long-term complications (8).

Abscess formation and pockets of extra-intestinal air (> 5 mm in diameter) are significant predictors of failure of non-operative treatment (22).

CT-based findings also help to predict the need for surgery during and after a first episode of diverticulitis : when graded severe on CT, with radiological signs of colonic perforation, the risk of surgery was as high as 26% compared with 4% when graded moderate on CT (22).

Moreover the exact site of inflammation can be identified by CT. This is particularly important when planning elective surgery to locate the proximal margin of resection (22). Thus CT not only provides prognostic information but also defines the topography of the disease.

# Colonoscopy

Colonoscopy is not recommended in the acute phase of acute diverticulitis. Possible difficulties of colonoscopy in the acute phase are incomplete examination due to pain, stenosis and incomplete bowel preparation. Discouragements to perform colonoscopy in the acute phase are based on the hypothesis that insufflation of air is associated with the risk of converting a sealed perforation to a free perforation. Classically it was done 6 weeks after acute diverticulitis in order to exclude colonic malignancy (2). Some authors reported no increased detection of advanced neoplasia in patients with a typical presentation of acute diverticulitis (2,11).

Although safe, routine performance of a routine colonoscopy in asymptomatic patients after an episode of acute diverticulitis to exclude other diagnosis was not found to be helpful (11). Some authors however advocated colonoscopy to exclude malignancy (2).

So the usefulness of colonoscopy after an episode of acute diverticulitis is still a matter of debate, excepted in the presence of a mass on CT.

# **Special patient group**

## Young patients

The definition of young age in patients with acute diverticulitis is either below 40 or 50 years. Off all patients hospitalized for this disease, 18-34% are younger than 50 years (9). Some authors have reported that young patients have an increased risk of complications and that they have a higher recurrence rate (9). Therefore elective (prophylactic) surgery was often advised after one episode of uncomplicated diverticulitis based on both the low surgical risk of an elective procedure in a young person and the many years of future risk of recurrence (9).

In a recent meta-analysis, patients younger and older than 50 years presenting with diverticulitis were compared with regard to complications, disease recurrence and the need for surgery (23). There was no significant difference in risk to require urgent surgery between both age groups. The cumulative risk of developing at least one diverticulitis recurrence varied between 20.9% and 53.6% in patients younger than 50 years with an estimated average risk of 29.9%. Patients older than 50 years had an estimated average risk of 17.3%. Patients younger than 50 years more frequently required urgent surgery during hospitalization for a subsequent recurrent episode. The cumulative risk was 7.3% in younger and 4.9% in older patients (significant).

Another meta-analysis compared outcomes of diverticulitis in patients of young age (< 40 years or < 50 years) and of older age (24). The rate of complicated disease at admission was not significantly different. Setting the age cut-off to 40 years had no impact on the results. Recurrence rate was significantly higher in young patients (31.6% in patients < 50 years as compared with 18.5% in patients > 50 years).

In a retrospective cohort study showed that a policy of routine elective colectomy in a younger population would require 13 elective surgeries to prevent 1 emergency colectomy (25).

It is suggested that 'younger patients will have a higher cumulative risk for recurrent diverticulitis, even if the virulence of their disease is not different than that of older patients'. However, there has been no long-term follow up of young patients. Furthermore, current studies may be biased toward younger patients as surgeons had a lower threshold for operative intervention in this subgroup (26).

The timing for elective surgery of colonic diverticulitis in young patients remains controversial. Researchers should no longer attempt to answer this question by metaanalyses (27).

As conclusion there is no evidence that younger patients should be treated differently than older patients. Recent studies have challenged the recommendation for elective surgery after an initial episode of diverticulitis in younger patients.

### Immunocompromised patients

In patients with a compromised immune system, an increased incidence of acute diverticulitis has been reported compared to healthy individuals, especially in patients with kidney failure, organ transplant or using corticosteroids. These patients have a 5-fold greater risk of complicated recurrence and perforation compared with non-immunosuppressed patients (36% vs 7%) (8). Patients with collagen vascular disease and malnutrition are also at higher risk and were significantly more often diagnosed with complicated diverticulitis (2).

