# Strategies in Perforated Diverticulitis

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# Strategies in Perforated Diverticulitis

Strategieën in geperforeerde diverticulitis

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# 1

## Outline of this thesis

# Outine of this thesis

Diverticular disease is one of the most common diseases related to the gastro-intestinal tract requiring in-hospital treatment in Western countries. Despite its high incidence, controversies remain about the optimal treatment of the different stages of this disease. Perforated diverticulitis, as the most severe and feared stage of diverticular disease, is only observed in about 2% of the cases. Therefore, strategies in treatment of this stage of diverticulitis are even less thoroughly investigated. To elucidate the problem and as a backbone of this thesis, a structured analysis of the vast existing amount of clinical data with regard to perforated diverticulitis available in the teaching hospitals of the Rotterdam region was undertaken.

As an introduction of this thesis, **Chapter 2** describes the clinical features of different stages of diverticulitis and discusses the controversies in current treatment strategies. The controversies in treatment clarify the importance of the three randomized clinical trials that have evolved under the auspices of the Dutch Diverticular Disease Collaborative Study Group.

The pathophysiology of diverticulitis and its perforation remains poorly understood. Good insight in the aetiology of diverticulitis and identification of risk factors for diverticular perforation might be important for improvement of surgical strategies in the treatment and prevention of perforated diverticulitis. **Chapter 3** gives an overview of the current evidence and theories in the pathophysiology of diverticulosis, diverticulitis and perforation and discusses its prevention.

Acute perforated diverticulitis is considered a very serious condition, which requires emergency surgery. The most commonly performed surgical procedure in these cases is Hartmann's procedure (HP). Improvements in surgical techniques, radiological intervention techniques, advances in intensive care medicine and progress in the management of peritoneal sepsis, has led to an increasing interest in resection with primary anastomosis (PA). Regardless of the selected surgical strategy emergency operations for diverticular disease are associated with mortality up to 30%. In **chapter 4** the factors related to in-hospital mortality after perforated diverticulitis are described. Postoperative outcome after HP and PA for treatment of acute perforated diverticulitis are compared in **chapter 5**. The incidence of reoperations or additional interventions to treat complications after HP and PA are discussed in relation to patient's characteristics, severity of the disease, surgeon's experience and time of operation.

The existing literature regarding perforated diverticulitis only reports about short-term postoperative mortality and postoperative complications. Less is

known about survival outside the hospital on the long term. Nevertheless, survival expectancy should be an important factor in decision making for initial treatment as it measures the patient's prognosis. **Chapter 6** describes the long-term survival of patients who were operated for acute perforated diverticulitis compared to the natural life span of the Dutch population.
Also quality of life is increasingly recognized as a crucial factor when assessing clinical outcomes after surgical interventions. It presents a patient's perspective, which is obviously a key outcome in clinical decision-making. **Chapter 7** discusses patient-orientated outcomes, such as quality of life, in relation to surgical technique (HP or PA), surgeon's experience in colorectal surgery, severity of the primary disease, and patients' characteristics.
Although the absolute prevalence of perforated diverticulitis is low, its importance is reflected in the significant postoperative mortality, especially when it is complicated by generalized peritonitis. During the last century, progress in sepsis management has led to more radical surgical procedures, but survival did not improve significantly. Mortality rates after emergency surgery for generalized peritonitis caused by perforated diverticulitis have remained high. Recently, laparoscopic damage control surgery (lavage and drainage, without resection) has been introduced and seems to reduce postoperative morbidity and mortality. In **chapter 8** a historic overview of the development of different surgical strategies in perforated diverticulitis is presented and perspectives for the future are discussed.
Evidence for different surgical strategies in treating perforated diverticulitis is mainly based on retrospective data or prospective studies with limited numbers of patients. Randomized controlled trials are lacking in current literature. In **chapter 9** the LADIES-trial protocol is described. This study is the first study designed as a multicenter randomized control trial to compare different surgical strategies in the treatment of acute perforated diverticulitis with generalized purulent or faecal peritonitis. The LADIES-trial is a joint initiative between the LOLA-trial, which compares laparoscopic lavage and drainage with open resectional surgery in perforated diverticulitis with purulent peritonitis and the DIVA-trial, which compares Hartmann's procedure with sigmoid resection with primary anastomosis in perforated diverticulitis with purulent or faecal peritonitis.
Although PA with or without a diverting loop ileostomy seems to be a good alternative, HP is still performed most frequently in patients with diverticular peritonitis. Patient who undergo HP are left with an end colostomy. Restoration of bowel continuity can eventually take place in a second operation. Stomal reversal rates and postoperative complications in patients who had undergone HP and patients after PA with diverting loop ileostomy for perforated diverticulitis are compared and discussed in **chapter 10**.

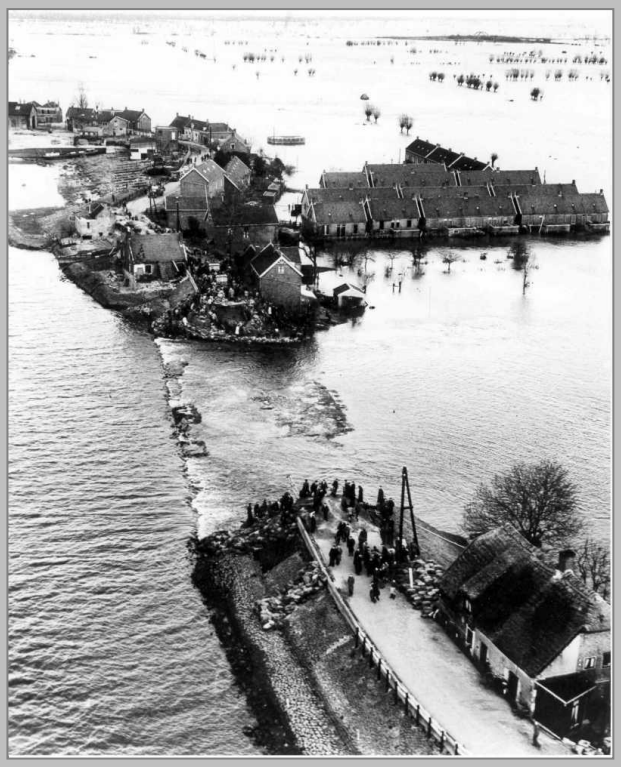
Stoma reversal is considered a contaminated operation. Therefore, morbidity after reversal of colostomy or loop ileostomy is rather high, with wound infection as one of the most commonly reported complications. **Chapter 11** described the rate of wound infection and its consequences in case of stoma reversal and primary closure of the skin at the stoma side, compared to stoma closure and leaving the skin at the stoma side open for secondary healing.
Although, HP is considered a two-stage procedure, restoration of bowel continuity after HP is still considered as a technically challenging operation, associated with significant morbidity and even mortality. These rates can be as high as 30% and 14%, respectively after stoma reversal in patients who had undergone a HP for perforated diverticulitis. This is the main reason why this second operation is never performed in more than half of the patients. **Chapter 12** describes a new technique for reversal of HP. We have called this procedure 'stomal incision reversal', as no additional incisions have to be made besides the one at the stomal side. It has the advantage that the amount of adhesiolysis is limited to the paracolic pathway to the rectal stump. By significantly reducing the operative trauma, it is suggested to reduce the postoperative complication rate. In **chapter 13** this new minimally invasive method of restoration of bowel continuity is compared to the standard technique by laparotomy in patients after HP for complicated (perforated) diverticulitis.

# 2

# Treatment for diverticulitis not thoroughly researched

*with*
Draaisma WA
Van de Wall BJ
Unlu C
De Korte N
Swank HA

On behalf of the
Dutch Diverticular Disease
Collaborative Study Group



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# Abstract

In the Netherlands approximately 14,000 patients are referred to the hospital for diverticular disease each year. Overall controversy persists about four aspects of treatment of the different stages of diverticulitis, i.e. the role of antibiotics in the treatment of mild diverticulitis, the question of whether elective surgical resection is justified in recurrent diverticulitis or in persisting abdominal symptoms after an episode of diverticulitis, the question of whether patients with purulent peritonitis due to perforation may be treated with laparoscopic peritoneal lavage instead of Hartmann's procedure, and finally, whether resection with a primary anastomosis is a feasible and safe alternative to Hartmann's procedure in the surgical treatment of Hinchey III or IV diverticulitis. These questions will be addressed in four upcoming Dutch randomized trials.

# Introduction

Diverticulosis is a common disorder of the colon wall in westernized countries. The pathogenesis of this structural abnormality is probably multifactorial involving low-fibre-dietary habits, changes in colonic motility and wall structure associated with ageing. The prevalence of diverticulosis is estimated at 50-70% in individuals older than 80 years. Below the age of 40, it is observed in less than 10% of the people.[1] Diverticulosis is most notable in the left colon, with up to 99% having some degree of sigmoid involvement
Several symptoms can be related to the presence of diverticulosis. Symptomatic diverticulosis refers to the condition in which the patient experiences recurrent abdominal pain and bloating. Complicated diverticulosis (diverticular disease) refers to the different stages of diverticulitis or diverticular bleeding. Left lower quadrant pain whether or not accompanied by fever is almost universal in sigmoid diverticulitis. The incidence of diverticular disease is estimated at 75-150 per 100.000 patients each year, which results in 14.000 hospital admissions each year. The annual costs to treat diverticular disease are 40-80 million Euros.[1,2]
Diverticulitis is the most usual complication of diverticulosis, affecting 15-20% of patients.[3] The pathophysiology of diverticulitis remains poorly understood. Due to a lack of good quality research, the optimal treatment of this ever more common disease is still debatable.
Four trials with different research questions all involving important issues concerning the treatment of different manifestations of diverticulitis have evolved in 2008. This has led to a joint Dutch initiative: the 'Dutch Diverticular Disease Collaborative Study Group' (3D-study group). Herein we outline the different trials of the 3D-study group and discuss their importance.

# Clinical features of diverticulitis

Patients suffering from diverticulitis will present with abdominal pain at the left lower quadrant, fever and an elevated white blood cell count (table 1).[4] Most often the diagnosis of diverticulitis can be made on clinical grounds, but sometimes clinical features can be non-specific and misleading. Other diagnoses like irritable bowel syndrome or gynaecological disorders must be excluded.

**Table 1.** Frequency of symptoms in diverticulitis

| Symptom | Frequency (%) |
|---|---|
| Abdominal tenderness in the left lower quadrant | 93-100 |
| Elevated white blood cell count | 69-83 |
| Fever | 57-100 |
| Nausea | 10-30 |
| Vomiting | 15-25 |
| Constipation | 10-30 |
| Diarrhea | 5-15 |
| Dysuria | 5-20 |
| Change in urinary habits | 6-25 |

In case of mild symptoms, additional radiographic modalities are not necessary to justify clinical diagnosis. These patients can be treated conservatively with oral fluids with or without additional antibiotics on an out-patient basis. Relief of symptoms is expected within 2-3 days. Imaging is indicated when complains persist or worsen.[5,6] If necessary, in-hospital treatment of diverticulitis with restricted oral intake and intravenous antibiotic treatment is initiated.[6,7]

Abdominal ultrasound is known as a relatively cheap and reliable non-invasive method to diagnose diverticulitis. In the hands of an experienced radiologist, ultrasonography has a reported sensitivity of 92% and a specificity of 90%. In computed tomography (CT) scanning, sensitivity and specificity are reported as high as 94 and 99%,[8,9] respectively. CT has the advantage that it defines the extent of the affected colon as well as it identifies abscesses and perforations more accurately than ultrasonography. However, CT is more expensive and involves radiation.[8,9]

## The Hinchey classification

Several classifying systems have been introduced to describe the different stages of diverticular disease. The Hinchey classification is most widely recommended.[10] Traditionally Hinchey's classification has been used to distinguish four different stages of perforated diverticulitis (figure 1), but improvements in imaging modalities has led to a modification of this classification. The modified Hinchey classification describes five categories of diverticulitis, with two subcategories in case of Hinchey stadium I (table 2).[11] In general, Hinchey Ia is regarded as mild diverticulitis, Hinchey Ib-II as moderate diverticulitis and Hinchey III-IV as severe complicated diverticulitis.

**Figure 1.** The Hinchey Classification of (perforated) diverticulitis

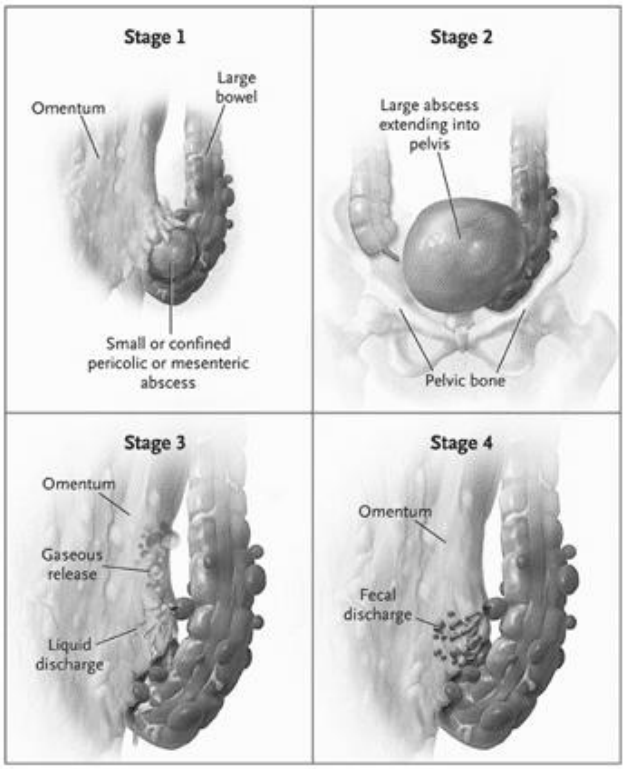




**Table 2.** Original and modified classification of (perforated) diverticulitis by Hinchey

| Hinchey classification | | Modified Hinchey classification | |
|---|---|---|---|
| Stadium | Findings | Stadium | Findings |
| | | 0 | Mild non-complicated diverticulitis |
| I | Pericolic phlegmon or abscess | Ia | Localized pericolic inflammation or phlegmon |
| | | Ib | Localized pericolic abscess |
| II | Pelvic, abdominal or retroperitoneal abscess | II | Pelvic, abdominal or retroperitoneal abscess |
| III | Generalized purulent peritonitis | III | Generalized purulent peritonitis |
| IV | Generalized faecal peritonitis | IV | Generalized faecal peritonitis |

# Controversies in the treatment of diverticulitis

## Literature

When discussing the optimal treatment for the different stages of diverticulitis, three main questions remain unanswered: 1) Is there a benefit of additional antibiotics in the treatment of mild diverticulitis?; 2) What is the benefit of elective surgery in case of recurrent or persistent complains in diverticulitis?; and 3) What is the optimal treatment strategy in Hinchey III and IV perforated diverticulitis? Recently, a systemic review concerning the above-mentioned issues was published, which showed that hard evidence is still missing.[12] Randomized trials are lacking in the current literature, at present evidence is only based on retrospective studies and some prospective cohort studies with limited numbers of patients.

## Antibiotics or not?

Most patients with mild (Hinchey I-II) diverticulitis can be treated conservatively without surgical intervention.[5] Recently, the benefit of additional antibiotics in the conservative treatment of these patients is debated. In 2007 the results of a retrospective study in which patients with mild diverticulitis treated with antibiotics (n=118) were compared with patients without additional antibiotics (n=193), were published.[13] Of the patients who were treated with antibiotics, 3% needed to undergo surgical intervention in a later stage during initial hospital admission, compared to 4% of the patients that were initially treated without antibiotics. After a mean follow up of 30 months, 29% of the patients with antibiotics developed complications that needed surgical intervention or recurrence of diverticulitis. This was 28% for the patients that were initially treated without antibiotics.

In conclusion, the authors of the study stated that additional antibiotics probably will not provide better outcome in the treatment of mild diverticulitis. However, selection bias may have played an important role, as the more severely affected patients are more likely to have been treated with additional antibiotics.

In 1996 questionnaires regarding the treatment of diverticulitis were sent to all surgeons and internists in the Netherlands. The results of this questionnaire showed that both specialists had different thoughts about the benefit of antibiotics in diverticulitis treatment. Surgeons were more conservatively in prescribing antibiotics compared to internists: 55% vs. 77%, respectively.[14] A similar questionnaire, provided by the 3D-study group in 2009, demonstrated a significant decrease in antibiotic use: currently, only 10% of both the surgeons

and internists recommend additional antibiotics in the treatment of mild diverticulitis (unpublished data).
As cost-effectiveness and antibiotic resistance are important issues in improving current health care, and hard evidence is lacking in current literature, prospective assessment of the benefit of antibiotics in the treatment of mild diverticulitis is warranted.

## Diverticular recurrence or persistent complaints: resection or not?

After a conservatively treated first episode of diverticulitis, 20-25% of patients will develop a recurrence of diverticulitis.[12] Traditionally, patients were advised to undergo resection of the affected colon segment after a second episode of diverticulitis,[6,7] because of a supposed higher risk on complications (fistula/ abscesses formation/ perforation) and mortality in case of another recurrence.[15] Today, surgeons and internists are more conservative. Recent studies have observed that the severity of recurrent diverticulitis is comparable to previous episodes. Only 5-8% of the patients that were treated conservatively for diverticulitis will develop complications due to recurrent diverticulitis requiring emergency surgery during follow-up.[16,17] Subsequently the benefit of elective surgery to prevent perforated recurrent diverticulitis is debatable.
On the other hand, a more specified subgroup of patients might benefit from prophylactic surgery. After conservative treatment, 40-80% of the patients will present with persistent complaints related to diverticular disease.[17,18] These patients complain of prolonged abdominal tenderness with or without changed stool habits for more than three months after recovery from the initial diverticular inflammation. It is important that other colonic disorders have been excluded.[12] The daily presence of abdominal tenderness affects the quality of life of these patients and is associated with higher costs due to frequent specialist consultation, analgesic use and absence from work.[18,19] The question remains, for how long can a conservative strategy be acceptable for patients with prolonged abdominal complains after diverticulitis?
Elective resections will not only prevent complicated recurrences, but might also be beneficial in treating prolonged abdominal complaints after diverticulitis.[20] However, the supposed benefit of elective surgery must be weighed against possible perioperative complications. Major complications, like anastomotic leakage, is observed in 5-10% of patients and there is even a risk on mortality (0-1%).[21] As good randomized clinical trials are lacking in current literature, the optimal treatment of patients suffering from recurrent diverticulitis or prolonged abdominal complaints after diverticulitis, is still a matter of debate.

## Surgical treatment of Hinchey III-IV diverticulitis

Free bowel perforation caused by diverticulitis is one of the most severe and complicated forms of diverticular disease. Perforation of a large diverticular abscess (Hinchey III) or the bowel wall itself (Hinchey IV) into the abdominal cavity is found in about a quarter of patients with acute diverticulitis. It will lead to generalized peritonitis, with a mortality rate up to 35%.[22] In this category of patients emergency surgery is indicated. The optimal strategy remains debatable.

*Hartmann's procedure* (HP). The most commonly performed surgical procedure in these cases is HP, in which the affected sigmoid is removed with the establishment of an end colostomy.[23] Restoration of bowel continuity can eventually take place in a second operation, but with a significant risk on postoperative morbidity and even mortality. This is the main reason why almost 40% of patients after HP will be left with a permanent end colostomy.[24]

*Resection with primary anastomosis* (PA). Alternatively, resection of the affected bowel with primary anastomosis with or without temporary 'protective' diverting loop ileostomy can be performed. Reversal of this loop ileostomy can be performed as a local procedure without the need for laparotomy.

Several studies have tried to compare both surgical strategies, including three systemic reviews.[22,23,25] In the latest review of 2007, postoperative mortality is estimated at 18.8% after HP and 9.9% after PA.[23] Anastomotic leakage was observed in 3 and 6% respectively. Postoperative complication rates varied from 25 to 50% and were not different between both procedures. However, patients with higher risks on postoperative complications were found to undergo more often HP than PA. The effect of this selection bias on the presented results is unknown, but makes it hard to make a good comparison between both surgical strategies. A randomized controlled trial between both strategies is warranted.

*Laparoscopic lavage*. Recently a new strategy for treating Hinchey III diverticulitis has been introduced: laparoscopic lavage and drainage without resection. A prospective cohort study of 92 patients, who were treated with laparoscopic lavage with 4 litres of warm saline and the placement of two abdominal drains, showed an uncomplicated outcome in 89%.[26] Three patients died due to multi organ failure (3%). Laparoscopic lavage seems to be a promising alternative for HP or PA, as the latter have higher mortality rates. It is therefore of interest to compare this new laparoscopic strategy with the current mostly performed open resectional strategies in a randomized controlled trial.

# Considerations

The optimal treatment for the several different stages of diverticular disease is still a matter of debate. Patients with mild and non-complicated diverticulitis can be treated conservatively, without the need for surgical intervention. It remains unclear if these patients need to be treated with antibiotics and if the use of antibiotics in the treatment of mild diverticulitis indeed leads to a faster recovery, shorter hospital stay and faster return to work, which have important socio-economic implications.
Prophylactic surgery seems not to be indicated for patients after one episode of diverticulitis, as only a small number of these patients will develop complications in the future that require emergency surgery. Nevertheless, patients with persistent complaints after diverticulitis could benefit from elective surgery. The suspected benefit from surgery needs to be weighed against general postoperative morbidity like wound infection, bleeding and severe complications like anastomotic leakage and even mortality.
The optimal treatment of Hinchey III and IV diverticulitis also remains controversial. Patients with generalized purulent peritonitis (Hinchey III) might benefit from laparoscopic lavage and drainage, if in these patients sigmoid resection by laparotomy, with accompanying high morbidity-and mortality rates, can successfully be withheld.
Understandably, patients with generalized faecal peritonitis (Hinchey IV) need to undergo emergency surgery. The question remains which strategy is superior. Possibly PA is a better and safer option in this category of patients than HP.

# Dutch trials

Recently, in the Netherlands the 3D-study group is established that will assess the abovementioned aspects with regard to the treatment of diverticulitis. Four randomized clinical trials have been designed in different hospitals under auspices of the 3D-study group. From the Amsterdam Academic Medical Centre, the Saint Lucas Andreas Hospital and the Haarlem Kennemer Gasthuis Hospital, the DIABOLO-trial is initiated. This study will randomize patients with mild diverticulitis between treatment with intravenous administered antibiotics, outpatient treatment with oral antibiotics, or treatment without antibiotics.

The Amersfoort Meander Medical Centre has designed another randomized trial: the DIRECT-trial. In this study patients with persistent complains after one or more episodes of diverticulitis will be randomized between elective resection of the affected bowel segment and a conservative policy.
From the Rotterdam Erasmus University Medical Centre and Amsterdam Academic Medical Centre the LADIES-trial is initiated. The LADIES-trial will assess the optimal surgical treatment for perforated diverticulitis. Patients with Hinchey III diverticulitis will be randomized between laparoscopic lavage and open resectional surgery (LOLA-arm). In addition, the patients with Hinchey III diverticulitis that are randomized for open resectional surgery and all patients with Hinchey IV will be randomized between HP and PA (DIVA-arm). The studies have started in 2010 and are intended to provide more evidence with regard to the optimal treatment for the different stages of diverticular disease.

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# Ernst Graser

(4-4-1860 – 19-11-1929)

*Ernst Graser was the first who described the anatomy and aetiology of sigmoid diverticula (known as Graser's diverticula since) and their inflammation.*

Ernst Graser studied medicine at the universities of Erlangen, Munich en Straßburg, where he graduated in 1883. He started working as a resident at the department of surgery of the Erlangen University Hospital in 1886. He became professor of surgery in Rostock in 1892. He returned to the Erlangen University clinics in 1901, where he was appointed director of the surgical department and dean of the medical faculty. He continued working in Erlangen until 1929. During the First World War he worked in the fighting zone as general physician (1906-1915). Afterwards he became head of physicians and was ranked Major-General. From 1920 until 1922 Ernst Graser was president of the Bayerischer Chirurgenvereinigung, which he was the founder of.

# George Emerson Brewer

(28-7-1861 – 24-12-1939)

*George Emerson Brewer was the first who reported about acute perforated diverticulitis in 1907.*

George Emerson Brewer studied medicine at the University of Buffalo and the College of Medicine at Harvard University, where he graduated in 1884. After a residency in obstetrics and gynaecology at the Columbia Hospital for Women of Washington D.C., he worked at the Johns Hopkins Hospital and finally at the New York City Hospital as an attending surgeon. At that time he had started his studies in operating room techniques. After two years he became surgeon in the Roosevelt Hospital and became surgical director of the Presbyterian Hospital in 1913.

George Brewer was one of the founders of the Society of Clinical Surgery and its first president. Later he became president of the American Surgical Association and Clinical Congress of Surgeons of North America.

During the First World War he served with an operating team in France as chief consultant of Surgery of the First Corps and First Army. George Brewer received many international honours, amongst them Officier de l'Ordre de la Couronne of Belgium and fellow of the Royal College of Surgeons of Ireland.