In patients HIV infection, diabetes, malignancy or chemotherapy no increased risk of complicated diverticulitis was found (11).

Surgeons should maintain a low threshold to recommend operative intervention as treatment during the first hospitalization for acute diverticulitis in patients at higher risk (8).

# Treatment of symptomatic, uncomplicated diverticular disease

### Fibre

A possible approach to the treatment of symptomatic diverticular disease is to increase dietary fibre. A systematic review found 4 studies on treatment of symptomatic diverticular disease (14). One randomized trial showed no treatment effect of fibre ingestion on resolution of symptoms, whereas the other 3 studies did show a significant treatment advantage with fibre ingestion.

So these results are inconsistent and the quality of the studies was low.

### Cyclic antibiotic therapy

A possibility to treat symptomatic, uncomplicated diverticular disease is to give cyclic antibiotics. In almost all the studies antibiotics were given one week a month for a longer period. Rifaximin is the only antibiotic with studies of some quality. It has inhibitory effects on intestinal microbiota, so that the intestinal gas production can be decreased. The question remains if this possible benefit could be maintained in the remaining 3 weeks without antibiotic treatment.

Different studies compared cyclic rifaximin treatment with fibres groups (28). Four controlled trials were found and the patients in the rifaximin plus fibres group had a higher chance to be symptom-free after 3 months. However, at 24 months, the most differences were not significant. The number needed to treat (NNT) to prevent 1 case of acute diverticulitis by adding rifaximin to fibres, was 58 (28).

A meta-analysis evaluated the long-term efficacy administration of rifaximin plus fibre supplementation vs fibre alone (29). Sixty-four per cent of the patients included in the rifaximin group were symptom-free at the end of follow-up (12 or 24 months) while only 34.9% of the patients in the 'only fibre group' were symptom-free. Acute diverticulitis occurred in 2.8% of the 'fibre alone group', as compared with 1% of the treatment. Similar results were obtained in another systematic review (30).

The question remains if there is only an effect on short term (3 months) or that administration of rifaximin one week a month might have an effect on longer term. Without RCT no firm recommendations can be given.

# Probiotics

A recent multicentre, double-blind, placebo-controlled study was conducted to assess the effectiveness of mesalazine and/or probiotics in maintaining remission in symptomatic uncomplicated diverticular disease (31). Lactobacillus casei subsp. DG 24 billion/day plus mesalazine (1.6 g/day) was used versus placebo (31).

The recurrence of symptomatic uncomplicated diverticular disease was 0% in the group with both Lactobacillus and mesalazine and 23% in the group with placebo. Conclusion was that both cyclic mesalazine and Lactobacillus casei treatments, particularly when given in combination, appeared to be better than placebo for maintaining remission of symptomatic uncomplicated diverticular disease.

The rationale about the use mesalazine with probiotics is that mesalazine controls inflammation, whereas probiotics restore colonic microenvironment.

A systematic review about the use of probiotica in patients with symptomatic, uncomplicated disease suggests that probiotics alone or in combination with 5-ASA are safe and potentially useful in the management of diverticular disease (32).

More RCT studies with larger populations are needed.

### Anti-inflammatory medication

The last few decades, the pathogenesis theory of diverticular disease has changed. It has been mentioned that the type of inflammation is similar to that occurring in chronic inflammatory bowel disease, suggesting that patients may benefit from anti-inflammatory medication.

Recently a multicentre study was published (33). Patients with symptomatic, uncomplicated diverticular disease were randomized to mesalazine 1000 mg 3 times daily or placebo (33). Primary efficacy endpoint was a change in lower abdominal pain at week 4. For this outcome there was no significant difference between the mesalazine and the placebo group. However, median time to complete pain relief was 8 days in the mesalazine group and 19 days in the placebo group.

A systematic review in 2011 about treatment with 5-ASA for diverticular disease was published founding 6 RCT's : 3 in patients with uncomplicated diverticulitis and the remaining in patients with symptomatic uncomplicated diverticular disease (34). The results showed that patients treated with 5-ASA had significantly better outcomes and that mesalazine scheduled daily was superior to cyclic administration to prevent relapse of diverticular disease.