# 3

# Pathophysiology and prevention of diverticulitis and perforation

*with*
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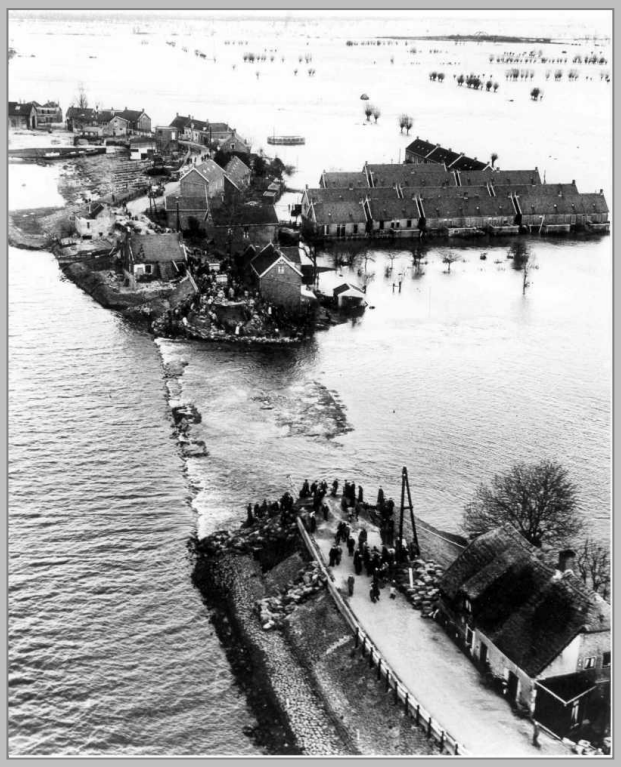

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# Abstract

This article gives an overview of the current evidence and theories in the pathophysiology of diverticulosis, diverticulitis and perforation and discusses its prevention.

Diverticular disease is one of the most common diseases related to the gastro-intestinal tract in Western countries. The pathogenesis of this disease process is probably multifactorial, but remains poorly understood and inadequately investigated.

A literature search was performed in order to give an overview of the current evidence and theories in the pathophysiology of diverticula formation and the factors related to progression towards inflammation and even perforation. Strategies for prevention of (perforated) diverticulitis are also discussed.

The pathogenesis of diverticular disease and its complications seems to be a result from a complex interaction between exposure to a low-fibre diet, possible genetic influences, the coexistence of other bowel diseases and the impact of medicine use. This eventually leads to alterations in colonic pressures and motility and structural changes of the colon wall. Unfortunately the evidence is frequently conflicting in present literature or lacking altogether.

# Introduction

The prevalence of diverticulosis is estimated at 5% by the age of 40 years, up to 65% at 80 years of age.[1,2] Its exact prevalence is difficult to assess because most people remain asymptomatic.[2] Only 10 to 25% of patients with diverticulosis will manifest any related clinical symptoms.[2,3]
The pathogenesis of this disease process is probably multifactorial involving dietary habits, changes in colonic pressure, motility and wall structure associated with ageing.[4] The reason why a subgroup of individuals progresses from asymptomatic to symptomatic or even complicated diverticular disease remains poorly understood. This article gives an overview of the current evidence and theories in the pathophysiology of diverticulosis, diverticulitis and perforation and discusses its prevention.

# Pathophysiology diverticula of the colon

In western nations diverticula are most common in the left colon. This is in contrast to Asian nations where they occur primarily in the right colon.[5] This difference suggests a role for genetic, environmental or lifestyle factors in the aetiology of diverticular disease.[6]
Diverticula are most notable in the left colon, with up to 99% having some degree of sigmoid involvement.[7] They protrude most commonly in four rows between the antimesenteric and mesenteric taenia.[8] The majority of diverticula pass through the bowel at weak points in the circular muscle layer where the blood vessels penetrate it to supply the mucosa.[8,9] This suggests that intraluminal pressure might play a role in their formation. These pulsion diverticula are in fact ‘false’ diverticula as not all layers of the bowel wall are involved.[4]
The maintenance of the colonic wall is provided by extracellular matrix, with components like collagen and elastin.[10] The mechanical characteristics of the bowel are maintained via circular and longitudinal muscle layers. The circular muscle thickens in regular bands of contraction (plicae circulares) which control peristalsis. The longitudinal muscle also condenses in thick bands (the taeniae coli) which serve to pull the colon to a relatively short functional length. Thickening of the muscular layer is one of the most consistent features of diverticulosis.7

Accumulation and aberrant deposition of connective tissue fibres (elastin and collagen) underlie the altered muscle morphology.[11] The muscle cells themselves do not change, but the taeniae become thickened secondary to elastin depositions, which leads to contraction in this layer and thickening of the circular muscle layer.[11-13] This narrows the lumen. In addition, systematic contractions of the circular muscle divide the bowel into a series of compartments. Altogether these colonic wall changes lead to an increase in intracolonic pressures.[14-16]

Elastin depositions and crosslinking of collagen continue throughout life in all layers of the colonic wall.[17] Increased elastin deposition may result from intermittently increased colonic pressure, which in turn is due to reduced faecal load produced by a Western low-fibre diet. Together with a decrease in tensile strength of the colonic wall, caused by an increase in cross-linking of collagen fibres with age and caused by a low fibre diet as well, these changes in muscle morphology will result in weakening of wall resistance.[13,18-20] The increased depositions of these two connective tissue fibres (elastin and collagen III) are observed more pronounced in diverticular disease.[21,22]

It is thought that a disruption of the balance between matrix metalloproteinases (MMPs) and their inhibitors (TIMPs) may be involved in the pathogenesis of diverticular disease, through remodelling of the colonic extracellular matrix, particularly collagen.[10] An overexpression of TIMPs in the muscular layer affects the turnover of extracellular matrix, resulting in the formation of diverticula and their complications.[7,10,22] An increased synthesis of type III collagen is observed in diverticulosis, but its significance remains to be elucidated.[21] The disturbance of the collagen texture (lower ratio of mature collagen type I and immature collagen type III), is thought to weaken the bowel wall, hence leading to the onset of diverticula.

Besides colonic wall changes, disordered motility has also been suggested as a cause of increased intraluminal pressure and hence as a pathogenetic factor in diverticulosis.[23] Colonic motility is influenced by the aging process of its smooth muscle, causing an increase in segmental contractile activity.[24] Patients with symptomatic diverticular disease have shown to have higher motility indices than asymptomatic patients or healthy persons.[23] Nevertheless, absolute evidence is still lacking, since most studies on colonic motility and myoelectrical activity were biased by poor patient selection, heterogeneity of clinical conditions, recording techniques, and duration of the recording and mostly based on small numbers of patients.[23]

Neurophysiopathological data to support the increased colonic motility are sparse in the present literature. The high intracolonic pressure might be related to an imbalance in usual excitatory and inhibitory neural influences (increased cholinergic stimulation). Cholinergic nerves were dominantly present in the

diverticular colon compared with controls.[25,26] Moreover, patients with diverticular disease have shown substantial structural alterations of the enteric nervous system mainly characterized by a significant lower number of glial cells and a lower number of interstitial cells of Cajal in the mesenteric plexus and within the muscle.[27] These cells are emerging as potential colonic pacemaker cells, and their loss might explain intestinal motor abnormalities reported in diverticular disease.

The influence of Western diet habits (red meat, low fibre) on the evolution of diverticular disease has been well established.[1,28,29] These dietary factors lead to increased colonic transit times, smaller stool volumes and subsequently to raised intracolonic pressures, all of which may contribute to the development of diverticulosis.[30] An increase in diverticular disease in developing countries has been documented, concurrent with the adoption of Westernised dietary habits.[4] An unexplained curiosity in the increase in diverticular disease in Asia is that it is mostly right sided, which suggest a genetic component in the development of diverticulosis.[31]

Some genetic disorders have been associated with a strong predisposition towards diverticula formation. Most of these syndromes are associated with a connective tissue disorder (Ehler-Danlos, polycystic kidney disease).[6] But literature is conflicting about this matter.[32] The same is thought about Saint's triad (the aggregation of gallstones, diverticulosis of the colon and hiatus hernia in elderly people). Connective tissue abnormalities causing herniosis might be the causing factor in this triad, although fibre-depleted diets may also be causatively related to Saint's triad.[33]

Recent studies show increasing mitochondrial dysfunction in the ageing colonic epithelia and this correlates well with diverticular disease prevalence.[34] It remains unclear whether these findings play a role in pathogenesis or are simply related to aging.

It has been suggested that the irritable bowel syndrome may be an early stage in the development of diverticulosis.[35,36] Although a lack of dietary fibre and higher colonic motility activities caused by changes in the enteric nervous system has been implicated as aetiological factors in both conditions, available evidence supporting this theory is conflicting in the present literature. As both conditions are relatively common, the likelihood of coincidental occurrence in the same individual is quite high.[37] It is therefore almost impossible to predict which patients are symptomatic as a direct result of their diverticulosis. In the same manner, persistence of symptoms after surgical resection for symptomatic diverticular disease can be explained.[37]

In conclusion, the evidence from studies in man suggests a relationship between diet/lifestyle and diverticular disease, but there remains a lack of robust definitive evidence.

# Pathophysiology of diverticulitis

It is estimated that 10 to 25% of patients with diverticulosis will experience inflammation at some point during their lives.[38] Like the pathophysiology of diverticula, the aetiology of diverticular inflammation is also speculative. Development of diverticulitis has been described similarly to that of appendicitis. Diverticula may become acutely inflamed through impacted faeces, leading to an obstruction of the lumen, raising intradiverticular pressure by continuing mucus formation and ultimately causing ulceration within the diverticular mucosa.[39] This event then allows for proliferation of bacteria, diverticula distension, and localised ischaemia. Eventually, perforation of variable extent may result, accounting for a range of symptoms.[40,41] It is possible that the increased colonic pressure in diverticular disease is also responsible for pushing fecaliths into the diverticula.

Dietary shifts during the past century have likely not only influenced colonic motility, but also altered colonic flora.[42] The colonic environment has likely undergone radical changes in the past century due to decreases in both soluble and insoluble fibre. Higher levels of *Bacteroides* and lower levels of *Bifidobacteria* have been found studies comparing gut flora between Westernised and rural populations. This change in colonic microbial environment may be an important element in the transformation of asymptomatic diverticular disease into diverticulitis, but its exact role has not been adequately defined.[43]

In addition to the 'typical' form of diverticulitis, it is increasingly recognised that luminal mucosal inflammation may coexist with diverticula.[44,45] This low-grade inflammation share histological features with inflammatory bowel disease. The pathogenesis of this so-called diverticular colitis, sigmoiditis, or segmental colitis is unknown, as is its relationship with inflammatory bowel disease.[45,46] Nevertheless, low-grade diverticular colitis might be the reason why some patients are chronically symptomatic. This phenomenon has been described before in inflammatory bowel disease, where colonic symptoms may persist after resolution of inflammation.[47] The acute diverticular inflammation may have provoked an alteration in colonic neuromuscular function and may be responsible for chronic symptoms, even in the absence of inflammation.

# Pathophysiology of perforated diverticulitis

Although diverticulosis is common, complications requiring surgery occur in only approximately 1% of patients with the disease.[48] The incidence of diverticular perforation has been estimated at 4/100.000 population per annum.[49] About 80% of patients presenting with perforated diverticulitis do not have a previous history of diverticular disease.[49]

The natural history of complicated diverticulitis remains poorly understood, probably because consultant surgeons see only two to three cases a year and almost a third of patients die from unrelated causes during follow up.[50] In case of perforated diverticulitis this percentage might be even higher, up to 50% within five years.[51]

The aetiology of perforation remains unknown, but as stated before, it is thought to be a result of excessive rise in intradiverticular pressure and focal necrosis.[52] This local perforation may form pericolic phlegmones and pus collections (Hinchey I).[53] If this process progresses localized abscesses may be formed between loops of small bowel or in the pelvic peritoneum (Hinchey II). If the pus cannot be contained, the abdominal peritoneum gets contaminated producing generalized purulent peritonitis (Hinchey III). The same is found when a large intraperitoneal diverticular abscess ruptures into the abdominal cavity.[54] If the initial perforation is large, faecal contamination of the abdominal cavity can occur (Hinchey IV).[53]

Patients with diverticular disease in general show raised intracolonic pressures, especially in the sigmoid colon.[14] As almost all diverticular perforations occur in the sigmoid colon, these pressure changes must be an important etiological factor. Besides that, the properties of the colonic wall are likely important, because diverticula consist predominantly of mucosa, lacking a smooth muscle layer. The mucosal barrier is vulnerable and may be impaired by various exogenous factors.[55]

NSAIDs have been implicated as a risk factor for perforation in diverticulitis.[49,56-58] NSAIDs inhibit the cyclo-oxygenase enzyme and causes topical mucosal damage, increasing colonic permeability. Besides, they reduce prostaglandin synthesis, which is important in maintaining an effective mucosal barrier.[59]

Corticosteroids and opiate analgesics are also related to an increased perforation rate.[60,61] Corticosteroids have strong immunosuppressive and anti-inflammatory effects, which may result in an impaired ability to contain the perforation initially.[57] This will lead to more severe inflammatory complications. Besides, symptoms and signs in the immunosuppressed patient may well be masked, often delaying and underestimating diagnosis and its

severity.[62,63] The prevalence of diverticulosis in immunosuppressed patients may not differ from that of the rest of the population, but there is undoubtedly a much higher incidence of complicated diverticulitis in such patients.[63] Opiates slow intestinal transit and raise intracolonic pressures.[61] By slowing transit time, the diverticular mucosa may have a prolonged exposure to potentially damaging pathogens, such as bacteria.

Unfortunately the causal relationship between these drugs and perforated diverticulitis is mainly based on (small) case series or case-control studies. Hard evidence is lacking in the present literature. Besides, if these drugs are a true risk factor for perforation, they would account for less than 20% of cases: other risk factors must be important.[54]

The role of smoking and alcohol intake in perforated diverticulitis is also unknown. Nicotine might predispose to diverticular inflammatory complication by reducing mucosal immunity,[64,65] but hard evidence is lacking in the present literature.[66]

Since the incidence of diverticulosis increases with age, the majority of patients presenting with symptoms are the elderly. Complicated diverticulitis is also observed predominantly in older patients. This problem is caused by an unusual presentation of diverticular complications in the elderly patient, with consequent delay in diagnosis. Polypharmacy may further exacerbate this problem and may even increase the risk of developing complications (NSAIDs, corticosteroids).[67] The relatively high incidence of comorbidities in the elderly and the unusual presentation of the disease will lead to a very high morbidity and mortality rate for this group of patients.[51]

On the other hand, complicated (perforated) diverticulitis is relatively frequently seen in younger (male) patients.[68] Although diverticulitis is uncommon in patients less than 40 years old, accounting for only 5% of all patients admitted for diverticulitis, it has been thought to be a more virulent condition in this age group.[69,70] But again the present literature is conflicting. Several recent publications have suggested that the disease is not more virulent in the younger patients.[71-73] The high rate of complications and perforations may be attributed to a high misdiagnosis rate because diverticulitis may not be suspected in younger patients with abdominal complaints.[74,75]

# Prevention of diverticulitis and perforation

The possible role of diet and lifestyle offers strategies for prevention. Large prospective studies have identified a preventive effect of both vegetable and

high fibre intake and physical exercise in the development of diverticular disease, as well as diverticulitis.[76-78] The protective action of dietary fibre would make the stools bulkier, thereby increasing the colon size and decreasing intraluminal pressures, and reducing colonic transit time.[79,80] Fibre as a dietary supplement may be beneficial in prevention. It is nevertheless remarkable that the incidence of diverticular disease has not been found to be reduced, while several studies have shown an increased intake of fibres in Western populations over the last three decades.[81] The exact role of fibres in the pathophysiology of diverticulosis and its prevention remains unclear. And when symptoms have developed, evidence of a benefit of fibre is even less convincing.[81]

A reduction in transit time was the consistent finding in most of the studies that addressed the effect of physical exercise on colonic function. An increase in colonic motor activity has been postulated; however, the exact mechanism of this effect is still not clear.[78]

As mentioned above, patients with symptomatic diverticular disease have shown to have higher motility indices than asymptomatic patients or healthy persons.[82] This suggests that anticholinergic or antispasmodic drugs might improve symptoms by diminishing muscular contractions. Nonetheless, there is no evidence to support this in the present literature.[40]

One of the latest therapies for the prevention of recurrent diverticulitis is the use of mesalazine, rifaximin or a combination of both.[83,84] The rationale for this is that mesalazine inhibits some key factors of the inflammatory cascade.[85] The protective role of mesalazine in the recurrence of symptomatic diverticular disease is thought to be similar to that for the use in chronic inflammatory bowel disease.[85,86]

Another very recent therapy is the use of probiotics.[87] Probiotics diminish changes in the spectrum of intestinal microflora and the adherence and translocation of pathogens. They also regulate production of antimicrobials and interact as competitive metabolites with pro-inflammatory organisms. Especially the combination of *Lactobacilli* spp. with Rifaximin seems effective in reducing severe forms of diverticulitis and the prevention of recurrences, hence reducing surgical treatment significantly.[88,89]

The role of surgery in the prevention of (complicated) diverticular disease is unclear. Formally, elective sigmoid resection was recommended after two episodes of uncomplicated diverticulitis to prevent serious complications of recurrent colonic diverticulitis.[90] This guideline was based on the assumption that recurrent episodes of diverticulitis will lead to more complications and higher mortality. The data to support this assumption are based on small and older studies. Advances in diagnostic modalities, medical therapy, and surgical techniques over the past two decades have changed both the management and

outcomes of diverticulitis.[91] Patients treated nonoperatively would be expected to do well without elective colectomy, since most patients will not have further episodes of diverticulitis.[92,93] Recurrent episodes of diverticulitis do not lead to more complications and more conservative treatment failure.[94,95] At present it is thought that elective resection for uncomplicated diverticulitis does not alter outcome, nor does it decrease mortality or prevent severe complications of the disease such as perforation.[96,97] For approximately 80% of the patients perforation is the first manifestation of diverticular disease.[49]
Finally an association between the use of calcium channel antagonists and perforated colonic diverticular disease was demonstrated.[98] Calcium channel antagonists, which reduce colonic contractility and tone, protected against perforation. Further studies are required to confirm this association, but it may represent a potentially useful preventive therapy.

# Conclusion

Although diverticular disease is one of the most common diseases related to the gastrointestinal tract in Western countries its pathophysiology remains poorly understood and inadequately investigated. Much of the evidence suggests that the pathogenesis of diverticular disease is a result from a lifelong exposure to a low-fibre diet, leading to alterations in colonic pressures and motility and colon wall structural changes. Unfortunately the 'evidence' is frequently conflicting in the present literature or lacking altogether. This complex interaction between colonic structure, motility and diet, the possible genetic influences, the coexistence of other bowel diseases and the impact of medicine use, makes it difficult to investigate. It may even be so that clinical subtypes of diverticular disease exist in terms of pathophysiology and symptomatology requiring different treatment strategies. Further basic and clinical investigations need to be done to fill up the several gaps in the knowledge of pathophysiology of diverticulosis and diverticulitis and its treatment and prevention. For the same reason, there is a need for further good quality epidemiological research to identify risk factors in diverticular perforation. Whether new insights in the aetiology will lead to new surgical strategies for prevention and treatment of perforated diverticulitis remains to be seen.

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# 4

# Hospital mortality after emergency surgery for perforated diverticulitis

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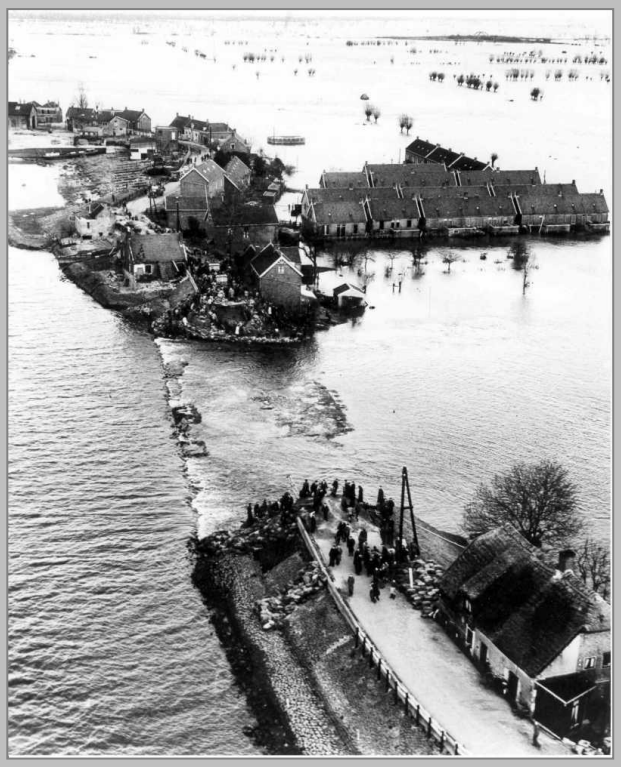
WCJ Hop
JF Lange
PPLO Coene
E van der Harst
WF Weidema
GHH Mannaerts



Nederlands Tijdschrift voor Geneeskunde 2009; 153(25): 1209-1214.

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# Abstract

Mortality and morbidity rates of acute perforated diverticulitis remain high. The ideal treatment is still controversial. The object of this study was to compare patients with perforated diverticulitis treated either by resection with primary anastomosis (PA) or Hartmann's procedure (HP) and to assess which factors predict hospital mortality after emergency surgery for acute perforated diverticulitis.

A multicenter study was carried out on 291 consecutive patients with acute perforated diverticulitis who were presented in the surgical units of five affiliated teaching hospitals in Rotterdam, The Netherlands between 1995 and 2005. Hospital mortality was assessed in relation to patient-related risk factors such as age, gender and classification according to the American Society of Anesthesiologists (ASA); disease severity factors such as Hinchey score and Mannheim peritonitis index (MPI); surgery-related risk factors, such as type of surgery, e.g. HP or PA; surgeon's experience and time of operation and was evaluated using multivariate logistic regression analysis.

The total postoperative in-hospital mortality was 29%. HP was performed 211 times and PA was performed 75 times. HP was significantly more frequently performed in patients with higher values of age, ASA, Hinchey and MPI (all $p<0.001$). Multiple logistic regression analysis showed that age, ASA classification, Hinchey score, MPI and the absence of a specialist colorectal surgeon during surgery, were important prognostic factors of mortality. Surgical technique was not related to postoperative mortality (adjusted odds ratio for mortality (HP versus PA): 1.3; 95% CI: 0.6-2.9; $p = 0.54$).

Hospital mortality after emergency surgery for acute perforated diverticulitis was only found to be associated with patient-related risk factors, like age and ASA, severity of disease scores, like Hinchey score and MPI and the absence of a specialist colorectal surgeon during surgery. As the type of surgery did not appear to be a risk factor, selected patients with perforated diverticulitis can well be managed by PA. This decision should be made while taking into account patient's concomitant diseases, response to preoperative resuscitation and the availability of a surgeon experienced in colorectal surgery.

# Introduction

Almost 14.000 patients are admitted to hospital with symptoms related to diverticular disease in the Netherlands each year.[1] Most of those patients can be successfully treated conservatively, but nearly a quarter develop complications, like perforation, stenosis and abscess or fistula formation.[2] Surprisingly, 80% of the patients presenting with acute perforated diverticulitis, have not had previous symptoms related to diverticular disease.[3]
Acute perforated diverticulitis is considered a very serious condition, which requires emergency surgery. The most commonly performed surgical procedure in these cases is the so called Hartmann's procedure (HP), in which the affected sigmoid is removed with the establishment of an end colostomy. Restoration of bowel continuity can eventually take place in a second operation. Nevertheless, this second operation is never performed in more than half of the patients.[4]
Sigmoid resection with primary anastomosis (PA), in which an end colostomy is avoided, is an alternative to HP. Although the poor general condition of the patients and the severity of the disease found during surgery often deter many surgeons from performing PA, several studies have shown that PA can be safely performed even in this group of patients.[5-8]
Regardless of selected surgical strategy emergency operations for diverticular disease are associated with mortality up to 30%.[9] This is mainly due to major emergency surgery being performed outside office hours in the severely affected and elderly patient with multiple comorbidities.
Herein we describe the factors related to hospital mortality after emergency surgery for acute perforated diverticulitis.

# Patients and methods

## Selection of patients

A total of 291 patients underwent emergency surgery for acute perforated diverticulitis in the academic centre and four affiliated teaching hospitals of Rotterdam, The Netherlands (Erasmus Medical Centre, Ikazia Hospital, Maasstad Hospital (previously St. Clara Hospital and Zuider Hospital) and Sint Fransiscus Hospital) between 1995 and 2005. Patients were selected from computerized surgery registration databases using the search codes: exploratory laparotomy; diverticulitis; perforated hollow viscus; Hartmann's

procedure; left hemicolectomy; sigmoid resection; low anterior resection. Using this searching strategy, a complete overview of all patients presenting to the surgical units of the abovementioned hospitals was obtained, as all patients with acute perforated diverticulitis undergo emergency surgery. After completion of selection of the patients, predetermined parameters (amongst mortality) were distracted from the computerized patient's registration databases. When data was missing the paper medical records were studied.