All the studies had a low quality.

Almost all the mentioned studies showed a positive effect for mesalazine. The optimal dose is yet to be determined, but the best results for cyclic use of mesalazine were obtained with 800 mg twice daily, 10 days a months (30).

However continuous treatment has been shown to be more effective than cyclic doses.

# Treatment of uncomplicated diverticulitis

# Antibiotics in acute phase

A common hypothesis is that diverticulitis is the result of an obstruction at the neck of the diverticulum. Mild diverticulitis is thought to be associated with microperforation and in more severe disease, gross perforation. In short, all manifestations of diverticulitis have been presumed to be caused by bacterial infection that should be treated with antibiotics.

However new insights in the pathophysiology showed that recurrent or chronic diverticulitis displays chemical and histological similarities to IBD and IBS. Should the statement that diverticulitis should be treated with antibiotics still stand ?

A review in 2008 found 3 RCT showing no significant difference between antibiotics and no antibiotics for the treatment of uncomplicated diverticulitis (26).

A recent, multicenter RCT included 623 patients, with CT-confirmed uncomplicated left-sided diverticulitis, treated with intravenous fluids and antibiotics or intravenous fluids only (35). The treatment was initiated with intravenous antibiotics. Orally administrated antibiotics such as ciprofloxacine combined with metronidazole were initiated subsequently on the ward or at discharge. The total duration of antibiotic therapy was at least 7 days.

The authors found that antibiotic therapy did not prevent complications, nor accelerated recovery nor prevent recurrence. This study did not address whether or not hospitalization is necessary or if outpatient treatment without antibiotics is appropriate.

Little is know about which antibiotics are the first choice for acute diverticulitis. This is because there are only a few studies comparing different antibiotics for dose and for oral or intravenous administration (30). Antibiotics should cover Gram-negatives and anaerobes (30). In our country, clavulanic acid is often used as first line treatment.

Most patients with uncomplicated diverticulitis can be treated conservatively with a success rate of 93-100%. Conservative treatment includes antibiotics, starvation and bed rest in almost all studies (11). There is no evidence that bed rest, dietary restrictions or laxatives positively influence the treatment outcome of acute diverticulitis. In patients who do not tolerate oral feeding, it is recommended to start parental feeding when oral feeding is not to be expected within 3 days. The use of antibiotics seems appropriate in patients presenting with signs of generalized infection (temperature >  $38.5^\circ$ ), affected general condition or signs of septicaemia and in immunocompromised patients (11).

The strong evidence from a large RCT showing no benefit of antibiotics in uncomplicated diverticulitis raises important questions about etiology and management of diverticulitis (9). Acute diverticulitis may be inflammatory rather than an infectious condition (9). Recently, a not common form of segmental colitis associated with diverticular disease that mimics chronic idiopathic IBD histologically has been recognized.

Further research is required before definitively adapting an antibiotic-free treatment strategy.

### Pain treatment

There is no evidence that acetaminophen, nonsteroidal anti-inflammatory drugs (NSAID's) or morphinomimetics have a negative effect on the course of acute diverticulitis (11). Multiple studies found that patients on home NSAID's present more often with complicated diverticulitis, i.e. perforation. Morphinomimetics can be safely administered to patients with acute abdominal pain (11).

### Diet restrictions

The rationale behind diet restrictions for treating the acute phase of a diverticulitis episode has never been throughly studied. Many physicians recommend diet restrictions assuming that this may result in a less active bowel with a positive effect on the healing of the infection and ultimately shortening hospitalization time. Furthermore, it is thought that a more restricted diet is mandatory with increasing disease severity.

The diet choice does not seem to depend on the severity of the disease, nor does it relate to the height of Creactive protein or leucocyte count (23).

In general, it seems that patients with increasing fever at presentation receive a more restricted diet. Notably, advising a more restrictive diet at presentation and hospitalization for a diverticulitis might lead to longer hospitalization duration (23).