## Surgeon and treatment

HP was performed in 211 patients and 75 patients underwent PA. In 20 patients after PA a diverting loop ileostomy was also performed. The remaining 5 patients underwent primary suture repair of the perforated diverticulum without resection. This group of 5 patients was excluded from the statistical analysis.

Perioperatively, the patients received broad-spectrum antibiotics: Cefazolin 1000 mg and Metronidazole 750 mg, or Amoxicillin and Clavulanate 1000mg-200mg. The decision regarding the surgical procedure was left to the discretion of the surgeon on call, who was not necessary a specialist colorectal surgeon. A specialist colorectal surgeon was stated as a surgeon that had successfully completed a fellowship in colorectal surgery with additional 2 or more years of practical experience, or a surgeon with 5 years or more practical experience in this type of surgery.

## Other prognostic factors

In this study, postoperative in-hospital mortality was retrospectively assessed in relation to age, gender, classification according to the American Society of Anesthesiologists (ASA), severity of disease, type of surgery, surgeon's experience and time of the operation, e.g. within or outside working hours and year. Severity of disease was stratified by the Hinchey score (table 1)[10] and the Mannheim Peritonitis Index (MPI) (table 2). An MPI≥26 is a significant predictor of mortality.[11]

## Statistics

Statistical analysis of the various parameters was performed using the Mann-Whitney test and the Fisher's exact test. Differences were considered significant at a two-tailed p-value of $<0.05$. A multivariate analysis of the significant clinical variables in univariate analysis was done using logistic regression models with mortality as the outcome.

**Table 1.** Classification of severity of perforated diverticulitis according to Hinchey[10]

| Score | Findings during surgery |
|---|---|
| Hinchey I | Confined paracolic or mesenteric phlegmon or abscess |
| Hinchey II | Distant (pelvic, abdominal or retroperitoneal) abscess |
| Hinchey III | Generalised purulent peritonitis |
| Hinchey IV | Generalised faecal peritonitis |

**Table 2.** Calculation of the Mannheim peritonitis index[11]

| Risk factor | Score |
|---|---|
| Age > 50 years | 5 |
| Female sex | 5 |
| Organ failure | 7 |
| Malignancy | 4 |
| Preoperative duration of peritonitis > 24h | 4 |
| Origin of sepsis not colonic | 4 |
| Diffuse generalised peritonitis | 6 |
| Exsudate | |
| Clear | 0 |
| Cloudy, purulent | 6 |
| Faecal | 12 |

# Results

## Patients and in-hospital mortality

Characteristics of the patients that underwent HP and PA are shown in table 3. The total postoperative in-hospital mortality was 29% (83 patients). Median survival of these 83 patients was 10 days (range 1-46). Patients who underwent HP were significantly older and with higher ASA classifications, higher Hinchey scores, and MPI (all $p<0.001$). A multivariate logistic regression analysis was performed using the prognostic parameters mentioned before: age, gender, ASA, Hinchey score, MPI, type of surgery and experience of the surgeon. Postoperative hospital mortality was found to be significantly related to the patient-related risk factors age and ASA-classification (ASA>II) (table 4).

Mortality was not related to gender: male 26% vs. female 31% (odds ratio (OR) 1.24; 95% CI 0.74-2.1). Also the year in which the operation had taken place or the hospital, in which the patient was operated, were not related to mortality.
Median hospital stay after HP was 17 days (range 1-137) compared to 13 days (range 5-112) after PA ($p<0.001$). Intensive Care Unit (ICU) stay was also significantly different (3 days (0-72) vs. 1 day (0-56), respectively; $p<0.001$).

**Table 3.** Characteristics of all patients that underwent emergency surgery in 5 hospitals of Rotterdam, The Netherlands between 1995 and 2005

| | Total | Hartmann's procedure | Primary anastomosis |
|---|---|---|---|
| Number of patients | 296 | 211 | 75 |
| Median age in years (range) | 70 (23-95) | 72 (23-95) | 64 (23-84) |
| Male/female; n | 126/165[1] | 92/119 | 29/46 |
| ASA classification; n (%) | | | |
| I | 50 | 32 (15) | 17 (23) |
| II | 91 | 57 (27) | 30 (40) |
| III | 99 | 78 (37) | 21 (28) |
| IV | 51 | 44 (21) | 7 (9) |
| Hinchey score; n (%) | | | |
| I | 71 | 50 (24) | 21 (28) |
| II | 48 | 22 (10) | 26 (35) |
| III | 123 | 95 (45) | 23 (31) |
| IV | 49 | 44 (21) | 5 (7) |
| MPI-points; n (%) | | | |
| <26 | 215 | 143 (68) | 68 (91) |
| ≥26 | 76 | 68 (32) | 7 (9) |
| Surgeon's experience; n (%) | | | |
| Specialist colorectal surgeon | 127 | 77 (36) | 49 (65) |
| Non-specialisist colorectal surgeon | 164 | 134 (64) | 26 (35) |
| Time of operation; n (%)[2] | | | |
| During office hours | 107 | 71 (49) | 36 (51) |
| Outside office hours | 109 | 74 (51) | 35 (49) |

*ASA = American Society of Anesthesiologist; MPI = Mannheim Peritonitis Index.*
*[1]Five patients underwent primary suture repair of the perforated diverticulum; these patients are left out this study. [2]Time of operation was not recorded in 75 patients.*

**Table 4.** Factors predicting postoperative in-hospital mortality after Hartmann's procedure or sigmoid resection with primary anastomosis for treatment of perforated diverticulitis; multivariate analysis

| | Postoperative mortality | | |
|---|---|---|---|
| | OR | 95% CI | p |
| Type of surgery (HP or PA) | 1.3 | 0.6-2.9 | 0.54 |
| Age (per year older) | 1.04 | 1.01-1.07 | 0.003 |
| ASA classification (vs. ASA I) | | | 0.014 |
| II | 2.7 | 0.7-10.4 | |
| III | 5.7 | 1.6-20.8 | |
| IV | 5.6 | 1.4-21.9 | |
| Hinchey score (vs. Hinchey I) | | | 0.012 |
| II | 0.7 | 0.3-1.9 | |
| III | 0.8 | 0.4-1.7 | |
| IV | 2.8 | 1.7-6.8 | |
| Specialist colorectal surgeon vs. non-specialist colorectal surgeon | 0.4 | 0.2-0.8 | 0.007 |

*OR = Odds ratio; HP = Hartmann's procedure; PA = sigmoid resection with primary anastomosis; ASA = American Society of Anesthesiologist.*

## Surgeon and type of surgery

The ratio of HP and PA performed each year did not change during the time period of this study. In 61% of the patients (72/119) with a Hinchey score of I and II, e.g. localised perforated diverticulitis, HP was performed. Patients with generalised peritonitis (Hinchey score III and IV) underwent HP in 83% of the cases (139/167). Specialist colorectal surgeons performed a PA significantly more frequently than surgeons without substantial experience in colorectal surgery: 39 vs. 16% (OR 3.28; 95% CI 1.89-5.70).

Mortality after HP was 34%, compared to 15% after PA. With univariate analysis HP adversely affected prognosis, however with multivariate analysis the type of surgery was not significantly related to postoperative mortality (table 4). The absence of a specialist colorectal surgeon during surgery remained a risk factor for postoperative mortality after multivariate analysis. In contrast with surgeon's experience, time of operation was not related to mortality: office hours compared to outside office hours showed an OR of 1.4 (95% CI 0.68-1.91).

The performance of a diverting loop ileostomy did not show any significant reduction in postoperative mortality. Ten patients died after PA without ileostomy (18%); only 1 of 20 patients after PA with diverting loop ileostomy died (5%): OR 3.2 (95% CI 0.38-27.13).

### Severity of disease

In-hospital mortality was significantly related to severity of disease. After adjusting for age, ASA, Hinchey, type of surgery and surgeon's experience, using multivariate analysis mortality was significantly related to Hinchey score, particularly Hinchey score IV (faecal peritonitis) (table 4). Similar results were observed when Hinchey score was replaced by MPI in the multivariate analysis (MPI=26 vs. <26: OR for mortality 13.5; 95% CI 6.6-27.7; p<0.001). Evaluation of Hinchey score and MPI together was not possible because of their strong correlation.

## Discussion

### Hospital mortality

In-hospital mortality after emergency surgery for acute perforated diverticulitis was high (29%). This reflects the poor general condition of these aged patients with multiple comorbidities. More than half of the patients were preoperatively classified ASA III or higher. Mortality was significantly related to age and ASA classification. Besides this, severity of disease (Hinchey score and MPI) was also significantly related to postoperative mortality. Although surgeons experienced in colorectal surgery had better outcomes compared to non-colorectal specialised surgeons, the type of surgical procedure (HP or PA) appeared not to be related to in-hospital mortality.

### Surgeon and type of surgery

The type of surgery was not significantly related to postoperative mortality. Although this has been described before,[12] this finding remains striking, as many surgeons still prefer HP over PA. Even patients with Hinchey I or II perforated diverticulitis underwent HP in 61% of the cases (table 3), although the existing literature advices otherwise.[5,9] Patients with Hinchey III or IV perforated diverticulitis will seldom undergo PA. The question is if the current strategy is right.[5,13]

Patient's prognosis appeared to be related to the surgeon's experience in colorectal surgery. As the operations were classified as emergency and hence

may be performed outside office hours, not all procedures were performed by specialist colorectal surgeons. It is known that non-colorectal surgeons prefer to perform HP for emergency management of colorectal disease.[14] Besides, an increase in postoperative morbidity and mortality is found for non-colorectal surgeons.[14] This study also showed the mortality after surgery performed by specialist colorectal surgeons was lower than when performed by general surgeons. In contrast with surgeon's experience, time of the operation did not influence outcome.

## Age and ASA classification

In this study, patients who had undergone HP generally had a higher age, ASA classification, higher Hinchey scores and MPI compared to patients who had undergone PA. Therefore, it seems that the more severely affected and high-risk patients underwent HP. A multivariate logistic regression analysis was performed to reduce the found bias in patient selection. Higher age and ASA classification were found to be independent risk factors for postoperative in-hospital mortality in case of perforated diverticulitis. The fact that the more severely affected patients underwent HP, could explain the longer hospital- and ICU stay in this group of patients.

## Severity of disease

Parameters significantly correlated with postoperative mortality were Hinchey score and MPI. Both scores reflect the severity of the disease. The Hinchey score is frequently used as a perioperative classification of severity of disease.[10] In the present study, only a Hinchey score of IV was found to increase the risk of postoperative mortality. Hinchey scores of I-III were not related to a patient's outcome.

Classifying severity of disease using MPI correlated better with postoperative mortality, with a MPI≥26 found to be a significant predictor of mortality. Nevertheless, higher Hinchey scores and MPI have not been associated with higher anastomotic leakage rates[6] and hence they should not be considered a contra-indication for performing PA.

## Considerations

In 1994, Gooszen et al published the results of a questionnaire concerning the treatment of diverticular disease, which they had sent to all members of the Dutch Society of Colorectal Surgeons.[15] This study shows that the ratio of HP and PA performed each year are similar to the ratios described in the publication of 1994 and did not change during the 10 years study period. Postoperative mortality did not improve either. In other words, for the last 10-

15 year, treatment of perforated diverticulitis has not changed, nor has its results. For many surgeons HP remains the favoured surgical procedure.
Randomised trials comparing HP and PA for perforated diverticulitis are lacking in the current literature. A few prospective studies tried to prevent confounding by selection by performing PA in all consecutive patients with perforated diverticulitis.[6,7,16,17] The results of these studies showed that PA seems not to be inferior to HP and are in concordance with the results of the present study. However, most studies are limited by small numbers of patients with generalised peritonitis and often the results of subgroups, for example patients with purulent or faecal peritonitis, are not mentioned separately.
In our opinion, the indication for HP is set too frequently. Especially in case of Hinchey I and II perforated diverticulitis, PA should be the surgical procedure of choice (if radiographic percutaneous intervention is not an option). Selected patients with generalised peritonitis (Hinchey III and IV) may also be managed well by PA. This decision should be made while taking into account patient's age and ASA classification and the availability of a specialist colorectal surgeon. It may seem that outcome after perforated diverticulitis depends mainly on intensive care and treatment of patient's comorbidities, by adequate perioperative fluid resuscitation and antimicrobial therapy. Especially in older patients this seems to be most important, as the type of surgery does not play a significant role.[12,18-22]

# Conclusion

Postoperative in-hospital mortality after acute perforated diverticulitis was very high, but seemed not to be related to the type of surgery: Hartmann's procedure or sigmoid resection with primary anastomosis. Reduction in mortality might be expected after intensive treatment of the patient's comorbidities. The availability of a specialist colorectal surgeon during the operation was also related to better outcomes.

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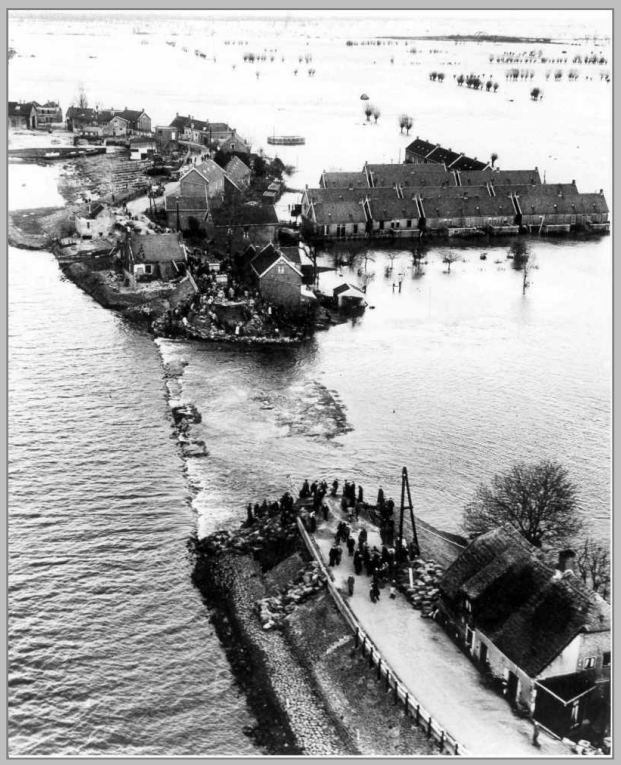
# 5

# Outcome after emergency surgery for acute perforated diverticulitis in 200 cases

*with*
GP Akkersdijk
MP Gosselink
WCJ Hop
GHH Mannaerts
E van der Harst
PPLO Coene
WF Weidema
JF Lange



Digestive Surgery 2007; 24(5): 361-366. Epub 2007 Aug 30.

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Autumn meeting of the Dutch Society of Gastroenterology 2006, Veldhoven (5-6 oct 2006)

# Abstract

Mortality and morbidity rates of acute perforated diverticulitis remain high. The ideal treatment is still controversial. The object of this study was to compare patients with perforated diverticulitis treated either by resection with primary anastomosis (PA) or Hartmann's procedure (HP).

A multicenter study was carried out on 200 consecutive patients with acute perforated diverticulitis who were presented in the surgical units of four affiliated teaching hospitals in Rotterdam, The Netherlands between 1995 and 2005. Mortality and morbidity were compared in relation to type of surgery, American Society of Anesthesiologist classification (ASA), age, gender, Mannheim Peritonitis Index (MPI), Hinchey score, surgeon's experience and time of operation.

There was a tendency for more severely affected patients (Hinchey, MPI, ASA and age) to undergo HP. Multivariate logistic regression analysis showed no significant difference in mortality between HP and PA. After HP, more patients needed one or more re-interventions to treat postoperative complications compared to PA. Besides, HP resulted in a longer total hospital and intensive care unit stay. Specialist colorectal surgeons performed significantly more frequent PA instead of HP. Time of operation did not influence the choice of surgical procedure.

Selected patients with perforated diverticulitis can well be managed by PA, as it seems not to be inferior to HP in terms of severe postoperative complications that need surgical or radiological re-intervention and mortality. This decision should be made while taking into account patient's concomitant diseases, response on preoperative resuscitation and the availability of a surgeon experienced in colorectal surgery.

# Introduction

Diverticular disease has emerged as a common problem in Western countries over the course of the 20th century. Up to two-third of individuals are affected with diverticulosis by the age of 70[1] and admission rates for diverticular disease are still increasing in the aged population.[2] Nearly a quarter of the patients require an emergency operation because of perforation, peritonitis, or systematic complications.[3]
Regardless of selected strategy emergency operations for diverticular disease are associated with substantial morbidity and mortality. Therefore the optimal treatment for complicated diverticulitis is still a matter of debate.[4] The current controversy is whether resection with primary anastomosis (PA) is safe or if a Hartmann's procedure (HP) still remains standard practice in case of generalized peritonitis complicating diverticulitis. For many surgeons HP still remains the favoured option in these patients.[5] Improvements in surgical techniques, radiological intervention techniques, anaesthesia, advances in intensive care medicine and progress in the management of peritoneal sepsis, has lead to an increasing interest in PA with or without diverting stoma or colonic lavage.[6-8]
The object of this study was to compare the mortality rates, the incidence of reoperations or additional interventions and length of hospital stay in patients with perforated diverticulitis treated by HP and PA in relation to patient's characteristics, severity of the disease, surgeon's experience and time of operation.

# Patients and methods

All consecutive patients between 1995 and 2005 that underwent HP or PA for acute perforated sigmoid diverticulitis in the surgical units of four affiliated teaching hospitals in Rotterdam, The Netherlands (St. Clara Hospital, Zuider Hospital, Sint Franciscus Hospital and Ikazia Hospital) were included in this study. The indications for surgery were clinical signs of diffuse peritonitis or presence of septic status with acute abdominal pain, free gas on plain abdominal radiography or specific findings at ultrasonography or computerized tomography. All but five patients were operated within 24 hours and received preoperative and postoperative broad-spectrum intravenous antibiotics. In none of the patients preoperative bowel preparation was used.

139 patients underwent HP and 61 patients underwent PA. Colon resections for perforated diverticulitis in the PA group were sigmoid resection (51), left hemicolectomy (8) and anterior resection (2). In the PA group 16 patients (26%) received a diverting ileostomy. The decision to perform one or the other procedure was left to the discretion of the surgeon on call. The operation was performed 84 times by a colorectal specialist surgeon and 116 times by a general surgeon.

In this study, all additional radiological interventions or reoperations after primary emergency surgery were recorded as re-interventions. Re-interventions were defined as radiological-assisted percutaneous drainage of abdominal or pelvic abscess, open abdominal wound management or reoperations because of ongoing sepsis, abdominal abscess, evisceration, anastomotic leakage or stoma-related complications.

A prospective computerized morbidity and mortality registration was carried out for all patients admitted to and operated in the surgical departments of all four hospitals. Patients who underwent emergency surgery for acute perforated diverticulitis could therefore be identified. Severity of disease was stratified with the Mannheim Peritonitis Index (MPI)[9] and Hinchey score.[10] The MPI was retrospectively calculated from the medical reports of all patients, whereas Hinchey score was distracted from the surgical reports. Patients with generalized peritonitis underwent 95 times an HP (Hinchey III, n=62; Hinchey IV, n=33), whereas only 26 patients underwent PA (Hinchey III, n= 21; Hinchey IV, n= 5). Age, gender, American Society of Anesthesiologist classification (ASA), severity of disease, postoperative mortality (30 days), number of re-interventions, surgeon's experience in colorectal surgery, time of operation, hospital stay and stay on the intensive care unit in the two groups were compared.

## Statistics

Data are represented as mean ± SD or median ± SD unless indicated otherwise. Comparisons between the two groups were made with Mann-Whitney tests for quantitative variables or graded outcomes and the Fisher's exact test for categorical data. A multivariate logistic regression analysis of the significant clinical variables in univariate analysis was done using logistic regression models with mortality or required re-intervention as the outcome. Differences were considered significant at a two-tailed p-value of $<0.05$.

# Results

A total of 200 patients underwent emergency operation between January 1995 and January 2005. During this period the percentages of HP and PA, which were performed each year, did not change with time (p=0.82). Patient's characteristics are mentioned in table 1.

**Table 1.** Patients' characteristics

| | Hartmann's procedure | Primary anastomosis | p |
|---|---|---|---|
| Patients (n) | 139 (70) | 61 (30) | |
| Age[1] (years) | 69±13 | 61±15 | |
| Sex | | | 0.54 NS |
| Male (89) | 64 (46) | 25 (41) | |
| Female (111) | 75 (54) | 36 (59) | |
| Hinchey score[1] | | | 0.01 |
| I (35) | 26 (19) | 9 (15) | |
| II (44) | 18 (13) | 26 (43) | |
| III (83) | 62 (45) | 21 (34) | |
| IV (38) | 33 (24) | 5 (8) | |
| ASA classification[1] | | | <0.01 |
| I (42) | 25 (18) | 17 (28) | |
| II (50) | 31 (22) | 19 (31) | |
| III (64) | 46 (33) | 18 (30) | |
| IV (44) | 37 (27) | 7 (11) | |
| MPI[2] (points) | 21±8.0 | 17±6.0 | <0.001 |
| Time of operation | | | 0.66 NS |
| During office hours (127) | 89 (64) | 38 (62) | |
| Outside office hours (73) | 50 (36) | 23 (38) | |
| Surgeon's experience | | | 0.01 |
| General surgeon (116) | 89 (64) | 27 (45) | |
| Colorectal surgeon (84) | 50 (36) | 34 (55) | |

*Values in parentheses are percentages. NS = Not significant.*
*[1]Mean age, Hinchey score, American Society of Anesthesiologist (ASA) classification ± SD.*
*[2]Median Mannheim Peritonitis Index ± SD.*

No differences in surgical procedure or baseline patient characteristics were noted between the series from the different hospitals. Patients who underwent HP were significantly older and showed higher Hinchey scores, higher ASA classifications and MPI. Specialist colorectal surgeons performed significantly more frequently a PA instead of HP. There was no relation found between time of operation and the type of surgical procedure (p=0.66) 16 PA patients (26%) received a temporary ileostomy. No differences were found between PA patients with or without a temporary ileostomy.

## Mortality

Total mortality was 27% after emergency surgery for perforated surgery. 47 patients died after HP compared to 7 PA patients (34 vs. 11%; p<0.01). Mortality seemed related to type of surgery, age, ASA classification, Hinchey score, MPI and surgeon's experience (table 2).

**Table 2.** Univariate analysis for relation between the listed variables and postoperative death (within 30 days) and the need for re-interventions

| | Mortality p | Re-interventions p |
|---|---|---|
| Surgical procedure | <0.01 | <0.01 |
| Age | <0.01 | 0.39 NS |
| Sex | 1 NS | 1 NS |
| ASA classification | <0.01 | <0.01 |
| Hinchey score | 0.012 | <0.01 |
| Mannheim Peritonitis Index | <0.01 | <0.01 |
| Time of operation | 0.37 NS | 0.22 NS |
| Surgeon's experience | 0.046 | <0.01 |

*NS = Not significant.*

Because of selection bias, patients who had undergone HP were significantly older of age, had more comorbidity, had a more severe disease and were more frequently operated by specialist colorectal surgeons, a multivariate logistic regression analysis was performed to compare both groups. After adjustment for these risk factors, mortalities in both groups did not differ significantly (OR 2.1; 95% CI 0.8-4.8; p=0.15). Age, MPI and ASA classification were still

significantly related to a higher mortality rate ($p<0.01$, $p<0.01$ and $p<0.01$, respectively) as shown in table 3.
The performance of a diverting stoma in the PA group did not show a significant advantage over PA without diverting stoma (mortality of 6 and 13%; $p=0.66$) after univariate analysis. These groups were too small (n=16 and n=45, respectively) for multivariate logistic regression analysis.
During the study period postoperative mortality rates remained constant ($p=0.18$). There were no significant differences in mortality between the four centres ($p=0.49$).

## Re-interventions

To treat their (severe) postoperative complications or sepsis 54 patients (27%) needed one or more reoperations or additional (radiological) interventions (HP, n=46; 33%, PA, n=8; 13%, $p<0.01$). Table 2 shows whether or not the need for radiological or surgical re-interventions was related to the listed factors.
Multivariate analysis, adjusting for Hinchey score, ASA, age, MPI and surgeon's experience, showed that HP necessitated significantly more frequently re-interventions compared to PA (OR 2.4; 95% CI 1.2-5.7; $p<0.05$). Higher ASA classification, Hinchey score, and MPI were also significantly related with need for re-interventions after primary surgery (table 4).

**Table 3.** Multivariate logistic regression analysis for postoperative death within 30 days

| | Postoperative mortality | | |
|---|---|---|---|
| | OR | 95% CI | p |
| HP vs. PA | 2.1 | 0.8- 48 | 0.15 |
| Age | 1.2 | 1.1 – 1.3 | <0.01 |
| ASA (vs. ASA I) | | | <0.01 |
| II | 2.2 | 0.6 – 9.3 | 0.29 |
| III | 5.8 | 4.7 – 22.7 | <0.01 |
| IV | 9.8 | 2.5 – 39.5 | <0.01 |
| Hinchey (vs. Hinchey I) | | | 0.06 |
| II | 1.5 | 0.5 – 5.7 | 0.52 |
| III | 1.2 | 0.4 – 3.7 | 0.78 |
| IV | 3.9 | 1.0 – 13.8 | 0.03 |
| MPI | 1.4 | 1.2 – 1.5 | <0.01 |
| Surgeon's experience | 1.3 | 0.7 – 2.5 | 0.45 |

*OR = Odds ratio; HP = Hartmann's procedure; PA = primary anastomosis; ASA = American Society of Anesthesiologist classification; MPI = Mannheim Peritonitis Index.*

**Table 4.** Multivariate logistic regression analysis for the need of reoperation or other additional interventions after surgery

| | Postoperative need for re-interventions | | |
|---|---|---|---|
| | OR | 95% CI | p |
| HP vs. PA | 2.4 | 1.1 – 5.7 | 0.05 |
| Age | 1.0 | 0.96 – 1.01 | 0.24 |
| ASA (vs. ASA I) | | | <0.01 |
| II | 1.2 | 0.4 – 3.7 | 0.81 |
| III | 6.4 | 2.2 – 18.3 | <0.01 |
| IV | 2.6 | 0.8 – 8.1 | 0.10 |
| Hinchey (vs. Hinchey I) | | | 0.02 |
| II | 1.0 | 0.3 – 3.3 | 0.98 |
| III | 1.0 | 0.3 – 2.9 | 0.98 |
| IV | 3.9 | 1.3 – 12.7 | 0.02 |
| MPI | 1.1 | 1.0 – 1.2 | <0.01 |
| Surgeon's experience | 4.9 | 2.5 – 9.7 | 0.04 |

*OR = odds ratio; HP = Hartmann's procedure; PA = primary anastomosis; ASA = American Society of Anesthesiologist classification; MPI = Mannheim Peritonitis Index.*

When comparing the need for re-interventions in high-risk patients (older age, generalized peritonitis, more comorbidities and higher MPI) between HP and PA groups, no significant differences could be found, as shown in table 5.
Within the PA group, univariate analysis showed no significant differences found in number of complications that needed re-intervention whether or not a diverting ileostomy was performed (19 vs. 11%; p=0.42). Three patients (5%) developed an anastomotic leakage after PA; 1 of them had received a diverting ileostomy during primary surgery and anastomotic leakage could be treated conservatively. The other patients needed reoperation because of their anastomotic leakage. There were no significant differences in number of re-interventions between the four centres (p=0.77).

## Hospital stay

The median postoperative hospital stay for hospital survivors after HP and PA was 22 days (± 22; range 6-120) and 13 days (± 18; range 6-112) respectively. The median hospital stay was significantly longer after HP compared to PA (p<0.01). Median stay at the intensive care unit was also significant longer for HP (2 days ± 10; range 0-61) than for PA (1 day ± 8; range 0-56) (p<0.01).

**Table 5.** The need for re-interventions in high-risk patients

| Risk factor | Hartmann's procedure n=48 | Primary Anastomosis n=8 | p |
|---|---|---|---|
| Age = 70 year | 24 (50) | 4 (50) | 1.0 |
| Hinchey score III and IV | 35 (73) | 4 (50) | 0.23 |
| ASA = III | 34 (71) | 6 (75) | 1.0 |
| MPI = 26 | 25 (52) | 2 (25) | 0.25 |
| 2 or more risk factors | 37 (77) | 5 (63) | 0.40 |
| 3 or more risk factors | 24 (50) | 2 (25) | 0.26 |

*Values in parentheses are percentages. ASA = American Society of Anesthesiologist classification; MPI = Mannheim Peritonitis Index.*

# Discussion

The prevalence of diverticulosis in Westernised countries is rapidly increasing and so are its complications.[11] Nevertheless, a perforated diverticulitis with generalized purulent and faecal peritonitis occurs less frequently. Therefore, recommendations in treating this stage of disease are based on small or retrospective studies. This multicenter report is the largest in the current literature including 200 consecutive patients with acute perforated diverticulitis.

As emergency surgeries for perforated diverticulitis may be associated with substantial morbidity and mortality optimalization of its treatment is important. Primary resection has become the standard practice for patients with generalised peritonitis complicating diverticulitis, but fear of anastomotic leakage often deters many surgeons from performing PA. A diverting stoma or intraoperative colon lavage seems to diminish the number of anastomotic leakages but not mortality.[12] This management by fear is supported by an experiment of Hawley,[13] demonstrating that faecal soiling or peritoneal sepsis may impair the healing of a colonic anastomosis. This is however not supported by clinical experience.[12,14,15] Gooszen et al. evaluated the relationship between severity of disease and the patient's general condition to adverse outcomes of PA and observed that the rate of anastomotic leakage was not related to a higher MPI, APACHE II score or the Hinchey score.[5] Outcome of purulent or faecal peritonitis was reported to depend mainly on preoperative fluid resuscitation and antimicrobial therapy, but not on primary repair.[16,17]

Although not proven in randomized controlled trials, it may seem that improvements in surgical and radiological intervention techniques, anaesthesia and intensive care medicine could favour for colonic resection with PA in emergency surgery for diverticular disease even if it is complicated by purulent or faecal peritonitis.[5,6,8,18]

Mortality rate and the rate of complications that needed radiological or operative re-interventions in this study was high (both 27%), which reflects the severity of the disease and the poor general condition of the patients. In this study significant higher severity scores (Hinchey score and MPI) were observed in the patients who underwent HP compared to the patients with PA. Besides that, patients of the HP group were of older age and had more comorbidity (higher ASA classification). Therefore, it seems that the more severely affected and high-risk patients underwent HP. This was also observed in a prospective multicenter study for surgical treatment of several different complications of diverticular disease.[19] In the latter study, a multifactorial analysis of predictors of HP was made in order to reduce selection bias. Multivariate analysis still showed a twofold increase in postoperative complications after HP compared to PA. There was no significant difference in mortality between the two surgical procedures.

As the operations were classified as emergency and hence may be performed outside office hours, not all procedures were performed by specialist colorectal surgeons. It is known that non-colorectal surgeons prefer HP in case of emergency surgery for colorectal surgery.[20] Besides, an increase in mortality and morbidity is found after emergency surgery performed by a non-colorectal surgeon in such cases.[20] In this study specialist colorectal surgeons performed significantly more frequently a PA instead of an HP. It also seemed that they had a better outcome than a general surgeon (table 2,4), but when comparing surgeons it is necessary to adjust for differences in case mix and type of surgery, as the best surgeon may get the most difficult job.[21] In contrast with surgeon's experience, time of operation did not influence the choice of surgical procedure in this study.

In this study, that exclusively covers patients with acute colon perforation due to diverticulitis, a multivariate logistic regression analysis was performed to reduce the found bias in patient selection and surgeon's experience in order to make a comparison between the results after HP and PA. After adjusting for age, ASA, MPI, Hinchey score and surgeon's experience mortality was not significantly different between HP and PA. As age, ASA classification and MPI are significant predictors of mortality (table 3) after perforated diverticulitis, it is suggested that further reduction in mortality will require improvement in medical management of pre- and perioperative sepsis and

comorbid conditions. Although this is a retrospective study, the analysis has found to be appropriate and therefore the conclusions can be sound.

MPI, ASA classification, age and Hinchey score could decisively affect postoperative morbidity.[22-24] This is in accordance with the results of this study for ASA classification, Hinchey score and MPI (table 4). It is important that surgical technique should not be a risk factor for severe postoperative morbidity. This study suggests that PA should not be regarded as an inferior procedure compared to HP, as patients who underwent HP seemed to have more postoperative complications that needed radiological or surgical re-intervention, especially when not performed by a specialist colorectal surgeon. These findings are in agreement with the result of other reports.[8,12,19] The difference in number of re-interventions is not necessary associated to a more advanced disease stage or more comorbidities of the patients in the HP group, as is shown in table 5. Besides a high complication rate when performing a HP, the reversal of HP is also known to be associated with substantial morbidity (9.1%) and even mortality (1.7%).[25] This is one of the reasons that HP often results in a permanent colostomy.[26]

Anastomotic leakage was found in 5% of the patients. This is in correspondence with the existing literature.[15] Whether or not a diverting stoma prevents against postoperative complications after PA for treatment of perforated diverticulitis remains unclear, as the groups were too small to compare in a multivariate analysis. In rectal cancer a diverting stoma seems to reduce the rate of anastomotic leakage that requires surgical intervention, rather than it protecting against the occurrence of leaks.[27] Finally, total hospital and intensive care unit stay seems to be in favour of PA compared to HP, but again the existing bias in patient selection probably is an important reason for this difference and therefore precludes clinical extrapolation.

In conclusion, this study shows that selected patients with acute perforated diverticulitis can be managed well by PA, as it seems not to be inferior to HP in terms of severe postoperative complications that need surgical or radiological re-intervention and mortality. This decision should be made while taking into account patient's concomitant diseases, response on preoperative resuscitation and the availability of a surgeon experienced in colorectal surgery and intensive care medicine. A prospective randomised trial to compare HP and PA with or without diverting stoma for treatment of perforated diverticulitis with generalised peritonitis is needed to confirm this last statement.

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# Edward John Hinchey

(23-3-1934 – present)

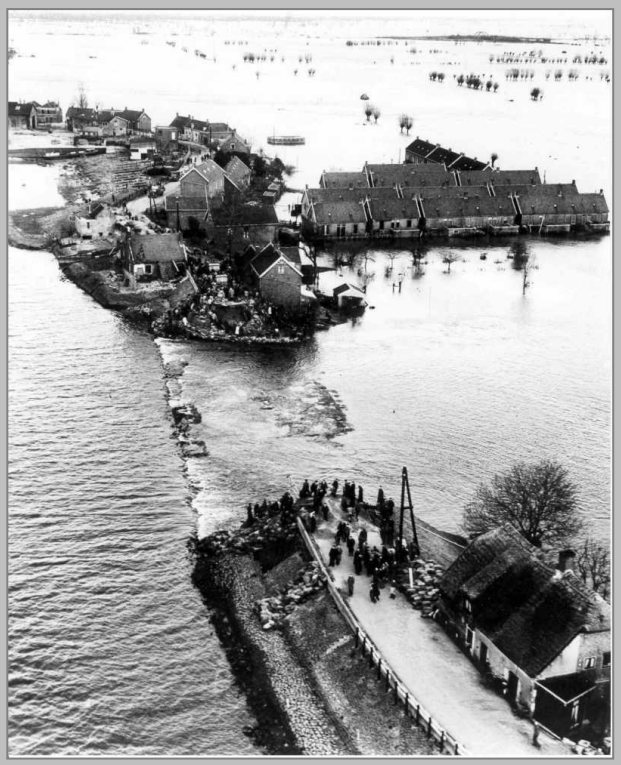
*Edward John Hinchey published the currently most frequently used classification of perforated diverticulitis.*

Edward John Hinchey studied medicine at the Queen's University's Medical School in Kingston, Ontario. He worked as an attending surgeon at the Montreal General Hospital from 1965, where he also had done his residency in General Surgery. He became professor of surgery three years later and finally became chairman of the division of general surgery in 1983.
He was president of the Royal College Examination Board in General Surgery, which he resigned to become the first president of the Canadian Association of General Surgeons in 1986. As recognition of his important achievements as the director of the Surgical Scientist Program at the faculty of medicine (which is still his main activity), he was appointed as an honorary professor emeritus at McGill University.

# 6

# Long-term survival after perforated diverticulitis

*with*
MP Gosselink
WCJ Hop
E van der Harst
BE Hansen
GHH Mannaerts
PPLO Coene
WF Weidema
JF Lange



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# Abstract

Short-term survival after emergency surgery for perforated diverticulitis is poor. Less is known about long-term survival. The aims of this study were to evaluate long-term survival after discharge from hospital and to identify factors associated with prognosis.

All patients who underwent emergency surgery for perforated diverticulitis in five hospitals of Rotterdam, The Netherlands between 1990 and 2005 were included. The association between type of surgery (Hartmann's procedure or primary anastomosis) and long-term survival was analysed by multivariate Cox's regression analysis taking account of age, American Society of Anesthesiology (ASA) classification, Hinchey score, Mannheim Peritonitis Index (MPI) and surgeon's experience. In addition, survival of the patients was compared to the matched general Dutch population.

A total of 340 patients were identified. Of these patients 49% were classified ASA III or IV. The overall 5-years survival was 53%. 250 patients were discharged from hospital alive after primary surgery. Median time of follow up of these 250 patients was 59 months. During follow up another 90 patients (58% was older than 75 year; 66% ASA III/IV) died. Survival was significantly impaired compared to the expected matched sex-, age- and calendar time-specific survival. Overall survival was significantly related to age and ASA classification. Hinchey score, MPI, number of re-interventions, the surgeon's experience and type of surgery did not influence long-term survival, although a trend was found towards Hartmann's procedure being a risk factor for poorer survival compared to primary anastomosis (hazard ratio for mortality 1.88; 95% CI 0.96-3.67; p=0.07).

Long-term survival of patients after perforated diverticulitis is limited and mainly caused by the poor general condition of the patients and not by the severity of primary disease or year and type of surgery.

# Introduction

Diverticular disease of the colon is common in westernized countries, especially in older people.[1,2] The large majority of patients remain asymptomatic. Only 1-2% of patients presenting for urgent abdominal evaluation have free perforation because of diverticulitis.[3] Nevertheless, the prevalence of perforated diverticulitis is increasing,[4] which parallels the ageing of the developed countries.

Emergency operations for perforated diverticulitis are associated with substantial mortality (8-26%),[5-8] which can increase up to 40% in the elderly.[8,9] The rate of severe postoperative complications is also high, which reflects the severity of the disease and the poor general condition of the patients.[10] After surviving primary surgery patients commonly face a long period of rehabilitation. Probably the majority of patients will never return to their prehospital health state because of postoperative side effects and complications. This might result into a shorter life expectancy.

The existing literature regarding perforated diverticulitis only reports about short-term postoperative mortality and postoperative complications. Direct postoperative mortality is known to be influenced by age and American Society of Anesthesiology (ASA) classification of the patient, the severity of the disease indicated by Hinchey score and Mannheim Peritonitis Index (MPI), type of surgery and surgeon's experience in colorectal surgery.[7-10] Less is known about survival outside the hospital on the long term. Survival expectancy could be an important factor in decision making for initial (surgical) treatment as it measures the patient's prognosis. The present study was undertaken to determine the long-term survival of patients who were operated for acute perforated diverticulitis. The issues of surgical technique, severity of primary disease and patients' characteristics will be addressed and compared with natural life span of the Dutch population.

# Patients and methods

A cohort of 340 consecutive patients were included provided they had undergone emergency surgery for perforated diverticulitis between January 1990 and December 2005 at the surgical departments of the academic and the four major teaching hospitals of Rotterdam, The Netherlands. Patients admitted for perforated diverticulitis could be identified and selected from

computerized surgery registration databases. The indications for surgery were clinical signs of diffuse peritonitis or the presence of sepsis with acute abdominal pain, free gas on plain abdominal radiography or specific findings at ultrasonography or computerized tomography. The type of surgical procedure was left to the discretion of the surgeon on call. As the operations were classified as emergency and hence frequently performed outside office hours, not all procedures were performed by specialist colorectal surgeons. Surgery consisted of Hartmann's procedure (HP; n=238), resection with primary anastomosis (PA; n=93), suture repair (n=7) and the performance of a diverting stoma without resection (n=2).

The database included patients' characteristics, year and type of surgical procedure, surgeon's experience, MPI, Hinchey score, postoperative medical and surgical adverse events, number of re-interventions, length of hospitalization and intensive care unit stay, the date of eventual death and the cause of death. Severity of disease was stratified with MPI[11] and Hinchey scores.[12] MPI was calculated from the medical reports of all patients, whereas Hinchey score was distracted from the surgical reports. A MPI≥26 is known to be a significant predictor of mortality.[11] In this study, all additional radiological interventions or reoperations after primary emergency surgery were recorded as re-interventions. These were defined as radiological-assisted percutaneous drainage of abdominal or pelvic abscess, open abdominal wound management or reoperations owing to ongoing sepsis, abdominal abscess formation, abdominal dehiscence, anastomotic leakage or stoma-related complications.

Follow up of all patients was conducted to July 2007. Data about the patients' course after initial hospital discharge were gathered from the medical reports and by telephone enquiry performed from the patients themselves, or when necessary, the patient's direct relatives or general practitioner. Patients lost to follow up were censored at the time of their last hospital visit. Long-term survival of patients who were operated for acute perforated diverticulitis was evaluated in relation to patient's characteristics, severity of the disease, type of surgery and postoperative course.

## Statistics

Kaplan-Meier survival plots with log-rank statistics were used in order to determine survival rates univariately according to various factors. The association between type of surgery (HP or PA) and long-term survival was analysed using multivariate Cox's regression analysis taking account of age, gender, ASA classification, Hinchey score and MPI. These analyses were performed with Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, Illinois, USA, 1998). In addition, observed survival was

compared with expected survival from matched sex-, age- and calendar time-specific death rates for the general Dutch population using life table method and Wilcoxon (Gehan) test. A test for a single proportion with continuity correction was used to evaluate differences between observed survival and survival predicted by the Mayo model (Mayo risk score).[13] Differences were considered significant at a two-sided p-value < 0.05.

**Table 1.** Characteristics of patients who survived emergency surgery for perforated diverticulitis (n=250)

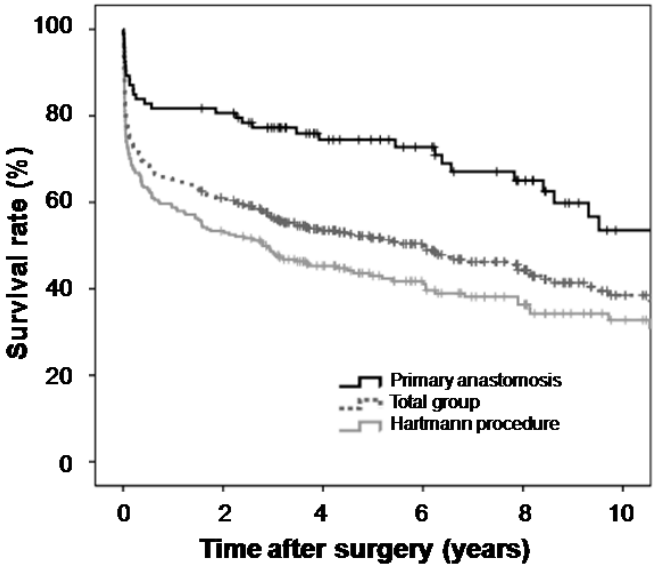
| | n (%) |
|---|---|
| Entire Cohort | 340 |
| Postoperative in-hospital death | 90 (26) |
| Survivors from initial surgery | 250 |
| Diseased during follow up (yes/no) | 90/160 (36/74) |
| Gender (male/female) | 110/140 (44/56) |
| Age (median (range)) | 66 (23-95) years |
| ASA | |
| I | 60 (24) |
| II | 93 (37) |
| III | 69 (28) |
| IV | 28 (11) |
| MPI | |
| <26 | 224 (90) |
| ≥26 | 26 (10) |
| Hinchey score | |
| I | 58 (23) |
| II | 56 (22) |
| III | 108 (43) |
| IV | 28 (11) |
| Type of surgery | |
| HP | 163 (65) |
| PA | 80 (32) |
| Other | 7 (3) |
| Hospital stay, median (range) | 17 (5-137) days |
| ICU stay, median (range) | 1 (0-61) days |

*Values in parentheses are percentages of patients unless indicated otherwise.*
*ASA = American Society of Anesthesiologist classification; MPI = Mannheim peritonitis index; HP = Hartmann's procedure; PA = resection with primary anastomosis; ICU = Intensive care unit.*

# Results

Between January 1990 and December 2005, 340 patients underwent emergency surgery for perforated diverticulitis. Of these 90 (26%) (HP: n=75; PA: n=13; other: n=2) died during their postoperative period at initial hospital stay. Characteristics of the 250 survivors are shown in table 1. At a median follow up of 59 months (range 1–210) after hospital discharge another 90 patients (36%; HP: n=68; PA: n=18; other: n=4) died. Causes of death are shown in table 2. Survival of all initial 340 patients is shown in figure 1. The overall 5-years survival of the total group (n=340) was 53%.
Of the 340 initial patients 49% was classified ASA III or higher, 33% was older than 75 years of age and 58% had generalized peritonitis because of perforation (Hinchey III 42%; Hinchey IV 16%). In these patients direct postoperative mortality was very high (41, 34 and 31%, respectively). In-hospital mortality of patients with Hinchey IV perforated diverticulitis was 48% (26/54). Long-term follow up of the survivors (n=250) revealed a mortality of 66% in ASA III or higher and 58% in patients older than 75 years. Long-term survival of patients who survived initial generalized peritonitis (Hinchey III and IV) was 41%, which is comparable to the whole survivors group (n=250).

**Figure 1.**




Kaplan-Meier plot illustrating survival of all 340 patients who presented with acute perforated diverticulitis and underwent emergency surgery between 1990 and 2005. Patients who underwent Hartmann's procedure (n=238) and those who underwent primary anastomosis (n=93) are also shown separately.

**Table 2.** Causes of death in 90 patients having survived emergency surgery for perforated diverticulitis and discharged from hospital (n=86)

| Cause of death | n (%) |
|---|---|
| Myocardial Infarction / Cardiac decompensation | 17 (19) |
| Age and general condition | 15 (17) |
| Cancer | 14 (16) |
| Exacerbation COPD / Pneumonia | 8 (9) |
| Cerebro-vascular accident | 5 (6) |
| Complicated reversal of Hartmann's procedure (HP) | 5 (6) |
| Recurrent complicated diverticulitis | 3 (3) |
| Urosepsis / Multi organ failure | 3 (3) |
| Complicated surgery for ileus | 2 (3) |
| Pancreas / Biliary tract infection | 2 (3) |
| Gastric ulcer perforation | 1 (1) |
| Ruptured abdominal aorta | 1 (1) |
| Unknown | 14 (16) |

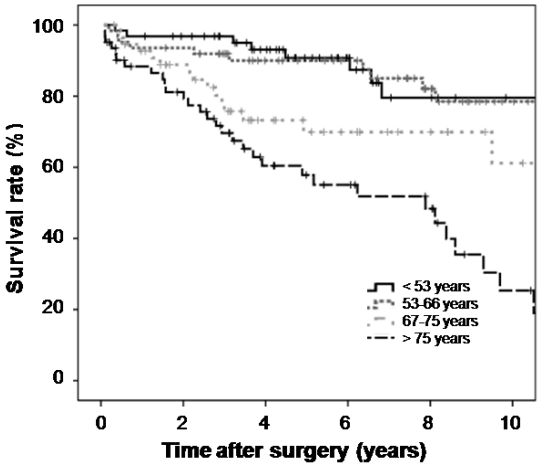
*Values in parentheses are percentages.*

Univariate and multivariate analysis of factors, which were considered potentially important in predicting survival of the 250 patients who survived beyond the perioperative period, were performed. In univariate analysis, age and ASA classification (figure 2 and 3) were both significantly associated with long-term survival (both $p<0.001$). Gender was not significantly related to long-term survival after perforated diverticulitis ($p= 0.91$).

No relation was observed between the severity of the primary disease at initial surgery and prognosis outside the hospital. Hinchey score had no influence on long-term survival after hospital discharge ($p=0.27$; figure 4). Also, discharged patients who had MPI =26 at initial surgery did not have a worse prognosis on the long term as compared with patients with MPI<26 ($p=0.31$). The need for re-interventions or reoperations to treat postoperative surgical complications after primary surgery during initial hospital stay was not related to long-term survival ($p=0.53$)

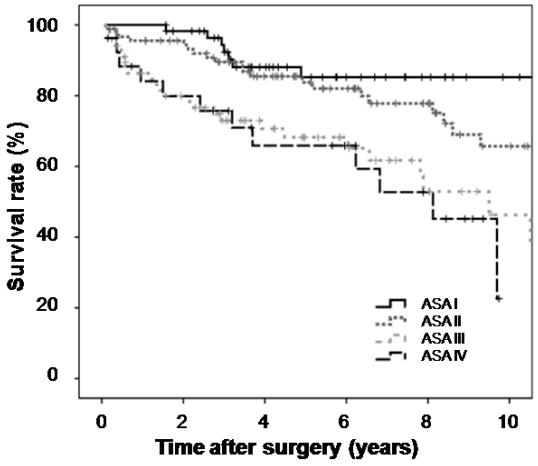
Type of initial surgery for perforated diverticulitis was related with long-term survival. Patients who underwent PA had better prognosis compared with those who underwent HP ($p=0.005$; figure 5). However, patients who underwent HP generally had a higher age and ASA classifications and had higher Hinchey scores and MPI at primary surgery (all $p<0.001$) in comparison with patients who underwent PA. When adjusting for these factors using multivariate analysis, long-term survival rates of PA and HP were not significantly different from each other. A trend was found towards patients who underwent HP being associated with poorer survival ($p=0.07$; table 3).