If the physician's choice of the diet is indeed a subjective issue, it may be questioned whether diet restrictions are even necessary (23).

It is impossible to draw conclusions if diet restrictions are advantageous in the treatment of patients with diveracute diverticulitis.

ticulitis. It seems that personal ideas of the treating physician and old principles determine diet restrictions in the no

# Medical treatment of recurrent diverticulitis

Traditionally the supplementary intake of dietary fibre was advised for patients after an episode of acute diverticulitis. A systematic review found no studies about the effect of dietary fibre on the recurrence rate (14). Recently, new theories about similarities between acute diverticulitis, IBD and IBS have been proposed, leading to new treatment possibilities for decreasing the recurrence.

Intermittent cyclic administration of rifaximin after an episode of acute diverticulitis decreased the chance of readmission by 50% and recurrent diverticulitis by 73% (11).

A study combined mesalazine (800mg twice daily 7 days every month) and rifaximin (400mg twice daily) versus rifaximin alone in recurrent acute diverticulitis (14). Symptomatic recurrence occurred significantly less in the group with the combination therapy (14).

# **Treatment of complicated diverticulitis**

Hinchey et al. proposed a classification based on CT evaluation for acute diverticulitis, that is useful in outlining successive stage of severity (36). The choice of treatment can depend on the stage of the Hinchey classifation :

- Stage 0 : Mild clinical diverticulitis
- Stage Ia : Confined Pericolic inflammation Phlegmon
- Stage Ib : Diverticulitis with pericolic or mesenteric abscess
- Stage II : Diverticulitis with walled off pelvic abscess
- Stage III : Diverticulitis with generalised purulent peritonitis
- Stage IV : Diverticulitis with generalised faecal peritonitis

A systematic review of the available evidence comparing the medical and surgical treatments in patients with diverticulitis was published (37). The majority of patients treated conservatively belonged to the group of patients with Hinchey score I or II, whereas emergency surgery was more common in patients with complicated diverticular disease (37). The in-hospital mortality of patients treated surgically was generally higher than that of patients treated medically. The readmission to the hospital due to diverticular disease during follow up was more common in the patients treated conservatively (18.6%) compared to those treated by emergency surgery (6.1%) (37).

## Hinchey Ib and II

A study promoted the non-operative management : there were more than 90% success rate in avoiding the

need for urgent operation and stoma creation. There was no difference in patients with abscess or in patients with remote free air (38). This approach requires a monitoring setting, appropriate antibiotic therapy, and adequate interventional radiology. But, most importantly, the patient must have a rapid clinical response to therapy (38).

The decision to use an aggressive approach to nonoperative therapy depends on the physiologic state of the patients, their physical examination and correlation with CT findings.

Other arguments to avoid surgery, are the mortality and morbidity rates. The mortality rate of emergency colorectal surgery across a number of studies has been reported to be 15 to 17%, with 1-year postoperative and overall mortality rates after emergency operation for diverticulitis reaching 22.6 to 35% (38). Furthermore, in patients that receive stomas during surgery, only 45 to 65% of these are eventually reversed, and reversal operations are associated with high morbidity (38).

Many of the discrepancies between this last (retrospective) study and studies in the past are probably due to a more aggressive use of percutaneous abscess drainage (56% of patients with grade 3 CT scans in this study while 3% in other studies) (38).

Contraindications to a non-operative approach include hemodynamic instability, generalized peritonitis, CT scan with diffuse free air and free fluid, immunosuppression and comorbidities that would not tolerate resolving sepsis (38).

There are no high-quality reports on the management of patients with acute diverticulitis and abscess formation and the literature shows no consensus about the most optimal treatment strategy. However treatment abscess formation has progressed from a surgical emergency to nonoperative management with antibiotics and percutaneous drainage, (eventually) followed by delayed resection (39). Conservative treatment with antibiotics was successful in up to 73% of patients presenting with an abscess of less than 4-5 centimetres (11).

A meta-analysis evaluated the management of acute diverticulitis and abscess formation. It showed that antibiotic therapy for abscesses (with diameter > 3 centimetres) was only successful in 14% of the patients. No association between abscess size and recurrence rates could be established (39).