**Figure 2.**



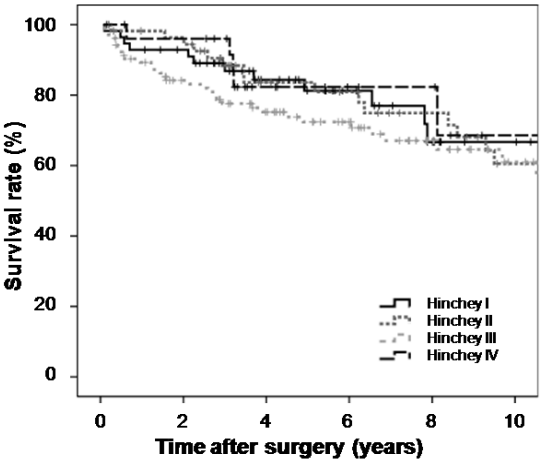

Kaplan-Meier plot illustrating survival of patients (n=250) after successful emergency surgery for perforated diverticulitis according to age (log-rank test, p<0.001).

**Figure 3.**



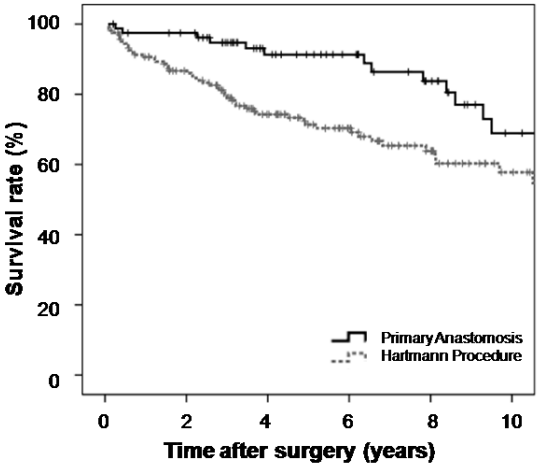

Kaplan-Meier plot illustrating survival of patients (n=250) after successful emergency surgery for perforated diverticulitis according to ASA classification (overall p-value <0.001).

**Figure 4.**




Kaplan-Meier plot illustrating survival of patients (n=250) after successful emergency surgery for perforated diverticulitis according to Hinchey score (p=0.27).

**Figure 5.**




Kaplan-Meier plot illustrating long-term survival of patients after successful emergency surgery for perforated diverticulitis according to type of surgery (log-rank test, p=0.005). HP, n=163; PA, n=80.

**Table 3**. Multivariate Cox's regression analysis for long-term mortality after surviving initial emergency surgery for perforated diverticulitis

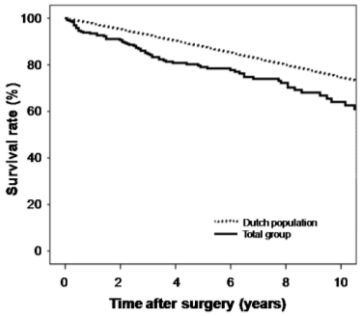
| | Long-term mortality | | |
|---|---|---|---|
| | HR | 95% CI | p |
| Surgical procedure | | | |
| HP | 1 | | |
| PA | 0.54 | 0.3 - 1.04 | 0.07 |
| Gender | | | |
| Male | 1 | | |
| Female | 1.1 | 0.6 – 1.8 | 0.87 |
| Age (years) | | | |
| <53 | 1 | | <0.001 |
| 53-66 years | 1.1 | 0.4 – 2.5 | 0.99 |
| 67-75 years | 2.7 | 1.1 – 5.7 | 0.05 |
| >75 years | 4.1 | 1.6 – 8.4 | 0.002 |
| ASA (vs. ASA I) | | | |
| I | 1 | | 0.002 |
| II | 1.8 | 0.7 – 3.9 | 0.29 |
| III | 4.2 | 1.5 – 8.6 | 0.004 |
| IV | 4.8 | 1.5 – 11.2 | 0.006 |
| Hinchey score | | | |
| I | 1 | | 0.75 |
| II | 1.2 | 0.5 – 2.5 | 0.71 |
| III | 1.1 | 0.6 – 2.2 | 0.79 |
| IV | 0.54 | 0.2 – 1.9 | 0.45 |

*Data given are Hazard ratios (HR) with 95% confidence intervals (95% CI).*
*HP = Hartmann's procedure; PA = resection with primary anastomosis; ASA = American Society of Anaesthesiologist classification.*

Similar results were observed when Hinchey score was replaced by MPI in the multivariate analysis. The time period in which the operation had taken place was not related to long-term survival (p=0.27), nor was the experience of the operating surgeon and (p=0.79).

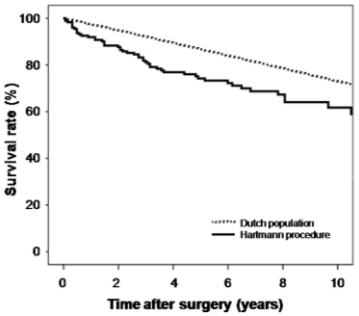
Long-term survival of the in-hospital survivors after perforated diverticulitis was significantly impaired compared to the expected matched sex-, age- and calendar time-specific survival of the general Dutch population (p=0.005; figure 6). This poorer overall survival seemed to be due to the poor survival of patients after HP (p=0.02; figure 7). Survival of patients who had undergone PA was not significantly different as compared to the sex-, age- and calendar time-matched control group of the general Dutch population (p=0.85; figure 8).

**Figure 6.**



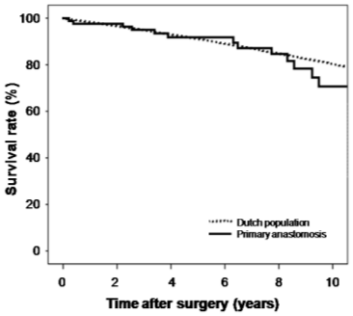

Kaplan-Meier plot illustrating survival of patients (n=250) after emergency surgery for perforated diverticulitis and the expected matched sex-, age- and calendar time-specific survival of the general Dutch population (log-rank test, p=0.005).

**Figure 7.**




Kaplan-Meier plot illustrating survival of patients (n=163) after Hartmann's procedure for perforated diverticulitis and the expected matched sex-, age- and calendar time-specific survival of the general Dutch population (n=163) (log-rank test, p=0.02).

**Figure 8.**




Kaplan-Meier plot illustrating survival of patients (n=80) after resection with primary anastomosis for perforated diverticulitis and the expected matched sex-, age- and calendar time-specific survival of the general Dutch population (n=80) (log-rank test, p=0.852).

# Discussion

The present study demonstrates reduced long-term survival for patients who survived initial emergency surgery for treatment of perforated diverticulitis compared with the general population. Besides a high direct-postoperative mortality rate (26%), each year about 5% of the patients died after having survived initial surgery and discharge from hospital. The observed 5-years survival after perforated diverticulitis was only 53%. The main reason for this observation is the poor general condition of the patients. Almost half of the patients that presented with acute perforated diverticulitis was classified ASA III or IV and one third was older than 75 years of age. The incidence of perforated diverticulitis is highest in older patients who suffering from multiple comorbidities as indicated by the higher ASA classifications.[14] These factors are not mutable and are known factors for mortality. Mortality after emergency surgery for perforated diverticulitis can increase to 40% in older patients.[8,9] It is therefore not surprising that these have a poor prognosis in the short and long term.

Besides patient-related risk factors, also disease related risk factors like Hinchey score and MPI are also known independent risk factors for in-hospital

mortality after emergency surgery.[15] The overall in-hospital mortality rate of patients with generalized peritonitis because of perforation was over 30% and increased towards almost 50% in cases with faecal peritonitis (Hinchey IV). However, when the patient survived primary surgery and was discharged from the hospital, the severity of disease at primary surgery did not appear to effect long-term survival. The need for one or more radiological-assisted drainage of abdominal abscesses or reoperations for ongoing sepsis, anastomotic leakage or stoma-related complications also did not influence long-term survival after hospital discharge. It seems that in surviving patients, initial severity of disease and the need for additional interventions do not affect the long-term outcome. Surgical experience and the year in which the operation took place were also not related with long-term survival.

The same was observed for the type of surgical procedure. In contrast with univariate analysis in which HP was related with poorer outcome in the long term compared with PA, multivariate analysis, adjusting for the differences in patients' characteristics, severity of disease and surgeon's experience, showed that type of surgery was no longer significantly related to long-term survival. Nevertheless a trend was found for better survival after PA. Compared with the general population survival after HP was restricted, whereas survival after PA was not. The more severely affected and high-risk patients are inclined to undergo HP.[10,16] In this study significant higher disease-severity scores (e.g. Hinchey score and MPI), older age and higher ASA classifications were observed in the patients who underwent HP compared with the patients with PA.[15] This could explain the poorer survival of the patients after HP and the similar survival of patients after PA compared with the general population.

As the optimal surgical strategy to treat perforated diverticulitis is still a matter of debate, it is important to be informed about the expected survival in the long term. Recommendations in treating patients with perforated diverticulitis with generalized peritonitis are mainly based on small or retrospective studies and short-term outcome. For many surgeons HP remains the standard treatment for this stage of disease, although a prospective multicenter evaluation of surgical procedures demonstrated that HP was associated with significantly more postoperative complications and a 1.8-fold increase in the likelihood of death compared with PA.[17] Fear of anastomotic leakage deters many surgeons from performing PA. As the operations were classified as emergency and hence may be undertaken outside office hours, not all procedures were performed by a specialist colorectal surgeon. It is known that noncolorectal surgeons prefer HP in the case of emergency surgery for colorectal surgery.[18] This preference is mainly based on the severity of disease and comorbidity and age of the patient in relation to the surgeon's experience in this field of surgery.

Patients who undergo HP have to deal with a colostomy. Additional stoma care might be a bridge too far for these (older) patients, as they face the physical (dehydration, leakage, parastomal hernia) and psychological (lifestyle alterations) challenges that are associated with having a stoma.[19] Probably they will never return to their prehospital health state owing to the stoma. Reversal of HP is associated with significant morbidity and even mortality,[19,20] especially in patients in a poor general condition with several comorbidities.[7,21] This is one of the reasons why HP often leaves the patient with a permanent colostomy.

It seems that PA for perforated diverticulitis compares equally well to HP in terms of long-term survival. Again it is essential to realise that high risk patients (higher ASA classification, older age, higher Hinchey score and MPI) were more likely to undergo HP. Nevertheless, after adjusting for these factors, survival after PA or HP was still not significantly different. Long-term survival was only related to patients' characteristics such as higher age and ASA classification III and IV. It was just this group of patients that was prominently present. Almost half of the patients was ASA III or higher and one third was older than 75 years. Within 6 years almost two third of these patients had died. One might postulate that particularly older patients with more comorbidity will present with a more severe inflammatory reaction causing perforation leading to death. This could also be an explanation for the statement that almost 80% of the patients present with perforated diverticulitis as the first manifestation of their diverticular disease.[22] The first attack in older ASA III and IV patients is especially hazardous.

All these aspects including short- and long-term survival, stoma care and patients' characteristics must be taken into account before performing primary surgery. HP should no longer be considered as the most likely treatment for perforated diverticulitis in all patients. In the younger healthy patients, PA may be the procedure of choice for all stages of severity of perforated diverticulitis when all short- and long-term outcomes are considered. In addition, in patients of older age and with ASA classification III or higher, HP must seriously be considered the surgical procedure of choice, because the long-term survival is limited and restoration of bowel continuity is therefore not an issue. A study comparing the quality of life after both procedures is warranted.

In conclusion, long-term survival of patients after emergency surgery for acute perforated diverticulitis is limited and mainly caused by the poor general condition of these aged patients. The severity of the primary disease, the type of initial surgical procedure and the surgeon's experience do not influence long-term out-hospital survival.

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# 7

# Avoiding or reversing Hartmann's procedure provides improved quality of life after perforated diverticulitis.

*with*
MP Gosselink
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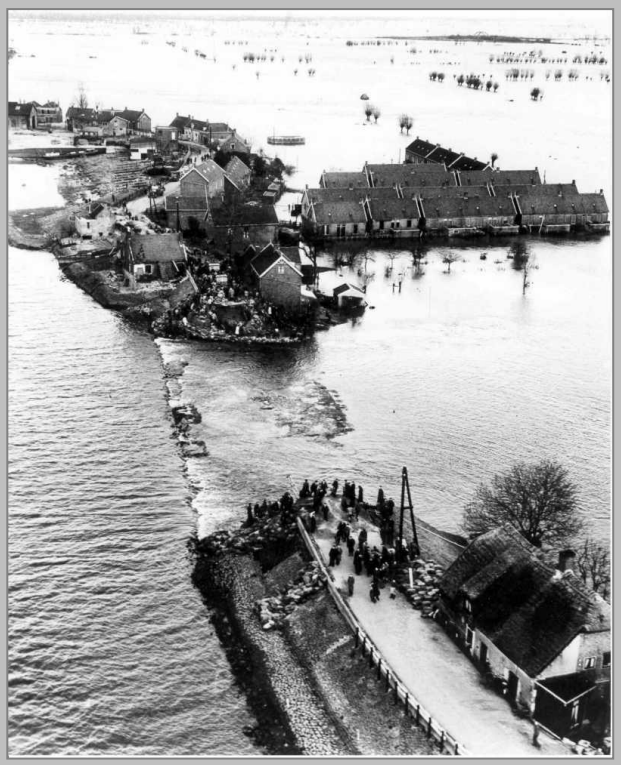

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# Abstract

The existing literature regarding acute perforated diverticulitis only reports about short-term outcome; long-term following outcomes have not been assessed before. The aim of this study was to assess long-term quality of life (QOL) after emergency surgery for perforated diverticulitis.

Validated QOL questionnaires (EQ-VAS, EQ-5D index, QLQ-C30, and QLQ-CR38) were sent to all eligible patients who had undergone emergency surgery for perforated diverticulitis in five teaching hospitals between 1990 and 2005. Differences were compared between patients that had undergone Hartmann's procedure (HP) or resection with primary anastomosis (PA) and also compared to a sex- and age-matched sample of healthy subjects.

Of a total of 340 patients, only 150 patients (44%) were found still alive in July 2007 (median follow-up 71 months). The response rate was 87%. In patients with PA, QOL was similar to the general population, whereas QOL after HP was significantly lower. The presence of a stoma was found to be an independent factor related to worse QOL. The deterioration in QOL was mainly due to problems in physical function and body image.

Survivors after perforated diverticulitis had a worse QOL than the general population, which was mainly due to the presence of an end colostomy. QOL may improve if these stomas are reversed or not be performed in the first place.

# Introduction

Diverticulitis is one of the most common diseases related to the gastrointestinal tract in western countries. In The Netherlands, 14.000 new cases have been estimated for 2006, which equals an incidence of 80/100,000 patients each year.[1] In spite of this, only 2% of these patients who present for urgent evaluation have acute perforation due to diverticulitis.[2]
Emergency surgery for perforated diverticulitis is associated with substantial morbidity and mortality, regardless of selected strategy.[3] For many surgeons, Hartmann's procedure (HP) still remains the favoured option, but it leaves the patient with an end colostomy. It is well known that patients with stomas may face both physical and psychological difficulties.[4] Reversal of HP is also associated with substantial morbidity and even mortality.[5] This is one of the main reasons why HP is never reversed in about half of patients.
Improvements in surgical and radiological intervention techniques and progress in the management of peritoneal sepsis have led to an increasing interest in colonic resection with primary anastomosis (PA). Although not proven in randomized controlled trials, PA seems not to be inferior to HP in terms of postoperative complications and mortality.[3,6-8] In these patients, a stoma can be withheld or, in case of a diverting loop ileostomy, reversed easily and quickly.[5]
The existing literature regarding perforated diverticulitis only reports on short-term outcome such as mortality and postoperative complications. Patient-orientated outcomes, such as quality of life (QOL), have never been assessed previously in patients needing emergency surgery for acute perforated diverticulitis. QOL is increasingly recognized as a crucial factor when assessing clinical outcomes after surgical interventions as it presents a patient's perspective, which is obviously a key outcome in clinical decision-making. To provide more data from a patient's perspective, the present study evaluates the long-term functional and health-related QOL outcomes of patients after emergency surgery for acute perforated diverticulitis. QOL will be examined in relation to surgical technique (HP or PA), surgeon's experience in colorectal surgery, severity of the primary disease, and patients' characteristics.

# Patients and methods

A cohort of 340 consecutive patients had undergone emergency surgery for perforated diverticulitis between January 1990 and December 2005 at the

surgical departments of the academic and the four major teaching hospitals of Rotterdam, The Netherlands (Erasmus University Medical Centre, Ikazia Hospital, Medical Centre Rijnmond-Zuid (formerly St. Clara Hospital and Zuider Hospital), and St. Franciscus Gasthuis Hospital). Patients were selected from computerized surgery registration databases using the search codes: exploratory laparotomy, diverticulitis, perforated hollow viscus, Hartmann's procedure, left hemicolectomy, sigmoid resection, low anterior resection. Using this searching strategy, a complete overview of all patients presenting at the surgical units of the hospitals mentioned above was obtained, as all patients with acute perforated diverticulitis undergo emergency surgery. The indications for surgery were clinical signs of diffuse peritonitis or presence of septic status with acute abdominal pain, free gas on plain abdominal radiography, or specific findings for perforated diverticulitis at ultrasonography or computerized tomography (CT). The type of surgical procedure (HP n=238; PA n=93; Suture repair n=9) was left to the discretion of the surgeon on call. There were no laparoscopic emergency operations performed during the study period.

Follow-up of all patients was conducted until July 2007. Data regarding the patients' course after initial hospital discharge was gathered from the hospitals' medical reports and by telephone inquiry from the patients themselves or when necessary, the patient's direct relatives and general practitioner. At 1 July 2007, 150 patients were still alive (HP n=90; PA n=58; suture repair n=3). Ten patients were lost in follow up as they moved abroad (n=3) or their home addresses were not available (n=7). Validated questionnaires were sent by post to all 150 eligible patients after they were asked by phone to participate. The response rate was 87% (131 patients).

In order to assess long-term QOL the patients filled in the EuroQol EQ-VAS, the EQ-5D index and the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-CR38 questionnaires. The EQ-VAS is a single-item visual analogue scale (VAS), ranging from 0 "worse imaginable health state" to 100 "best imaginable health state". The EQ-VAS represents the "value" of the current health state from a patient perspective. Next to the EQ-VAS, the patients classify their current health state using the five items of the EuroQol EQ-5D. This classification can be transformed to a so-called index score representing "the societal value" of the health state. Such societal value represents the value the general public attaches to current health state of the patient.[9]

Disease-specific QOL was measured according to the official scoring procedures for the EORTC QLQ-C30 and EORTC QLQ-CR38 questionnaires. Both were originally developed to assess the QOL of cancer patients from a patient's perspective.[11] Other than the EuroQol, the outcomes of the EQRTC

questionnaires are multidimensional. EORTC QLQ-C30 contains 30 items that can be computed in five functional scales (physical, role, emotional, cognitive, and social functioning), three symptom scales, and six single items (fatigue, nausea and vomiting, pain, dyspnoea, insomnia, loss of appetite, constipation, diarrhoea and financial difficulties).[12]
The EORTC QLQ-CR38 is subdivided into two functional scales (i.e., body image and sexual functioning), seven symptom scales (micturition problems, gastrointestinal tract symptoms, chemotherapy side effects, defecation problems, stoma-related problems, and male and female sexual problems), and three single-item measures (sexual enjoyment, weight loss, and future perspective).
The validity and reliability of both the EORTC QLQ C30 and QLQ-CR38 have been established in Dutch patients with colorectal cancer.[11] In both questionnaires, scores are summed within scales and rescaled from 0 to 100. A higher score indicates better functioning, future perspective, and a lower level of symptomatology.
Differences in QOL were determined and compared between patients that underwent HP or PA. Both groups were also compared to a sex- and age-matched community-based sample of healthy people in The Netherlands.[10] Categorical variables were compared using the Chi-square test or Fisher's exact test. Continuous variables were compared using the Mann-Whitney test. Differences in QOL between the two surgical groups were determined with multivariate logistic regression analysis, adjusting for age, gender, American Society of Anesthesiologist (ASA) classification, Hinchey score, and the presence of a stoma. These variables were a priori hypothesized as potential confounders based on literature and/or significant clinical variables in univariate analysis. Differences were considered statistically significant at a two-tailed p-value of $< 0.05$.

# Results

Patient characteristics regarding type of procedure and clinical data are listed in table 1. Responders were similar to the nonresponders regarding gender, age, and surgical procedure. Patients that had undergone HP had significant higher ASA and Hinchey scores during primary surgery compared to patients that underwent PA ($p<0.01$ and $p=0.04$, respectively). PA was more frequently performed by specialist colorectal surgeons ($p=0.03$). At time of the questionnaire, 30 HP patients (39%) still had an end colostomy. Two PA

patients still had a loop ileostomy (4%). The median duration of time interval between the operation and the questionnaire was 71 months (range 23-205 months).

**Table 1.** Baseline characteristics of the responders

| | Primary Surgery | | |
|---|---|---|---|
| | HP | PA | Suture |
| Number of patients | 76 | 53 | 2 |
| Age (years) | 62 | 59 | 56 |
| Stoma (%) | 39 | 4 | 0 |
| Follow-up (months) | 72 | 69 | 56 |
| Gender (%) | | | |
| Male | 52 | 40 | 50 |
| Female | 48 | 60 | 50 |
| ASA (%) [a] | | | |
| I | 25 | 41 | 100 |
| II | 28 | 34 | 0 |
| III | 33 | 17 | 0 |
| IV | 14 | 8 | 0 |
| Hinchey score (%) [a] | | | |
| I | 24 | 23 | 50 |
| II | 12 | 43 | 0 |
| III | 52 | 26 | 50 |
| IV | 12 | 8 | 0 |
| MPI (%) | | | |
| <26 | 93 | 86 | 100 |
| ≥26 | 7 | 14 | 0 |
| Re-intervention (%)[b] | 19 | 13 | 100 |
| Specialist colorectal surgeon (%) [a] | 41 | 62 | 50 |

*Data are median numbers with percentages in parentheses, unless otherwise specified. HP= Hartmann procedure, P = primary anastomosis., ASA= American Society of Anaesthesiologist classification, MPI= Mannheim peritonitis index. a= PA vs. HP: P<0.05; b= Re-interventions were defined as radiological-assisted percutaneous drainage of abdominal or pelvic abscess, open abdominal wound management or reoperation for ongoing sepsis, abdominal abscess, evisceration, anastomotic leakage or stoma-related complications.*

The mean scores and ranges of the EQ-VAS and EQ-5D index are presented in Table 2. From the patient perspective, the mean general QOL score (EQ-VAS) was better after PA compared to HP. Also from the social perspective, the mean EQ-5D index score was better in patients after PA. In patients who had undergone PA, the EQ-VAS and EQ-5D index score was similar to that of the general population. The patients who had undergone HP had a significantly lower EQ-VAS and EQ-5D scores compared to the sex-age-matched general population (EQ-VAS $p<0.01$; EQ-5D $p=0.02$).

The presence of a stoma was found to be an independent factor related to the QOL, with patients without a stoma having a better QOL (EQ-VAS $p=0.03$; EQ-5D $p=0.04$). When assessing a subgroup containing patients after HP who had undergone restoration of bowel continuity (n=46) differences in QOL from the patients perspective and the social perspective were no longer significant compared to the general population and the patients after PA.

No difference in QOL was found between patients who were operated by an experienced colorectal surgeon or a general surgeon. There was no correlation between Hinchey scores and QOL scores. Higher ASA classifications were associated with a lower QOL (EQ-VAS $p=0.04$; EQ-5D $p=0.01$). ASA classification and type of surgery were significantly related to QOL in bivariate analyses but were not found to be significant in multivariate analysis. Only the presence of a colostomy was found to be an independent predictor for lower QOL (EQ-VAS odds ratio 2.4; 95% CI 1.2 to 4.8; $p=0.03$) after multivariate logistic regression analysis.

Scores of the EORTC QLQ-CR30 and the QLQ-CR38 for the patient groups are presented in table 3 and 4. Differences between HP and PA were found on five scales. PA patients had significantly higher scores with regard to global health status, physical function, fatigue, dyspnoea, and body image compared to HP patients.

**Table 2.** General quality of life scores

| | HP | PA | Population |
|---|---|---|---|
| EQ-VAS | 65 (20-100) | 74 (10-100) [a] | 79 (68-87) [b] |
| EQ-5D index | 67 (-18 -100) | 77 (67-93) [a] | 77 (67-92) [b] |

*Data are mean scores with ranges in parentheses. EQ-VAS= Quality of life from the patient perspective, EQ-5D index = Quality of life from the social perspective. HP= Hartmann procedure, PA= primary anastomosis. Population= a sex- and age-matched community-based sample of healthy Dutch persons. a= PA vs HP: $p<0.05$; b= Population vs. HP: $p<0.05$.*

**Table 3.** Disease specific quality of life scores (EORTC QLQ-C30)

| | HP | | PA | |
|---|---|---|---|---|
| | Mean | Median (range) | Mean | Median (range) |
| Physical function [a] | 66 | 67 (0-100) | 79 | 87 (13-100) |
| Role function | 70 | 92 (0-100) | 76 | 100 (17-100) |
| Emotional function | 77 | 92 (0-100) | 81 | 92 (0-100) |
| Cognitive function | 78 | 83 (17-100) | 85 | 100 (17-100) |
| Social function | 75 | 83 (0-100) | 76 | 89 (0-100) |
| Global health status [a] | 69 | 71 (14-100) | 79 | 86 (14-100) |
| Fatigue [a] | 64 | 67 (0-100) | 76 | 89 (0-100) |
| Nausea/vomiting | 92 | 100 (33-100) | 94 | 100 (50-100) |
| Pain | 74 | 100 (0-100) | 79 | 100 (0-100) |
| Dyspnoea [a] | 65 | 67 (0-100) | 80 | 100 (0-100) |
| Sleep disturbance | 70 | 100 (0-100) | 67 | 67 (0-100) |
| Appetite loss | 85 | 100 (0-100) | 85 | 100 (0-100) |
| Constipation | 86 | 100 (0-100) | 77 | 100 (0-100) |
| Diarrhoea | 87 | 100 (0-100) | 87 | 100 (0-100) |
| Financial worries | 85 | 100 (0-100) | 91 | 100 (0-100) |

*A high subscale score indicates low distress and good functioning. HP= Hartmann procedure, PA= primary anastomosis. a= PA vs HP: p<0.05.*

**Table 4.** Disease specific quality of life scores (EORTC QLQ-CR38)

| | HP | | PA | |
|---|---|---|---|---|
| | Mean | Median (range) | Mean | Median (range) |
| Micturition problems | 75 | 78 (0-100) | 78 | 78 (22-100) |
| Gastrointestinal problems | 82 | 87 (13-100) | 81 | 87 (13-100) |
| Weight loss | 86 | 100 (33 - 100) | 93 | 100 (33 - 100) |
| Body image [a] | 72 | 85 (0 - 100) | 80 | 89 (0 - 100) |
| Defecation problems | 86 | 90 (43 - 100) | 89 | 95 (48 - 100) |
| Stoma problems | 73 | 76 (0 - 100) | 81 | 81 (81 – 81) |
| Chemo side-effects | 82 | 89 (33 - 100) | 83 | 100 (33 - 100) |
| Sexual function | 21 | 17 (0 - 67) | 20 | 17 (0 - 67) |
| Sexual enjoyment | 48 | 33 (0 - 100) | 58 | 67 (0 - 100) |
| Male sex problems | 61 | 67 (0 - 100) | 69 | 100 (0 - 100) |
| Female sex problems | 86 | 100 (17 - 100) | 81 | 83 (33 - 100) |
| Future perspective | 64 | 67 (0 - 100) | 74 | 67 (0 - 100) |

*A high subscale score indicates low distress and good functioning. HP= Hartmann procedure, PA= primary anastomosis. a= PA vs HP: p<0.05.*

The QOL from the patient perspective (EQ-VAS) was affected by the presence of physical function problems and body image problems ($p<0.01$ and $p=0.04$, respectively). Global health status, physical function, fatigue, and body image were predictors of QOL in social perspective (EQ-5D) (global health status, physical function, and fatigue, all $p<0.01$; body image $p=0.04$). Again, after assessing the patients who had undergone HP followed by restoration of bowel continuity, the EORTC QLQ-CR30 and QLQ-CR38 scores were not significantly different compared to those of patients that had undergone PA.

# Discussion

The present study compared long-term QOL among patients that underwent HP and PA for acute perforated diverticulitis. The QOL outcomes were also compared to the general Dutch population. Survivors from acute perforated diverticulitis reported worse QOL compared to the Dutch population. QOL in patients who had undergone HP was lower compared to patients who underwent PA, both from the patient's and a social perspective. After reversal of HP, this difference disappeared, but HP reversal was performed in only 61% of the patients. QOL in patients after perforated diverticulitis was mainly influenced by the presence of a stoma postoperatively.

Functional aspects and QOL of survivors have become increasingly important for patients with perforated diverticulitis because survival after emergency surgery for perforated diverticulitis is poor, both in the short and long terms.[13] Previously, we described the long-term survival after perforated diverticulitis.[13] The 5-year mortality after perforated diverticulitis was approximately 50%. The main reason for this observation was the poor general condition of the patients. Almost half of the patients that presented with acute perforated diverticulitis were classified ASA III or IV, and one third was older than 75 years of age.[13] It is stated before that the incidence of perforated diverticulitis is highest in elderly patients, suffering from multiple comorbidities as indicated by a higher ASA classification.[14] These factors are known to be correlated with mortality. Direct postoperative mortality after perforated diverticulitis can increase to 40% in patients of older age.[15] It is therefore not surprising that this group of patients have a poor prognosis in the short and long term.

QOL of patients is also important for surgeons when making a decision about the strategy of primary surgery. The optimal surgical treatment of perforated diverticulitis is still a matter of debate; neither PA nor HP has been proven the

superior surgical strategy in terms of mortality and morbidity. Because the impairment of function that may occur after different operations varies considerably, an assessment of QOL for each type of surgical procedure is becoming an essential principle to follow in a successful healthcare system.[16] A very small number of studies have evaluated QOL in patients with (complicated) diverticulitis, but the literature is diverse and frequently based on heterogeneous pathologies. The present study is the first to assess patient's long-term QOL after emergency surgery for acute perforated diverticulitis.

One study used questionnaires to examine whether diverticular disease has an impact on QOL. The authors suggested that the lower QOL scores found in diverticulitis patients compared to healthy controls could be useful in decision making and selection of patients for elective surgical treatment.[17] Two studies assessed long-term QOL after laparoscopic or open sigmoid resection for uncomplicated diverticulitis. Both found no significant differences between the two surgical techniques.[18,19] A recent study comparing two surgical strategies for treatment of complicated diverticular disease showed no difference in QOL in patients after PA or HP.[20] Unfortunately, this study was performed in a heterogeneous group of patients varying from emergency surgery for diverticular peritonitis to elective laparoscopic surgery in patients failing conservative treatment of diverticulitis. A recent study of quality-adjusted life-years after surgery for diverticular peritonitis concluded that PA was superior to HP, unless the risk of postoperative complication was higher than 40%.[21] The conclusions were based on decision analysis techniques for a hypothetical 65-year old, with the use of so-called utilities (a measure of the patient's or surgeon's relative preference for each individual outcome) to calculate. Unfortunately, there are no available published utilities specifically for diverticular disease and therefore, many of the used utilities arose from studies assessing other colorectal diseases, small or dated studies, expert judgment, and assumptions. Given the state of imperfect evidence and the high degree of uncertainty, the conclusion that PA was superior to HP in terms of quality-adjusted life expectancy is at least doubtful.

This study, however, included only patients with acute perforated diverticulitis and supports the conclusion that PA is superior to HP in terms of QOL. The indications for surgery were clinical signs of diffuse peritonitis or presence of septic status with acute abdominal pain or specific findings for perforated diverticulitis at radiographic investigations. The decision for surgical management was made by the surgeon on call, and not all patients had undergone preoperative CT-scanning. Therefore, some patients showed Hinchey I or II perforated diverticulitis at surgery. It is now recognized that patients with small, contained perforations, who are not systemically ill can be treated initially with antibiotics alone or by CT-guided percutaneous

drainage.[22] In this study, all patients that underwent emergency surgery for acute perforated diverticulitis were examined. Patients underwent either HP or resection with PA.

QOL in patients who underwent HP and PA were compared after a median of 71 months after primary surgery using the EQ-VAS, EQ-5D, and QLQ-C30 and QLQ-CR38. These questionnaires have proven to be efficient and reliable tools for establishing the health status within the Dutch community.[12,23] General QOL scores were significantly lower in patients that had undergone HP compared to patients after PA. HP patients were associated with lower physical performances mainly due to a lower physical function and more complains of fatigue. They also showed a diminished body image compared to PA patients.

QOL of patient after PA was comparable with the general population both from the patient's and societal perspective. Although not significant, QOL from the patient's perspective (EQ-VAS, table 2) in PA patients was lower than the general Dutch population. This might not be so much a difference in perspective as it is a difference in the methods: the societal perspective of the EQ-5D is based on "time trade off" (TTO), and the patient perspective is based on a VAS. TTO is a more conservative valuation of burden of disease than VAS.[24] Furthermore, the EQ-5D societal perspective is known to produce a ceiling effect.[25] This could explain why EQ-VAS remained significantly higher in PA patients than HP patients, whereas EQ-5D did not, after multivariate analysis.

Patients that had undergone HP and subsequent reversal of their end colostomy in a second operation showed comparable QOL outcomes to patients that had undergone PA and the general population. HP reversal was performed in only 61% of the patients, which is in reflective of the literature.[26] It has been stated previously that patients with a stoma may face many difficulties both physical and psychological.[4] It is known that patients with direct intestinal continuity after surgery for colon cancer showed better QOL scores than those who received an end colostomy.[27] Also, when having a stoma, reversal of it can result in significant improvements in global QOL and physical and social function.[28] In the present study, patients without an end colostomy (PA) and the HP patients who had their stoma reversed showed similar QOL scores from a social perspective to the general population, whereas patients with an end colostomy (HP without reversal) showed a worse QOL. QOL was independently related to body image problems, e.g., the presence of a stoma.

In the light of body image problems, the use of minimally invasive treatment strategies for perforated diverticulitis may be an interesting development. Although its exact role is still unclear, several studies have shown excellent

results in treatment of patients with peritonitis due to perforated diverticulitis by laparoscopic peritoneal lavage and drainage.[29-31] Compared to HP or PA, laparoscopic lavage and drainage seems to have a lower morbidity and mortality rate. And in most patients a subsequent elective resection is probably unnecessary so a stoma can be avoided.[30,31] As the presence of a stoma plays an important role in QOL in the patients after perforated diverticulitis, laparoscopic procedures might not only appear to be superior over HP and PA in the short term (postoperative morbidity and mortality) but also in the long-term (QOL). Future comparative studies must confirm these statements.

Although QOL was mainly affected by body image problems, it is also important when interpreting the QOL scores to consider that the outcomes are dependent on patient's preoperative expectations. Fear or ignorance of the long-term consequences of the operation is associated with lower QOL.[32] Optimistic and well-informed patients may be more resistant to the negative influence of limitations (caused by their stoma) on their QOL. Surgeons, with support from the stoma care therapist and the multidisciplinary team, can anticipate this by offering appropriate education regarding a colostomy. Ideally, education should start preoperatively so patients require less time and have fewer problems with their rehabilitation.[33] When a colostomy becomes necessary, modern stoma appliances are so effective that most patients with a colostomy can enjoy normal lives. Engel et al. who reported that patients after an abdominal perineal resection have a consistently lower quality of life stated that 60% of the patients in their sample were poorly informed about stoma irrigation techniques.[34] This underlines the importance of instruction and education by stoma care therapists on colostomy care and washout, enabling more bowel control. In patients with acute perforated diverticulitis, preoperative counselling is not possible, as these patients require immediate surgery. Postoperative counselling of the patient (and family) is therefore very important to obtain better control of their bowel function and hence improve long-term outcome.

General health prior to surgery is also associated with postoperative QOL. In general, patients with more than one comorbid condition report the poorest level of QOL.[35] It is known, for example, that neurological comorbidities, like cerebral vascular accident or multiple sclerosis, may be a reason for stoma care problems, causing lower quality of life.[36] Patients with higher ASA classifications (multiple comorbidities) experience more functional limitations and show a lower QOL life than ASA I patients.[32] In this study, patients who underwent HP had significant higher ASA classifications and Hinchey scores prior to initial surgery compared to patients after PA. Therefore, it seems that the more severely affected and high-risk patients underwent HP. These patients appeared to have lower postoperative QOL scores than patients after

PA and the general Dutch population. To assess whether the lower QOL was caused by differences in patient's characteristics and severity of disease scores (selection bias), a multivariate analysis was performed. After adjusting for the differences between the groups, QOL remained worse after HP compared to PA.

In conclusion, survivors after perforated diverticulitis had a worse QOL compared to the general Dutch population, which is mainly related to the presence of an end colostomy. When such stoma can be avoided (PA) or reversed, the QOL in these patients may improve.

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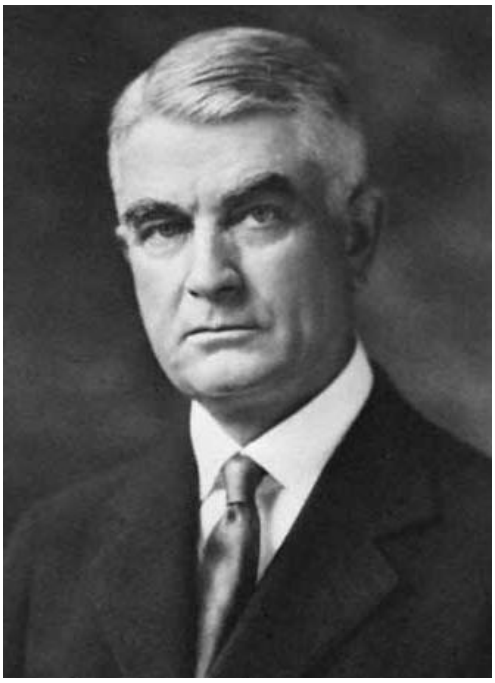


# William James Mayo

(29-6-1861 – 28-7-1939)

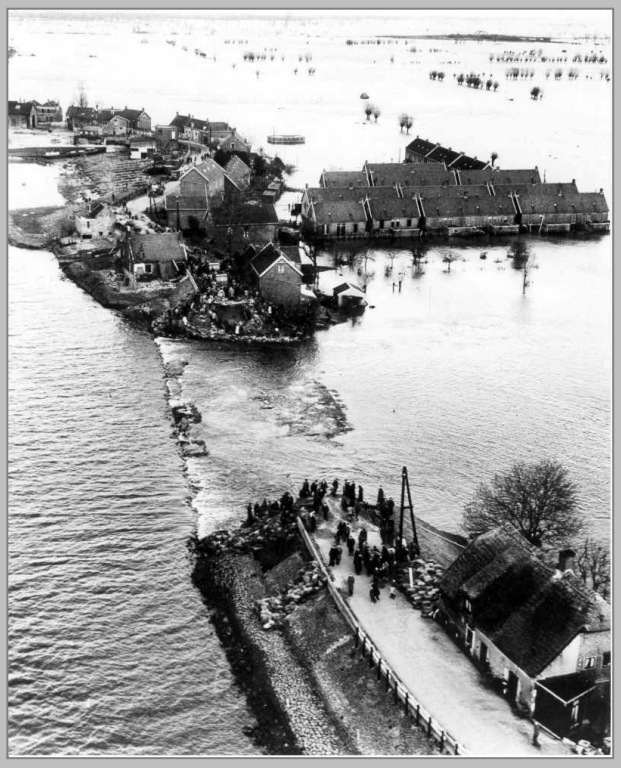
*William James Mayo was the first who established therapeutic surgical guidelines for perforated diverticulitis.*

William James Mayo studied medicine at the University of Michigan, where he graduated in 1883. He also took medical degrees at the New York Post-Graduate Medical School and Hospital. Together with his brother he worked at his father's private medical practise, which was later called the Saint Mary's Hospital. In 1889 William Mayo and his brother Charles Horace developed the Mayo Clinic. The not-for-profit clinic became famous throughout the world for the number and success of operations performed.
William Mayo was chairman of the Committee of American Physicians for Medical Preparedness. He was elected president of the Society for Clinical Surgery in 1911 and the following year president of the American Surgical Association. On America's entrance into the World War he was appointed colonel in the Medical Corps

# 8

# Treatment of perforated diverticulitis with generalized peritonitis
## Past, present and future

*with*
JF Lange



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# Abstract

The first cases of complicated perforated diverticulitis of the colon were reported in the beginning of the twentieth century. At that time the first therapeutic guidelines were postulated in which an initial nonresectional procedure was provided to be the safest plan of management.
After many years in which resection had become standard practice, today, one century later, again (laparoscopic) nonresectional surgery is presented as a safe and promising alternative in treatment of complicated perforated diverticulitis. The question rises what had happened to close the circle?
This paper includes a historic summary of changing patterns in surgical strategies in perforated diverticulitis complicated by generalized peritonitis.

# Introduction

Perforation with generalized peritonitis is the most common life-threatening emergency requiring surgical intervention in diverticular disease of the colon.[1] Whereas most people with diverticular disease remain asymptomatic, approximately 15% develop symptoms, and of these 15% will develop significant complications, such as perforation.[2] In most cases perforation is the first manifestation of the disease.[3] Although the absolute prevalence of perforated diverticulitis complicated by generalized peritonitis is low, its importance lies in the significant postoperative mortality, ranging from 4-26% regardless of selected surgical strategy.[1,4-6]

Until today the optimal treatment for perforated diverticulitis has been a matter of debate. During the last decades, the 'gold standard' has changed several times. Primary resection has become the standard practice, but fear of anastomotic leakage often deterred many surgeons from performing primary anastomosis. Therefore, for many surgeons Hartmann's procedure (HP) has remained the favoured option for these patients.[1] Nevertheless, improvements in surgical techniques, radiological intervention techniques, anaesthesia, advances in intensive care medicine and progress in the management of peritoneal sepsis have led to an increasing interest in resection with primary anastomosis (PA) with or without diverting stoma or colonic lavage.[5,7,8]

Recently, laparoscopic lavage and drainage without resection has successfully been used for patients who have generalized peritonitis caused by perforated diverticulitis (PPD).[9] Because this nonresectional mini-invasive surgical strategy was associated with a reduction in morbidity and mortality, it might be a promising alternative to the standard open resectional practice.[9-11]

This paper includes an overview of the development of different surgical strategies in PPD through the years, and based on this overview we present our personal opinion in the management of this surgical emergency.

# Three-staged procedure

Since the beginning of the previous century, a three-stage operation strategy was common practice in the treatment of diverticular disease. The first report of surgical treatment for complicated diverticulitis was by Mayo in 1907.[12] The classic three-stage operation includes an initial diverting colostomy and drainage followed by resection of the involved colon and, finally, a colostomy

closure as the third stage. This nonresectional surgery strategy was reaffirmed and advocated by the experiences at the Mayo Clinic, which presented the results in 1924, to be the safest.[13]

During the next two decades, indications for emergency surgery evolved towards complicated diverticulitis, such as perforation, obstruction and fistula formation, only. A preliminary transverse colostomy was advised in all cases in which resection was contemplated, and the period of delay before this resection should be from 3 to 6 months.[14,15] The rationale for this strategy was that primary resection is too difficult in the acute stage of the disease, often causing iatrogenic complications and hence mortality. After the faecal stream was diverged by performing a transverse colostomy during the first surgical stage, drainage of the abdomen and pelvic cavity was initiated to diminish sigmoid inflammation. After several months the second stage -resection of the involved bowel- could be performed to treat and prevent relapse of the disease. Smithwick[15] advocated this procedure in favour towards resectional operations. He reported a postoperative mortality after a three-stage procedure of nearby 12%, compared to 17% if the involved colon segment was resected during initial surgery.[15] Considering that antibiotics were not discovered yet, these results can be regarded as remarkable.

In 1945 Florey was responsible for the development of penicillin for use as a medicine.[16] Since then antibiotics were more frequently used during colonic surgery. Partly, this led toward a shift in the continuing controversy between three- and two-staged operations in favour of primary resection of the involved colon. Although at that time Smithwick,[17] amongst others, still recommended the three-stage and initially nonresectional operation,[18,19] more publications advocating primary resection in case of PPD arose.[20-22] Initial improvement after colostomy and drainage, without resection, was often followed by severe deterioration several days later when the involved perforated bowel was left in situ.

Since the 1960s combinations of antibiotics were used against gram-negative bacteria and anaerobic bacteria. Combination antibacterial therapy had shown better survival in septic patients.[23] Unfortunately, mortality rates in patients with PPD remained high. The basic cause of this high mortality was that the source of infection remained in the peritoneal cavity.[21] Painter and Burkitt[24] documented the increased intraluminal pressures and muscle abnormalities being the cause for diverticula formation in the sigmoid. When left in situ, the perforated segment remains a source of sepsis as bowel contractions continue evacuating infective material. Clinical observations and this new understanding of pathophysiology of diverticulitis led to the conviction that the colonic perforation had to be removed primarily.[21,22] Nevertheless,

controversy persisted because the ‘evidence’ was only based on expert opinion and some (small) non-comparative case series.

## Two-staged procedure with primary resection

Since the 1980s and 90s standard practice of PPD has definitively changed from nonresectional surgery towards primary resection of the involved sigmoid. A two-stage operation with the initial operation being resection of the diseased segment with the construction of a colostomy proximally and suture closure of the distal rectal stump became the preferred surgical strategy in these category patients.[25] The second stage was represented by the colostomy closure. Among surgeons this operation has been known since as Hartmann’s procedure (HP), although Hartmann[26] himself only performed such a procedure for rectum carcinoma and had advocated that the patient should not undergo restoration of bowel continuity.

This change in strategy was mainly based on the results of two reviews published in 1980 and 1984 by Greif et al.[27] and Krukowski and Matheson.[28] Mortality after primary resection was reported to be lower compared to those procedures in which the perforated segment could not be removed at initial operation.[27,28] Unfortunately both reviews were not systematic, containing a wide range of different surgical techniques and covering more than 25 years during which substantial improvements in antibiotic and other perioperative supportive therapies has taken place. Furthermore, it is not known whether the patients of both groups were comparable for a number of essential variables, such as age, ASA classification, and Hinchey and Mannheim Peritonitis Index scores.

Between 1993 and 2000, two randomized controlled trials (RCT) assessing primary versus secondary resection were published.[29,30] These RCTs drew opposite conclusions. Kronborg[29] concluded that three-stage nonresectional surgery (suture and transverse colostomy) in PPD was still superior to primary resection because of a lower postoperative mortality rate. Mortality in Hinchey IV patients was not different in both groups. Unfortunately, the study was preliminary stopped because of low recruitment (an average of four patients each year) and hence underpowered. A total of 62 patients were included and operated by 27 different surgeons during a period of 14 years.

Zeitoun et al.[30] concluded that primary resection was superior to nonresectional surgery because of less postoperative peritonitis and fewer reoperations. Nevertheless, postoperative mortality after primary resection was

higher compared with nonresectional surgery (24% vs. 19%), but this difference was not significant. Although the evidence was weak, the American Society of Colon and Rectal Surgeons has published practice guidelines in which the three-stage operative approach strategy (nonresectional surgery) was no longer recommended for most patients because of high associated morbidity and mortality.[31] As a result of improvements in radiological intervention techniques, postoperative complications and ongoing abdominal sepsis could be treated percutaneously, which made more radical resections during initial surgery possible.[32] HP had become mandatory for emergency indications in PPD. But scepticism about primary resection remained through the years.[33]

## Resection with primary anastomosis

Improvements in surgical and radiological intervention techniques and progress in the management of peritoneal sepsis led to an increasing interest in colonic resection with primary anastomosis (PA) since the 1990s. Although not proven in RCTs, PA with or without diverting loop ileostomy seemed not to be inferior to HP in terms of severe postoperative complications and mortality.[1,5,7,34,35] Probably, even the presence of faecal peritonitis was no longer considered an absolute contraindication to immediate bowel reconstruction.[36] However, fear of anastomotic leakage often deters many surgeons from performing a one-stage procedure (e.g., PA) in PPD.