There is some evidence that supports the use of percutaneous drainage for accessible, larger abscesses in patients not improved with medical therapy (8). This might be successful in up to 81% of the patients (11). A success rate of 49% of patients with abscesses more than 3 centimetres was found (39).

Patients require an adequate radiographic window for safe percutaneous drainage. Otherwise laparoscopically operative drainage is required (8).

Future research is needed to better determine which patients with Hinchey Ib and II can be managed nonoperatively.

# Hinchey III and IV

Peritonitis is the most life-threatening complication of acute diverticulitis, with a mortality of 14%. Perforation of the colon results in a purulent or faecal peritonitis. In a large population-based study, only 1.5% of patients with acute diverticulitis were found to have a perforation, and 9.6% were found to have an abscess (11). Early treatment in patients with peritonitis significantly improves outcome.

Recurrent diverticulitis associated with generalized peritonitis requiring surgery is very rare (0.7%). On long-term follow-up (9,5.years) emergency surgery was rarely required and none of the patients died of the disease. The risk of free perforation in acute diverticulitis decreases with the number of previous episodes, from 25% for the first episode to 12% for the second, to 6% for the third and 1% for the fifth (22).

Currently, there is an increasing trend for 'damage limitation surgery', that is to perform as little as possible during the acute phase and definitely treat the patient when the severity of the disease will be decreased (11). By applying certain 'down-staging surgery' protocols, a single-stage procedure can be eventually achieved in most of the cases and the current literature shows promising results in patients morbidity and mortality (11).

There are different surgical options for patients with Hinchey III and IV peritonitis : Hartmann's procedure is the most performed (11). However studies comparing mortality, morbidity, wound complications, operative time and antibiotic treatment of Hartmann's procedure and primary anastomosis did not show significant differences. It is likely that choice of operation is influenced by patient conditions and perioperative findings (11).

After resection, the decision to restore bowel continuity must incorporate patient factors, intraoperative factors and surgeon preference (8). The clinician must weigh the risks associated with anastomotic failure and of prolonging the operation, while recognizing that end-colostomies, created under these circumstances, are often permanent (8). Parameters generally favouring proximal diversion include patient, intraoperative factors and comorbidities as well as surgeon experience (8).

An systematic review found no direct information from RCT's about whether surgery is better than conservative treatment in people with acute diverticulitis and peritonitis (30).

Surgery is usually performed for people with perforation and peritonitis but it is unknown whether it improves outcomes compared with no surgery. Mortality at 30 days may be the same with acute sigmoid colonic resection compared with no acute resection (30).

# **Treatment of complications**

# Diverticular bleeding

Colon diverticula are responsible for rectal bleeding in 24-42% of the cases, and 5% of the diagnosed diverticu-

lar disease patients will bleed at least once in the course of their disease (40). Bleeding recurs in 22-38% and the risk of recurrence after the second episode is as high as 50% (40). Although diverticular most commonly appear in the left colon, diverticular haemorrhage originates from the right colon in 50% of the cases. Most bleedings stop spontaneously (77.6% in a large series) (40).

### Stenosis or obstruction

Intestinal obstruction is uncommon in diverticulitis, occurring in approximately 2 percent of patients (7). Small bowel obstruction is rare and usually caused by adhesions (7). Patients can present acutely, requiring emergent operation, or with chronic symptoms (40). Multiple attacks can lead to progressive fibrosis and stricture of the colonic wall. Obstruction generally responds to conservative therapy but can if needed be treated by different surgical techniques (7).

# Fistulae

Fistulae are uncommon, but are responsible for 5-9% of the indications for surgery in complicated diverticulitis (40). They result from drainage of the inflammatory process toward a neighbouring organ (bladder, vagina, uterus, small bowel) or more rarely toward the skin (40). Colovesical fistulae are more common in men and are the most common variety. They require surgical treatment (7). In women, the uterus is interposed between the colon and the bladder (7).