Although HP is considered a two-stage procedure, the second stage (reversal of colostomy) will never be performed in a large number of patients.[37,38] Restoration of bowel continuity after HP is a technically challenging operation and is associated with significant morbidity and mortality.[39] These rates can be as high as 25% and 14%, respectively, after colostomy reversal in patients who had undergone HP for PPD.[1,5] Together with the debilitated condition of many of these patients this is one of the main reasons that HP often results in a permanent colostomy. They face the physical (leakage, parastomal hernia) and psychological (lifestyle alterations) challenges that are associated with having a stoma.[40,41] The risk of a permanent ileostomy is recognizably less than that of HP and with fewer complications.[38,42]

The performance of a diverting loop ileostomy has been reported to decrease the rate of symptomatic anastomotic leakage in patients operated for rectal cancer.[43,44] The same is found in case of diverticular peritonitis. However, the quality of the present studies is poor. Besides, a diverting loop ileostomy

seems not to diminish postoperative mortality.[5] The use of perioperative colonic lavage appears to lower postoperative complications in case of PA, but the evidence in the present literature is limited.[45,46]
Postoperative morbidity and mortality rates of patients after emergency surgery for PPD are still high and mainly caused by the poor general condition of the frequently aged patients and the severity of disease.[47-49] This suggests that further reduction in mortality will require improvement in medical management of pre- and perioperative sepsis and comorbid conditions. Type of surgery seems no longer significantly related with postoperative mortality, although many recent studies favour PA, with or without loop ileostomy, instead of HP in purulent of faecal PPD.[6-8,34-36,50] These statements were confirmed by a systematic review of Salem and Flum in which mortality rates after HP and PA of 19% and 10% respectively, were reported.[5]

## Nonresectional laparoscopic lavage

The role of laparoscopic resectional surgery in PPD is limited. In acute complicated diverticulitis without peritonitis, laparoscopic sigmoid resection with PA seemed to be a safe procedure.[51] Outcome after laparoscopic PA in PPD is lacking in present literature. Laparoscopic HP seems to be a technically feasible procedure with reasonable outcomes for patients in this category.[52] In 1996, Faranda et al. first described a nonresectional laparoscopic procedure that seemed to be a more promising alternative.[53] In patients with peritonitis without gross faecal contamination, laparoscopic peritoneal lavage, inspection of the colon, and the placement of abdominal drains appear to diminish morbidity and improve outcome.[10,11,53] In a series of 100 patients with PPD, Myers et al. showed excellent results after laparoscopic lavage and drainage of the peritoneal cavity, with morbidity and mortality rates <5%.[9]
Laparoscopic damage control surgery seems to decrease the rate of more radical procedures, including HP.[11,54] In patients who were found to have faecal peritonitis or who fail to improve after lavage, acute resection should still be performed.[54] A comparative study between laparoscopic peritoneal lavage and open PA with diverting loop ileostomy for the management of PPD found no differences in postoperative morbidity and mortality.[55] Laparoscopic peritoneal lavage reduced the length of hospital stay and a stoma could be avoided in most patients.
In a second elective stage definitive surgery can take place, e.g., laparoscopic resection and PA,[10,11] although, subsequent elective resection is probably

unnecessary.[9,56] Nevertheless, the number of studies are rather limited and mostly based on small groups of patients. Besides, the rates of additional radiological interventions and conversion to an open procedure are high.[54] Finally, for many hospitals it will not be possible to have a surgical team with expertise in colorectal laparoscopic surgery present all the time. Therefore, laparoscopy is of unclear or limited value in the emergency setting caused by PPD. However, diagnostic laparoscopy may be useful if no diagnosis can be found by conventional diagnostics.[57]

Some authors have expressed their concerns with laparoscopic nonresectional treatment of perforated diverticulitis. They state that the decision to perform nonresectional surgery is influenced by the surgical access to the abdomen, i.e., laparoscopy, rather than based on evidence in literature.[58] Patients should undergo primary resection, whether the surgical access to the abdomen is conventional or laparoscopic, because there is 'evidence' in the literature that resectional surgery leads to lower postoperative peritonitis, and mortality rates, compared with nonresectional surgery.[58,59] Unfortunately, the evidence, to which they referred[28-30] -resection favouring nonresectional surgery- is equivocal or to the contrary as stated before. The major criticism of the nonresectional laparoscopically lavage technique is the continued presence of the perforated colon as a septic focus as well as the column of faeces remaining in the colon proximally to the perforation as a potential ongoing source of contamination. This was also the main criticism towards the three-stage procedure that was used to treat PPD until the 1970s. Classen et al. had observed that postoperative mortality related to sepsis was lowered after addition of more effective antibiotics to treat gram-negative and anaerobic bacteria since 1970.[19] Besides, PPD is accompanied by ileus and hence it is not likely that the faecal column is propelled towards the perforation. A patent communication between the colonic lumen and the peritoneal cavity usually cannot be found during laparoscopy because the site of the original perforation has become sealed by the inflammatory process and omentum and seems efficient to control the source of contamination. If the perforation site is too large to be sealed before peristalsis resumes, resection of the bowel segment is advocated.[60]

The suggestion that nonresectional surgery in combination with more advanced antibiotics have never proven to be an inferior strategy could explain the excellent results after laparoscopic lavage in combination with modern management of peritoneal sepsis with improved antibiotics and intensive care medicine. Naturally the latter technique has several advantages over the open three-stage procedure, of which less wound complications (such as infections and hernias), no stomal complications, and avoidance of a second operation are the most important.[9,19] Nevertheless, because the evidence is weak, until

now primary resection remains the standard treatment for PPD, although the European Association for Endoscopic Surgery Evidence-based Guidelines stated that laparoscopic nonresectional surgery may be considered in selected patients.[57]

## Nonresectional nonsurgical lavage

Until the 1990s, all stages of perforated diverticulitis were treated by surgery. The principles of primary treatment of abdominal infections caused by perforation, as outlined by Polk in 1979[61] have not changed much during the years. These principles includes alimentary tract decompression, fluid resuscitation, antibiotics to cover gram-negative aerobes and anaerobes, and so-called ‘source control‘. Source control consists of all measurements to eliminate the source of infection, to control ongoing contamination and to restore premorbid anatomy and its function.[61,62]
The progress in antibiotic development and interventional radiographic techniques has changed management of perforated diverticulitis. The high specificity of CT scan has allowed this modality to become a surrogate to the perioperative assessment made by the Hinchey classification.[63] Furthermore, CT scan has become an important therapeutic modality. It is now recognized that patients with small, contained perforations, who are not systemically ill can be treated initially with antibiotics alone, or by CT-guided percutaneous drainage.[62,64] Source control by percutaneous drainage has become the treatment of choice for most abscesses, provided that adequate drainage is possible and no debridement or repair of anatomical structures is necessary.[65] The size of the drain used is very important because complete evacuation of the abscess must be obtained. If the abscess cannot be drained sufficiently, source control will fail. Although mechanical control of the source of infection remains important, several studies have found that abscesses up to 4 cm seem to respond better to antibiotics alone.[62,64] Currently, the only patients who do require surgery (laparoscopically or open) for source control are those that fail conservative treatment and those that require emergency surgery, mostly patients with PPD.[64,65]
If nonresectional laparoscopic lavage and drainage to treat PPD is found to be a safe and better alternative for resectional surgery in the future, why should this be different from nonresectional nonsurgical, e.g., CT-guided, percutaneous lavage and drainage? Present literature as yet does not report about this (hypothetical or future) treatment strategy. Is it possible that this

will be the next step in the ever more conservative management of different stages in diverticular disease?
To answer this question, it is important to take into account the main principles of abdominal infection treatment when using percutaneous lavage and drainage. Fluid resuscitation and modern antibiotic strategies will not be different from laparoscopically lavage procedures. In order to gain source control in percutaneous techniques, it is important that large size catheters will be used for adequate drainage of thick and viscous purulent contents.[66] The main problem is the inability for inspection of the abdominal cavity to localize the site and size of the perforation. In laparoscopically procedures to treat PPD, careful removal of adherent omentum or bowel is tried to locate the site of perforation. If clearly adherent, the adhered omentum or small intestinal loops can be left in place and the abdominal cavity is irrigated with litres of warm saline.[9] At the end of the procedure, one or more drains are inserted. Such a careful adhesiolysis and inspection of the abdominal cavity, to look for or exclude other causes of generalized purulent peritonitis, is not possible using today's radiographic modalities. Furthermore, in case of a large perforation, causing faecal peritonitis, source control by percutaneous lavage and drainage is impossible and hence surgical treatment will be necessary to achieve source control and restore premorbid anatomy and function. It is, therefore, not likely that percutaneous (nonsurgical) nonresectional lavage and drainage will play a prominent role in the treatment of PPD in the near future, because it cannot meet to the principles of abdominal infection treatment yet.

# Conclusions

During the last century, mortality rates after emergency surgery for PPD have remained high: nearby 20%. Progress in (antibiotic) sepsis management has led to more radical surgical procedures, but survival did not improve significantly. The reason for this remains unclear. The question rises whether 'old-fashioned' (laparoscopic) nonresectional surgery in combination with 'modern' sepsis management is the key to success. The last reports are promising.
In our personal opinion, supported by the existing literature about treatment of PPD, resection with PA should be the standard procedure in emergency surgery for perforated diverticulitis with generalized peritonitis. HP must seriously be considered the surgical procedure of choice for older patients with multiple comorbidities, realizing that restoration of bowel continuity is not an

issue. Laparoscopic nonresectional surgery is regarded as a good alternative in case of purulent peritonitis, provided that it is performed by a surgeon experienced in laparoscopic surgery. Although currently, percutaneous drainage of abdominal abscesses is the preferred treatment strategy in contained diverticular perforations, it is not likely that nonresectional interventional radiographic techniques will play a prominent role in initial treatment of PPD in the near future. Clearly, more (prospective randomized) research is warranted to confirm all these statements.

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# Sir Howard Walter Florey

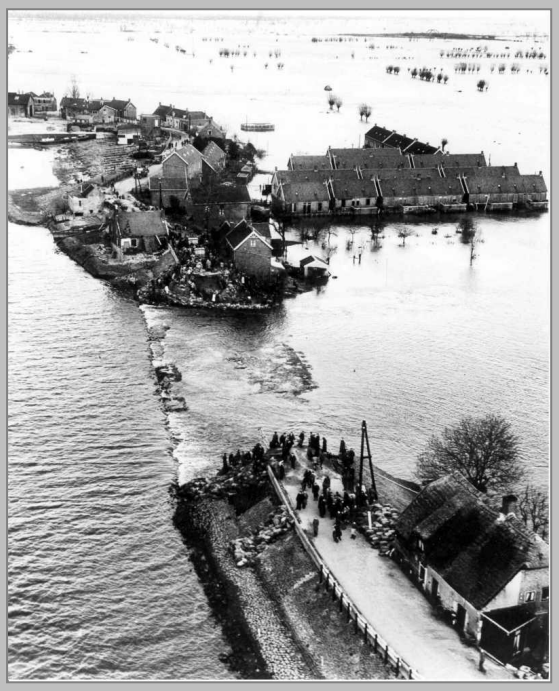
24-9-1898 – 21-2-1968)

*Howard Walter Florey developed penicillin, which was discovered by Alexander Fleming, into a useful treatment.*

Howard Florey studied medicine at the University of Adelaide, where he graduated in 1921. He continued his studies at Magdalen College in Oxford and in 1926 he was elected to a fellowship at the Cambridge Gonville and Caius College. In 1931 he started working as a pathologist at the University of Sheffield. Four years later he was appointed Professor of Pathology in Oxford. Alexander Fleming first observed the antibiotic properties of the mold that makes penicillin, but it was Howard Walter Florey (together with Ernst Boris Chain) who developed it into a useful treatment. In 1941, they treated their first patient. In 1945 the three were awarded with the Nobel Prize in Physiology or Medicine. Florey has had many honours bestowed upon him, amongst them the Lister Medal at the Royal College of Surgeons of England. In 1959 he was elected president of the Royal Society. He was made as Baron Florey, of Adelaide in the Commonwealth of Australia and of Marston in the County of Oxford in 1965.

# 9

# The Ladies trial: laparoscopic peritoneal lavage or resection for purulent peritonitis and Hartmann's procedure or resection with primary anastomosis for purulent or faecal peritonitis in perforated diverticulitis



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# Abstract

Recently, excellent results are reported on laparoscopic lavage in patients with purulent perforated diverticulitis as an alternative for resectional surgery (Hartmann's procedure or sigmoid resection with primary anastomosis). The objective of this nationwide multicenter randomised trial is to determine whether laparoscopic lavage and drainage is a safe and effective treatment for patients with purulent peritonitis (LOLA-arm) and to determine the optimal resectional strategy in patients with a purulent or faecal peritonitis (DIVA-arm).

This trial randomizes patients with perforated diverticulitis. Upon laparoscopy, patients with purulent peritonitis are treated with laparoscopic lavage and drainage (LL), Hartmann's procedure (HP) or sigmoid resection with primary anastomosis (PA) in a ratio of 2:1:1 (LOLA-arm). Patients with faecal peritonitis will be randomised 1:1 between HP and PA (DIVA-arm). Primary endpoint of the LOLA-arm is the combined number of major morbidity and mortality in the group of patients with purulent peritonitis. A sample size of 132:66:66 patients per treatment arm will be able to detect a difference in the primary endpoint from 25% in the HP and PA groups compared to 10% in the LL group (two sided alpha = 5%, power = 90%). Endpoint of the DIVA-arm is stoma-free survival one year after initial surgery. In this arm 212 patients are needed to significantly demonstrate a difference of 30% (log rank test two sided alpha = 5% and power = 90%) in favour of the patients with PA. Secondary endpoints for both arms are number of days alive in- and outside the hospital; health related quality of life, health care utilisation and associated costs.

The LADIES-trial is a nationwide multicenter randomised trial on perforated diverticulitis that will provide evidence on the merits of laparoscopic lavage and drainage for purulent generalised peritonitis and on the optimal resectional strategy for both purulent and faecal generalised peritonitis.

# Introduction

Diverticular disease is an important condition in terms of healthcare utilisation and it is one of the five most costly gastrointestinal disorders in westernised countries.[1] Despite the high prevalence, treatment of all different stages of diverticular disease is still hardly evidence based and containing a lot of controversies.

Perforated diverticulitis is a perforation of a diverticulum of the large bowel, mostly the sigmoid, resulting in either purulent or faecal peritonitis (Hinchey stadium III or IV). Both conditions require emergency surgery.[2,3] Regardless of selected strategy emergency operations for acute perforated diverticulitis are associated with substantial morbidity (up to 50%) and mortality (15-25%).[3-8] Primary sigmoid resection with or without anastomosis has become the standard practice for patients with generalised peritonitis complicating diverticulitis [6-10] and for many surgeons the Hartmann's procedure (HP) remains the favoured option.[11] Restoration of bowel continuity after this procedure is a technically difficult operation, with high morbidity and mortality rates.[12-14] Therefore stoma reversal after HP is only performed in 50 to 60% of patients, thereby compromising quality of life and increasing costs.[15,16] Recently laparoscopic lavage (LL) emerged as an effective alternative for patients with perforated diverticulitis with purulent peritonitis.[17] This nonresectional procedure has first been described by Champault in 1996.[18] In 2009, a systematic review on all studies on laparoscopic lavage with a total number of 231 patients was performed. Mortality was less than 2% and a (permanent) colostomy could be avoided in the majority of these patients.[17,19-24] It seems that LL for treating perforated diverticulitis will have great potential in improving health and reducing costs.

Since sigmoid resection is still considered the standard of care for perforated diverticulitis, implementation of LL might be variable. Some surgeons will embrace lavage because of its technical simplicity; others might be reluctant fearing failure of this novel strategy. Only a head to head comparison of both surgical strategies will provide evidence based surgical treatment strategies for patients with perforated diverticulitis with purulent peritonitis (LOLA-arm).

In case of faecal peritonitis there is no evidence that LL is a valid alternative for resectional strategies. But again, the optimal surgical treatment is still a matter of debate. The available literature suggests equality of HP and PA regarding postoperative mortality and morbidity.[5-9,25,26] The likelihood of stoma closure seems higher after sigmoid resection, primary anastomosis and diverting loop ileostomy (85%) compared to sigmoid resection with end colostomy (e.g., HP) (60%), but hard evidence is missing.[12-14] Therefore, HP

and PA are compared to determine the optimal resectional treatment for perforated diverticulitis with generalised purulent or faecal peritonitis, regarding stoma-free survival (DIVA-arm).

### Study objectives

For this two-armed randomised trial two objectives can be defined to determine the optimal strategy for the treatment of perforated diverticulitis. First, is laparoscopic lavage for patients with purulent peritonitis superior compared to open sigmoid resection, in terms of mortality, morbidity, quality of life, health care utilisation and associated costs (LOLA-arm)? Second, is HP or PA the superior strategy for patients with purulent or faecal generalised peritonitis in terms of stoma-free survival, quality of life and cost-effectiveness (DIVA-arm)?

## Patients and methods

### Study design

The LADIES-trial is a nationwide multicenter trial in which patients with generalised peritonitis caused by perforated diverticulitis are randomised to undergo either laparoscopic lavage and drainage or resectional surgery by laparotomy.

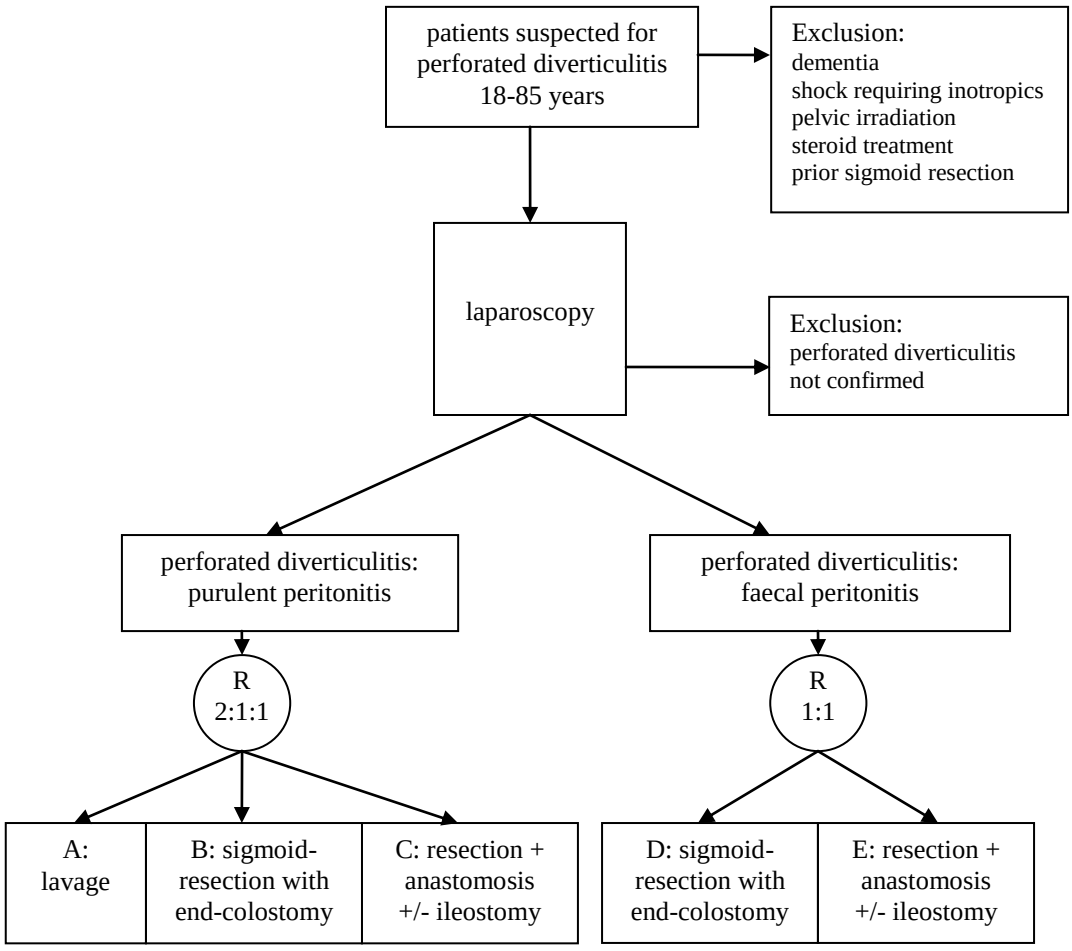
Patients presenting with clinical signs of diverticulitis with diffuse peritonitis can be included upon the finding of free gas on plain abdominal radiography, or upon the finding of peritonitis with diffuse fluid or free gas on computed tomography scan (CT). All patients need to fulfil the in- and exclusion criteria and will need to give written informed consent; exclusion criteria are dementia, pelvic irradiation, steroid treatment, prior sigmoidectomy and preoperative shock requiring inotropics.

All eligible patients will undergo diagnostic laparoscopy to exclude other causes of generalised peritonitis. If the diagnosis perforated diverticulitis is confirmed, the patient can be enrolled and randomised. Block-randomisation is performed during laparoscopy via the trial website according to figure 1.

In case of purulent peritonitis (Hinchey III), patients are randomized to laparoscopic lavage or laparotomy followed by HP or PA (LOLA-arm). The best evidence indicates that the latter two resectional strategies are equal in terms of postoperative morbidity and mortality in case of generalised peritonitis.[7,8] For this reason a three way 2:1:1 randomisation is performed. In case of an overt perforation with faecal peritonitis (Hinchey IV) patients will

undergo laparotomy and are randomised 1:1 to either undergo HP or PA (DIVA-arm).
Patients who are either ineligible for trial entry, who show other causes of peritonitis than diverticulitis at laparoscopy or who do not wish to take part in the study are treated at the discretion of the surgeon on call.

**Figure 1.** Flowchart of the both arms of the LADIES-trial




*The LADIES-trial with two study-arms: LOLA-arm: primary endpoint is mortality and major morbidity at one year (A versus B + C); DIVA-arm: primary endpoint is stoma-free survival at one year (B + D versus C + E).*

## Endpoints

Primary endpoint of the LOLA-arm is the combined number of mortality and major morbidity, twelve months after initial surgery. Secondary endpoints are quality of life, health care utilisation and associated costs.
Primary endpoint of the DIVA-arm is the stoma-free survival within twelve months after initial surgery. Secondary endpoints are quality of life and cost-effectiveness.

## Participating centers

More than thirty-five teaching hospitals in the Netherlands are participating in this trial, including six academic centres.

## Study population

This study consists of patients eligible for surgical treatment of perforated diverticulitis. Inclusion criteria are age between 18 and 85 years, a clinical suspicion for perforated diverticulitis and free gas on plain abdominal radiography, free gas on CT, or peritonitis with diffuse fluid or gas on CT.

## Ethics

This study will be conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Medical ethics approval has been obtained by the medical ethics committee from the Academic Medical Centre of Amsterdam on September 30th, 2009.
Prior to randomisation, written informed consent must be obtained from all patients.

## Study outline

*Diagnostic laparoscopy:* a careful inspection of the stomach, duodenum and sigmoid is performed to localise the site of perforation. In case of peritonitis due to a perforated diverticulum it must be attempted gently to locate the site of perforation. Careful removal of adherent omentum or bowel is tried. If clearly adherent, it should be left in place.
If no obvious perforation is apparent and faecal content is absent, the patient is randomised online between treatment with LL, HP or PA in a ratio 2:1:1.
In case of an overt perforation or intra-abdominal contamination with faeces, the patient is not eligible for LL and is randomised between HP and PA.
*LL*: the abdominal cavity is irrigated with six litres of warm saline. At the end of the procedure a Douglas drain is inserted via the right lateral trocar port.
*HP:* The perforated diseased part must be resected. There is no need of having the distal transsection line on the proximal rectum. An end-colostomy is

performed according to the preference of the operating surgeon, as for closing the rectal stump.
*PA:* Sigmoid resection is done according to the guidelines of the American Society of Colon and Rectal Surgeons.[27,28] The distal transsection margin has to be on the proximal rectum, the proximal margin is determined by the absence of wall thickening due to diverticulitis. The type of anastomosis and the decision to perform a diverting loop ileostomy are to the discretion of the surgeon on call.
Leaving a Douglas drain after resectional surgery is at the discretion of the operating surgeon. The resected tissue is sent for histological investigation to exclude malignancy. Antibiotics are administered for seven days in both groups. Postoperatively, oral diet and mobilisation are advanced as soon as possible. Within four to six weeks after LL a sigmoidoscopy is performed to exclude malignancy as the underlying cause of the perforation.
After the sigmoidoscopy is performed, the patient will be offered reversal of the stoma, when found eligible for surgery by the surgeon and anaesthesiologist.

## Intention to treat

The analysis will be performed in accordance with the intention to treat principle.

## Sample size calculation

In the LOLA-arm of the study, the supposed difference in the combined number of mortality and major morbidity between laparoscopic lavage and resection is 15%. With a two sided likelihood ratio test and a significance level of 0.05, a sample size of 132:66:66 will be necessary to detect this difference. With a group size of a hundred patients per arm it is also possible to find a significant difference (alfa=0.05, beta=0.1) of at least 10% in subscales of the SF-36, a validated Quality of life Questionnaire, at two, four, thirteen, 26 and 52 weeks after initial surgery.
In the DIVA-arm 212 patients are needed to significantly demonstrate a difference in stoma-free survival between both treatment arms, using log rank statistics with a power of 90% and a type I error of 5%. The suspected postoperative mortality for HP and PA is equally high (+ 15%).[7] About 60% of the patients that underwent HP have their stoma reversed.[12,13] When corrected for the expected mortality before reversal, the reversal rate will be 50%. Patients with a diverting loop ileostomy after PA will have their stoma reversed in over 85%.[13] When correction for expected mortality before reversal, this will result in a 72% stoma reversal rate in the initial patient population.

## Economic evaluation

Comparisons of the different surgical strategies in the economic evaluation will be analogous to the analyses of the clinical endpoints. The economic evaluation will be performed from a societal perspective, with the costs per unit improvement on the primary clinical endpoints, defined as combined mortality and morbidity for the LOLA-arm, and stoma-free survival for the DIVA-arm.

We hypothesise that a more effective intervention will be associated with less health care utilisation as well as absence from paid work (productivity costs). Therefore, the primary analysis will be a cost-effectiveness analysis that evaluates costs associated with an improved surgical outcome.

In addition, a secondary analysis will evaluate cost differences in relation to differences in quality-adjusted life-years (QALY's). This cost-utility analysis, resulting in an incremental cost-effectiveness ratio expressed in costs per QALY, will be included to allow comparison with other health-related interventions or programs. With a study horizon of twelve months, no discounting will be applied. We will differentiate between direct medical, direct non-medical and indirect costs.

## Data collection and monitoring

An electronic Case Report Form (CRF) will include general patients data: sex, age, medical history, POSSUM-score, preoperative APACHE-score, surgical parameters, Hinchey score, data concerning type of intervention, complications, mortality, duration of hospital and intensive care stay and the patients response to the questionnaires.