### Caecum diverticular perforation

Caecum diverticular perforation is rare and can clinically mimic appendicitis. It is usually encountered in emergency operations (40). Malignancy is not always excluded and a right hemicolectomy is usually the treatment of choice (40).

### **Elective surgery**

### Acute diverticulitis without complications

Most of the guidelines in the past suggested an elective resection after two attacks of uncomplicated diverticulitis, in order to prevent further attacks and the development of complications. However, this "evidence" is based on limited data and information from more than two decades ago (41).

New epidemiologic studies confirmed that recurrence of acute diverticulitis is rare and is a relatively benign process for the substantial majority of patients. 86% of a large cohort with an episode of acute diverticulitis required no further inpatient care for diverticulitis over the 8.9 years of follow-up (2). Recurrence occurred in only 13.3% of patients and only 3.9% had a second recurrence (2). No patient with a second recurrence required an operation, and repeat recurrences plateaued after 4 episodes (2). Recurrence overall is rare and therefore does not warrant elective colectomy (2). A review found 14 studies evaluating patient-specific risk factors for recurrence and complications showing that the importance of age is increasingly downplayed (42). Observational studies have identified family history, retroperitoneal abscess and length of the colon segment involved as factors associated with increased risk of recurrence (42). However, it remains unclear the factors can justify prophylactic surgery (42).

On above multiple episodes of diverticulitis do not seem to be associated with increased mortality or an increased risk of complicated diverticulitis. The overall mortality rate for patients with a prior history of diverticulitis was 2.5% comparing with a mortality rate of 10% for patients with an complicated diverticulitis (14). The most patients who present with complicated diverticulitis do so at the time of their first attack (14).

The likelihood of free perforation seems to be higher in patients with no history of diverticulitis than those who have recovered from 1 or more episodes decreasing from 25% at the first episode to 12% at their second, 6% at<sup>2</sup> their third and 1% thereafter (42). Recurrent diverticulitis even seems to reduce the risk of perforation, possibly due to adhesion formation (42).

Another argument against elective surgery after two episodes is that morphologic characteristics of recurrent diverticulitis may differ considerably from the first episode. A study of 60 patients with recurrent disease after initial medical management of uncomplicated diverticulitis compared CT scans from the index and second admission (11). At the time of recurrence, 6 patients (10%) had complicated diverticulitis and 3 patients underwent an urgent Hartmann procedure. Among the 54 patients with a CT-defined recurrence that was uncomplicated, 19 (35%) had a recurrence of diverticulitis at an average of 8 centimetres from the previous site (11).

So CT is not only important for the diagnosis of acute diverticulitis, but also to determine the location of the disease. This is particularly important when planning elective surgery (22). CT not only provides prognostic information but also defines the topography of the disease.

Elective surgery is associated with its own morbidity, an incidence of stoma formation, postoperative recurrence and persistent abdominal symptoms. These observations are not always based on studies because many are retrospective or report experiences on open surgery (25). The mortality associated with elective resection ranges from 1.0 to 2.3% and morbidity rates ranges from 25 to 55%, including a 10-14% incidence of stoma formation (22). Furthermore, elective resection is not curative in all patients, with recurrence rates of acute diverticulitis following surgery estimated at 2.6-10% (22).

The decision to recommend elective surgery should be individualized to each patient and should take in consideration the risks of operative therapy, the overall medical condition of the patient, patients preferences and other factors such as the effects on quality of life imposed by recurrent attacks, and severity of the attacks (8).

# Complicated diverticulitis

Studies indicate that elective sigmoid resection should be recommended for patients who have had a prior episode of complicated diverticular disease (such as fistula or stenosis) (22,40). Patients with pelvic abscess formation are at high risk of further complications and surgery should be seriously considered (22). Conversely, in asymptomatic patients after successful conservative treatment of a mesocolic abscess with or without drainage, surgery is not necessary, and therefore the indication for surgery in asymptomatic patients should be considered on a case-by-case basis, taking into account age, operative risk and the number and CT-graded severity of acute episodes of diverticulitis (22).

Other authors however stated that elective surgery must be recommended to every patient with complicated diverticulitis, especially among the patients with a pelvic or paracolic abscess that required percutaneous drainage (2,42), based on a higher incidence of late complications.

# Persistent colonic symptoms after acute diverticulitis

Persistent colonic symptoms, particularly abdominal pain, have been reported in patients after episodes of diverticulitis. These patients might benefit from early colonic resection after an episode of acute diverticulitis. It is also important to exclude other diagnoses such as IBS, which increase the likelihood of persistent symptoms after resection (11).

However, approximately 27-33% of patients remain symptomatic after elective surgery (4). But this percentage has decreased since it has become accepted that the anastomosis must be performed on the healthy upper rectum (4).

In 2 other reports resection relieved symptoms in 77 to 89% of cases, with persistent symptoms mostly related to comorbid IBS (42).

The decision to perform elective surgery for persistent colonic symptoms after an episode of acute diverticulitis needs to be taken on a case-by-case basis, weighing the severity of the ongoing syndrome and the likelihood of improvement against the short-term morbidity and longterm functional consequences of sigmoid resection (42).

# Discussion

Most of the knowledge and the guidelines about diverticular disease and acute diverticulitis are based on old and low quality studies.

The longstanding hypothesis that the development of diverticulosis is the consequence of a low fibre diet is contested by new studies. At this moment there is no clear answer in the literature if fibres should be recommended for the prevention of diverticulosis and the recurrence of acute diverticulitis.

Given the high cost of clinical trials, a for-profit organisation is unlikely to undertake a trial on dietary fibre, which is not patentable. Currently, companies are more interested in developing acceptable and patentable treatments (43).

The prevalence of diverticulosis approaches 80% in 80 years olds, the vast majority of those individuals do not have symptoms. In the future it will be important to determine why certain patients develop symptoms and why other patients do not (9). Another challenge for future research is differentiating the symptoms of IBS and IBD from those of chronically symptomatic diverticular due to a potential pathogenic role for inflammation.

Cyclic administration of antibiotics like rifaximin for patients with symptomatic, uncomplicated diverticular disease shows some promising results in reducing symptoms, but the quality of these studies was not high enough to make definitive statements. Recent data show that antiinflammatory medical therapy (mesalazine) may contribute to decrease symptoms in diverticular disease.

A recent RCT of high quality suggests that antibiotics may no longer be the keystone in the treatment for acute, uncomplicated diverticulitis, although further research will have to confirm this (35). Some studies suggest that rifaximin and mesalazine might reduce the risk of recurrent diverticulitis.

There are now several arguments against the traditional recommendation for surgical resection after 2 episodes of acute diverticulitis without complications. There are now several arguments against this hypothesis : recurrence of acute diverticulitis is rare and multiple episodes of diverticulitis are not associated with increased mortality or with increased risk of complicated diverticulitis. It seems that most serious complications are linked to the first episode (14).

Moreover, morphologic characteristics of recurrent diverticulitis may differ considerably from the first episode. At last persistent gastrointestinal symptoms, which are not improved with resection, are common after elective surgery, suggesting overlap between chronic or recurrent diverticulitis, IBD, and IBS.

A CT scan is very important before (elective) surgery, not only because it provides prognostic information but also because it defines the topography of the disease.

Elective surgery is typically advised for fistula and stenosis. Patients with pelvic abscess formation have higher risk on further complications and surgery should be seriously considered.

Recent evidence shows that younger patients (under 40 or 50 years) are not at higher risk for complications. Therefore elective surgery after one episode of diverticulitis is no longer applicable. Estimated on recent investigations, these group of patients is comparable with 'older' patients.

Immunosuppressed patients have a significantly higher risk on recurrent, complicated diverticulitis, and therefore a low threshold for emergency and elective surgery must be maintained.

An important limitation for this review was the lack of uniformity in terminology between the different studies. It seems therefore impossible to make a meta-analysis for the prevention and the treatment of acute diverticulits because of the heterogeneity of the study design, patients characteristics, type and regimens of therapy under study and outcome measures assessed (44).

Only the last two years there are a few randomized controlled trials of good quality.

There is an urgent need for high quality trials in all domains of diverticular disease.

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