Patients will be followed for a period of twelve months. During this follow-up period patients will complete a set of standardised questionnaires (SF-36, EQ-5D and GIQLI) 2, 4, 13, 26 and 52 weeks after the initial surgery. The questionnaires will be sent to the patients by mail accompanied by a stamped return envelope. Collection of the questionnaires will be safeguarded by the trial coordinator.

At 4, 13, 26, 39 and 52 weeks after initial surgery, the patients will be asked to complete questionnaires to assess complications, additional interventions, readmissions, duration of hospital and intensive care stay and visits to the outpatient clinic, number of days of sick leave and of social in attendance.

An independent trial monitor will monitor the study procedure and the data of included patients. A data monitoring committee will make early (after every 25 included patients) statistical analysis to guard the methodological quality of the study, the safety of the patients, and to monitor any early significant differences between the groups of treatment.

### Patient safety

An independent data monitoring and safety committee has been established to interpret the data from the current trial and to make interim analyses to decide on continuation of the study after every 25 included patients.

A data management bureau created the online database of the study to guard the entry of data by the local co-investigators. The same bureau has trained all local head investigators, trial coordinators and local co-investigators on the guidelines of Good Clinical Practice.

The trial coordinators have trained all other personnel on the protocol, on asking patients informed consent, on reporting Serious Adverse Events and on data entry.

According to the Good Clinical Practice guidelines, a list of Serious Adverse Events is defined. All events on this list have to be reported by the local co-investigators to the trial coordinators within 24 hours after the event. These events will be reported to the central Medical Ethics Committee within 24 hours afterwards. With this measure, the central Medical Ethics Committee compares the incidence of complications between the different arms of the trial and might decide to not continue the trial.

## Discussion

Since the introduction of LL for purulent peritonitis for perforated diverticulitis in 1996, the number of patients treated with this new method had gradually increased. However, there have been no publications of high methodological quality on this topic.[29] Therefore we do not know whether laparoscopic lavage is in fact a safe and effective treatment. Since the existing publications do promise a significant reduction in mortality and major morbidity, a randomised trial is appropriately warranted. A data monitoring committee will guard the methodological quality of the study, the safety of the patients, and monitor any early significant differences between the different surgical strategies. We have not found any evidence that laparoscopic lavage is a safe treatment for perforated faecal peritonitis; therefore in this group of patients randomisation will only take place between the two resectional strategies: HP and PA.

In the presented study all patients suspected for perforated diverticulitis are included and will undergo diagnostic laparoscopy. A midline laparotomy can be avoided in patients with other pathology and treated likewise. We do not know whether the lavage itself is important to the treatment of the peritonitis,

since there are no publications on the treatment of purulent perforated diverticulitis with diagnostic laparoscopy and antibiotic treatment alone. Laparoscopic lavage in combination with antibiotic treatment however, has been examined in a systematic review with very promising results.[29]
The stoma reversal rate is the primary endpoint for the DIVA-arm of the trial. Questions could be raised about the benefits of this reversal for a patient that is incontinent for faeces. A definitive colostoma for this specific group of patients might be preferable considering daily care. However this group of patients will be small and no studies have compared quality of life for incontinent patients with or without a stoma. An end colostomy and loop ileostomy show equal impact on patient's quality of life[16] and quantification of incontinence problems is unpractical in the emergency setting. Therefore incontinence is not established as an exclusion criterion. All resections will be performed with the intention of stoma reversal.
In the Netherlands the standard of care for perforated diverticulitis is either HP or PA. Resection with primary anastomosis is a type of treatment not mastered by every gastrointestinal surgeon. In the emergency setting, some surgeons might prefer HP, fearing anastomotic leakage. However, there is no clear evidence available showing a difference in mortality and major morbidity between HP and PA. Therefore we decided to include treatment with PA in the randomisation process of the LOLA-arm as well. Our hypothesis is that PA leads to a 22% higher stoma-free survival, and that this procedure might be advocated as the new standard of care in selected patients with generalised peritonitis caused by perforated diverticulitis.

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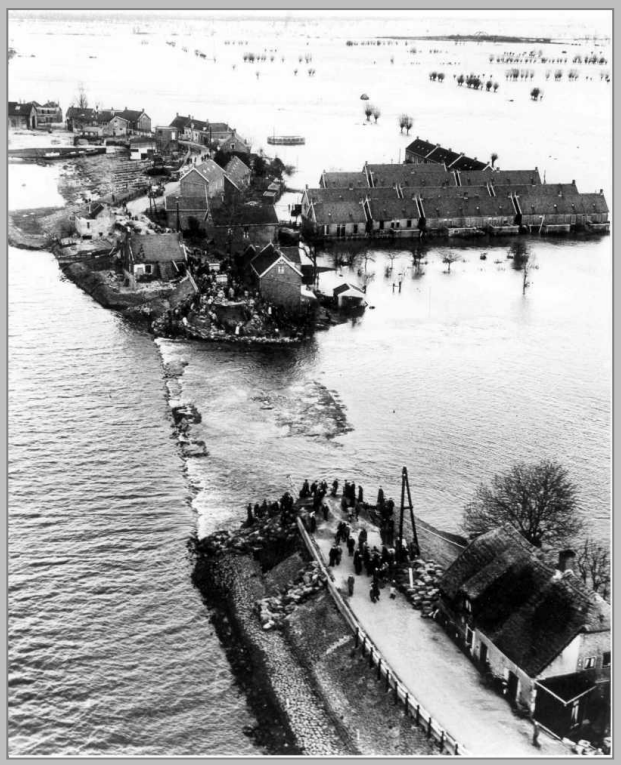
# 10

# Restoration of bowel continuity after surgery for acute perforated diverticulitis

## Should Hartmann's procedure be considered a one-stage procedure?

*with*
PPLO Coene
NM van Hout
E van der Harst
MP Gosselink
GHH Mannaerts
WF Weidema
JF Lange



Colorectal Disease 2009; 11(6): 619-624. Epub 2008 Aug 21.

# Abstract

Hartmann's procedure (HP) still remains the most frequently performed procedure in acute perforated diverticulitis, but it results in an end colostomy. Primary anastomosis (PA) with or without diverting loop ileostomy (DI) seems a good alternative. The aim of this study was to assess differences in the rate of stomal reversal after HP and PA with DI and to evaluate factors associated with postreversal morbidity in patients operated for acute perforated diverticulitis.

All 158 patients who had survived emergency surgery for acute perforated diverticulitis in five teaching hospitals in The Netherlands between 1995 and 2005 and underwent HP or PA with DI were retrospectively studied. Age, gender, ASA-classification, severity of primary disease, delay of stoma reversal, surgeon's experience, surgical procedure and type of anastomosis were analysed in relation to outcome after stoma reversal.

Of the 158 patients, 139 had undergone HP and 19 patients PA with DI. The reversal rate was higher in patients with DI (14/19; 74%) compared to HP (63/139; 45%) ($p=0.027$). Delay between primary surgery and stoma reversal was shorter after PA with DI compared with HP (3.9 vs. 9.1 months; $p<0.001$). Cumulative postreversal morbidity after HP was 44%. Early surgical complications occurred in 22 of 63 patients. Morbidity after DI reversal was 15% ($p<0.001$). Three patients died after HP reversal, none died after DI reversal. Anastomotic leakage was observed in 10 patients after HP reversal. This was less frequently observed when the operation was performed by a specialist colorectal surgeon (10 vs. 33%; $p=0.049$) and when a mechanical anastomosis was performed (4 vs. 24%; $p=0.037$).

Reversal of HP should only be performed by an experienced colorectal surgeon, preferably performing a stapled anastomosis, or probably not be performed at all, as it is accompanied by high postoperative morbidity and even mortality. It is important that these findings are taken in account for when performing primary emergency surgery for acute perforated diverticulitis.

# Introduction

Primary resection has become standard practice for patients with generalised peritonitis complicating diverticulitis, but fear of anastomotic leakage often deters many surgeons from performing primary anastomosis (PA). Adding a diverting loop ileostomy (DI) after resection and PA decreases the rate of symptomatic anastomotic leakage.[1,2] Nevertheless, for many surgeons Hartmann's procedure (HP) still remains the favoured option in perforated diverticulitis, in spite of improvements in surgical technique, radiological intervention techniques, anaesthesia, advances in intensive care medicine and progress in the management of peritoneal sepsis.[3]

Besides high morbidity and mortality rates of HP performed in complicated diverticulitis, reversal of HP is also known to be associated with substantial morbidity (rate of anastomotic leakage up to 25%) and mortality (up to 14%).[4,5] This is one of the reasons that HP often results in a permanent colostomy. Only about half of patients have their colostomies closed after HP, but the literature is not uniform and is frequently based on heterogeneous pathologies.[5,6]

The object of this study was to assess differences in the rate of stomal reversal after HP and PA with DI and to evaluate factors associated with postreversal morbidity. The results are discussed in the context of primary surgery for acute perforated diverticulitis.

# Patients and methods

Clinical variables of all 291 consecutive patients who underwent emergency surgery for acute perforated sigmoid diverticulitis in the surgical units of the academic centre and four affiliated teaching hospitals in Rotterdam, The Netherlands (Erasmus Medical Centre, Ikazia Hospital, Medical Centre Rijnmond-Zuid (formerly St Clara Hospital and Zuider Hospital) and St Franciscus Hospital) between 1995 and 2005 were retrospectively studied. The in-hospital survivors were included in this study. Follow up was conducted until July 2007.

A total of 291 patients underwent emergency surgery because of acute perforated diverticulitis of who 83 died in the hospital.[2] Of the survivors, 139 had undergone HP, 64 patients underwent PA, of whom 19 received DI and 5 patients underwent suture repair. In all hospitals the decision to perform one or

the other procedure was left to the discretion of the surgeon on call. A computerised surgery registration was carried out for all patients admitted to and operated in the surgical departments of all five hospitals. All patients who underwent reversal of HP or DI could therefore be identified.
Prior to surgery all patients underwent colonoscopy or barium enema to evaluate the rectal stump or colorectal anastomosis. Although the indication for restoration of bowel continuity was set by a specialist colorectal surgeon, the actual operation was not necessary performed by him or her. Age, gender, American Society of Anaesthesiologist classification (ASA), severity of primary disease (Hinchey score),[7] interval between primary surgery and stoma reversal, postoperative morbidity and mortality, surgeon's experience in colorectal surgery, surgical procedure and type of anastomosis were studied.
Data are represented as mean (range) unless indicated otherwise. Comparisons between the two groups were made using the Mann-Whitney test for quantitative variables or graded outcomes and the Fisher's exact test for categorical data. Differences were considered significant at a two-tailed p-value less than 0.05.

# Results

## Reversal of Hartmann's procedure

A total of 63 patients (age 61 (23-85) years) who survived surgical treatment of acute perforated diverticulitis underwent HP reversal (45%) between February 1995 and November 2005. Patients' characteristics are mentioned in table 1. No differences in baseline patient characteristics were noted between the series from the different hospitals.
The mean delay between HP and its reversal was 9.1 (0.4-25) months. Reversal was performed by a specialist colorectal surgeon in 76% of cases. They performed a handsewn anastomosis in 60%, whereas noncolorectal surgeons did so in 53%. Reasons for not performing stomal reversal are shown in table 2.
The cumulative postoperative morbidity was 44%: 28 patients had one or more minor or major postoperative complications. In total, early surgical complications occurred in 22 patients (table 3). Early surgical complications seemed not to be related to the severity of primary disease (e.g. Hinchey score >II; p=0.57), delay after primary surgery (p=0.46), ASA classification (e.g. ASA>II; p=1), gender (p=0.43), age (p=0.56), experience of the performing surgeon (p=0.76), or type of anastomosis (p=0.60).

**Table 1.** Patients' characteristics, severity of previous disease and surgical procedure in patients who underwent restoration of bowel continuity

| | **Primary surgery** | |
|---|---|---|
| | **HP** | **PA+DI** |
| Number of patients | 139 | 19 |
| Reversal of stoma | 63 (45) | 14 (74) |
| **Patient characteristics** | | |
| Age in years (range) | 61 (23-85) | 63 (38-82) |
| Male/female | 35/26 | 6/8 |
| ASA classification | | |
| I/II | 40 (63) | 7 (50) |
| III/IV | 23 (37) | 7 (50) |
| **Primary disease** | | |
| Hinchey score (%) | | |
| I/II | 19 (30) | 3 (21) |
| III/IV | 44 (70) | 11 (79) |
| Delay between procedures in months (range) | 9.1 (0.4-25.8) | 3.9 (0.7-7.5) |
| **Surgical procedure** | | |
| Specialist colorectal surgeon | 48 (76) | 6 (43) |
| Noncolorectal surgeon | 15 (24) | 8 (57) |
| Midline laparotomy | 48 | -- |
| Laparoscopy | 3 | -- |
| Through stomal side | 1 | 13 |
| Handsewn anastomosis | 37 (59) | 8 (57) |
| Stapled anastomosis | 26 (41) | 6 (43) |
| Side-to-side/side-to-end/end-to-end | 15/31/17 | 9/1/4 |

*Values in parentheses are percentages unless indicated otherwise.*
*HP = Hartmann's procedure; PA = resection with primary anastomosis; DI = diverting loop ileostomy; ASA = American Society of Anesthesiologist classification.*

Complications concerning anastomotic healing, including leakage and anastomotic or presacral abcesses formation, were significantly less frequently observed when the operation was performed by a specialist colorectal surgeon (10 vs. 33%; p=0.049). Anastomotic leakage was significantly less frequent after a stapled anastomosis (p=0.037) as shown in table 4. Complications relating to the rectal stump were not observed.
Incisional hernia as a long-term surgical complication occurred in 17 patients (27%) and repair was carried out in 13 using a prosthetic mesh. Postoperative

mortality after HP reversal was 5%. One patient died of pneumonia and two patients died of severe abdominal sepsis after anastomotic leakage.

**Table 2.** Reasons why bowel continuity was not restored

| | **HP** | **PA+DI** |
|---|---|---|
| **No restoration** | 76 (55) | 5 (26) |
| Comorbidity | 20 | 1 |
| Age | 15 | 1 |
| Satisfied/refusal | 14 | -- |
| Rectal stump complications | 3 | -- |
| Diseased in follow up | 14 | 2 |
| On waiting list for reversal | 2 | -- |
| Unknown | 8 | 1 |

*Values in parentheses are percentages. HP = Hartmann's procedure; PA = resection with primary anastomosis; DI = diverting loop ileostomy.*

**Table 3.** Postoperative complications

| | **HP** | **PA+DI** |
|---|---|---|
| Restoration of bowel continuity | 63 (45) | 14 (74) |
| Early surgical complications | 22 (35) | 1 (7) |
| Anastomotic leakage/abcess | 10 (16) | -- |
| Abdominal abcess | 4 | -- |
| Stomal complications | 2 | |
| Evisceration | 1 | -- |
| Fistula formation | 1 | -- |
| Ileus | 2 | -- |
| Wound infection | 7 | 1 |
| Bleeding | 1 | -- |
| Late surgical complications | | |
| Incisional Hernia | 17 (27) | 1 (7) |
| Medical complications | 8 (13) | 0 |
| Pulmonary infection/insufficiency | 4 | -- |
| Lung embolus | 1 | -- |
| Cardiac decompensation | 1 | -- |
| Urinary tract infection | 3 | -- |
| Catheter-related bloodstream infection | 1 | -- |
| Mortality | 3 (5) | 0 |

*Values in parentheses are percentages. HP = Hartmann's procedure; PA = resection with primary anastomosis; DI = diverting loop ileostomy.*

## Reversal of loop ileostomy

A total of 14 patients (age 63 (38-82) years) underwent reversal of DI. This rate (14/19; 74%) was significantly higher compared with the reversal rate of HP (63/139; 45%) (p=0.027). The mean delay between primary surgery and reversal of DI was 3.9 (0.7-7.5) months. This was significantly shorter than for reversal of HP (p<0.001). Reversal was performed by a specialist colorectal surgeon in only 6 patients (HP vs. DI: 76% vs. 43%; p=0.022). A handsewn anastomosis was performed in 67%, whereas noncolorectal surgeons did so in 50%.

There was no postoperative mortality after closure of DI and the cumulative postoperative morbidity was 15%. One patient showed a wound infection and one patient developed an incisional hernia at the stomal site after 7 months. Postoperative morbidity after reversal of DI was significantly lower compared with HP reversal (p<0.001).

**Table 4.** Influence of patient's characteristics, severity of previous disease and surgical procedure on impaired anastomotic healing after reversal of Hartmann's procedure

| | **Complicated anastomotic healing** | **p** |
|---|---|---|
| Number of patients | 10/63 | |
| Age of patients (years) | | 0.77 NS |
| With leakage | 61 | |
| Without leakage | 60 | |
| Gender | | 1.0 NS |
| Male | 6/35 | |
| Female | 4/28 | |
| ASA classification | | 0.73 NS |
| ASA = II | 7/40 | |
| ASA > II | 3/23 | |
| Hinchey score | | 1.0 NS |
| Hinchey I+II | 3/19 | |
| Hinchey III+IV | 7/44 | |
| Surgeon's experience | | 0.049 |
| Specialist colorectal | 5/48 | |
| Noncolorectal | 5/15 | |
| Anastomosis | | 0.037 |
| Handsewn | 9/37 | |
| Stapled | 1/26 | |

*NS = Not Significant; ASA = American Society of Anesthesiologist classification.*

# Discussion

The prevalence of diverticulosis in westernised countries is rapidly increasing and so are its complications.[8] Nevertheless, perforated diverticulitis with generalised purulent and faecal peritonitis occurs less frequently. As emergency surgery for perforated diverticulitis may be associated with substantial morbidity and mortality optimizing of its treatment is important.[9] Although not proven in randomised controlled trials, improvement in surgical and radiological intervention techniques, anaesthesia and intensive care medicine might favour colonic resection and PA with or without DI, in emergency surgery for diverticular disease even when complicated by purulent or faecal peritonitis.[10-13] However fear of anastomotic leakage often deters many surgeons from performing PA. In spite of the fact that DI seems to decrease the number of anastomotic leakages,[4] HP is still performed most frequently in patients with diverticular peritonitis.[3]

Although HP is considered a two-stage procedure, the second stage (reversal of colostomy) is never performed in a large number of patients.[5,14] Restoration of bowel continuity after HP is technically challenging. It is associated with significant morbidity, with reported rates of anastomotic leakage of 4-16% and a mortality of up to 4%.[5] These rates can be as high as 25% and 14% after colostomy reversal in patients who had undergone HP for complicated diverticulitis.[4] Whereas reversal of DI can be performed as a local procedure at the stomal site, HP reversal usually requires a midline laparotomy, adhesiolysis and pelvic dissection to identify the rectal stump. It is therefore not surprising that the greater complexity of HP reversal results in more postoperative complications compared with DI.[15] This is one of the reasons why HP often results in a permanent end colostomy. These patients face the physical and psychological disadvantages associated with having a stoma.[16] The risk of permanent stoma after PA is less than that of HP.[10,12]

The present study, which exclusively analysed patients who underwent emergency surgery for acute colonic perforation due to diverticulitis, is in agreement with the above. The reversal rate of HP was only 45%. Reversal of HP was associated with high postoperative morbidity (44%) and even mortality (5%), which reflects the difficulty of the procedure in these patients. This is even more striking, considering that only patients in a good general condition were selected for stoma reversal. Patients with advanced age (n=15) and several comorbidities (n=20) were considered too high a risk to have the colostomy reversed. Despite being less frequently performed by colorectal surgeons, reversal of DI was performed more frequently than reversal of HP.

There was a shorter delay after primary surgery and there were fewer postoperative complications. All these were statistically significant.

Anastomotic leakage was observed in 16% after HP reversal, similar to the existing literature.[4,5,17] Although a specialist colorectal surgeon decided on the indication for restoration of continuity, not all patients were actually operated by specialist. When considering the surgeon as a risk factor, it has been shown that postoperative morbidity, mortality and outcome after (colorectal) surgery vary considerably among surgeons.[9,18,19] An experienced, trained colorectal surgeon familiar with this type of surgery has a better outcome than a general surgeon.[9,19] This study clearly showed that anastomotic leakage was observed more frequently when the reversal was not performed by a colorectal surgeon.

Since intra-abdominal infection often persists long after the diseased colon has been removed, timing of restoration of bowel continuity might influence anastomotic healing and the difficulty of the procedure.[19,20] Operative difficulty appears to be less after a delay of 15 weeks.[21] Of 63 HPs that were reversed restoration took place within 15 weeks in only four cases. Another important surgical consideration is the suggestion that resection for diverticular disease needs to extend into the upper rectum, rather than the distal sigmoid to ensure removal of the diseased bowel and to minimize recurrence.[22] Stapling has largely been preferred to handsewn anastomosis, because of technical difficulty and complexity of the procedure.[17] In this study handsewn anastomosis resulted in significantly more anastomotic leaks and abscess formation compared with stapled anastomosis. The reason for this is unclear. One hypothesis is that handsewn anastomosis were more likely to be performed above the level of the pelvic peritoneal reflection, and hence within inflamed bowel.

The fewer postoperative anastomotic leaks after stapled anastomosis may also be related to the fact that adhesiolysis is limited to the paracolic area when approaching the rectal stump which can be easily identified using a rigid sigmoidoscope or the circular stapler introduced per anum. When performing a handsewn anastomosis it is necessary to create enough space for safe suturing which extends the degree of adhesiolysis required. Whether or not anti-adhesion agents such as Seprafilm can reduce adhesion formation is still a matter of debate. It is possible that the incidence of adhesive small-bowel obstruction requiring reoperation might be lower after placement of Seprafilm compared with no placement,[23] but when Seprafilm is wrapped around an anastomosis, there is some evidence that anastomotic leakage might occur more frequently.[24]

When treating a patient with acute perforated diverticulitis it is essential to decide on the optimal operative strategy. This involves not only the type of primary surgery, but other aspects must be taken into consideration. Before

primary surgery a balance must be made between morbidity and mortality of the primary operation, stoma reversal operation, the risk of a permanent stoma and the quality of life. All these should take into account the individual characteristics of the patient and the severity of the disease. Morbidity and mortality after PA may be similar to HP,[4,9,25] but reversal of HP is associated with significantly higher postoperative morbidity. Thus PA (with or without DI) may be the procedure of choice for perforated diverticulitis when long-term outcomes are considered.[4,25] HP should only be reserved for patients with a high risk of complications regarding long-term implications. Furthermore in these patients HP should no longer be considered as a two-stage procedure. HP for treatment of perforated diverticulitis should only be performed, provided that restoration of continuity will never take place. HP must be considered as a one-stage procedure, resulting in a permanent colostomy.

Laparoscopic surgery may be a promising alternative strategy to open surgery to decrease the rate of HP in patients with perforated diverticulitis.[26] Generalised peritonitis can be treated by laparoscopic peritoneal lavage and the placement of abdominal drains. Definitive elective surgery can than take place subsequently in the form of laparoscopic resection and primary anastomosis. The number of studies reporting this approach is limited, however, and is mostly based on small numbers of patients. There may be higher rates of additional radiological interventions and conversion to an open procedure.[27]

In conclusion, restoration of bowel continuity in patients with perforated diverticulitis by resection with primary colorectal anastomosis and DI can easily be performed in almost all patients with very low postoperative morbidity. In contrast, restoration of bowel continuity in patients treated by HP is only feasible in less than half of patients. As HP reversal is a difficult operation with a high postoperative morbidity and even mortality, reversal when indicated should be performed by a specialist colorectal surgeon, preferably using a stapled anastomosis.

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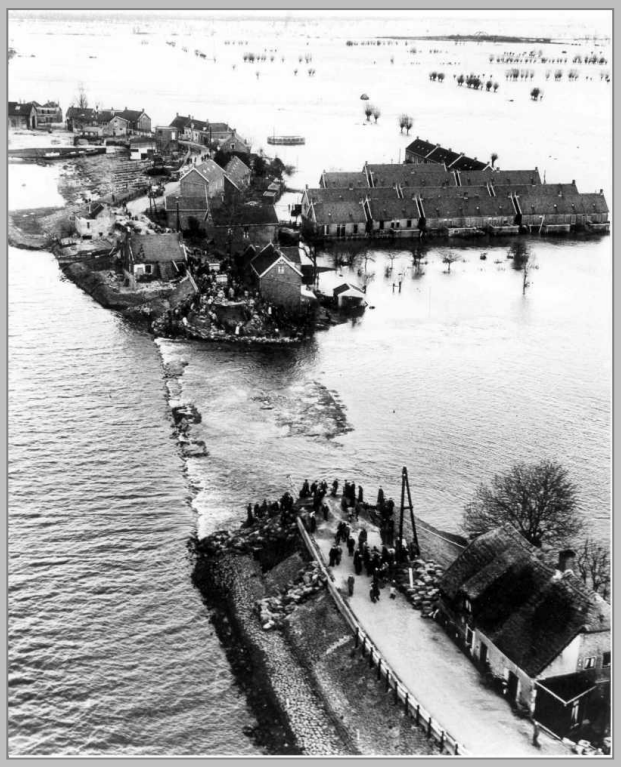
# 11

# Primary closure of the skin after stoma closure

## Management of wound infections is easy without (long-term) complications

*with*
N Vermulst
EJ Hazebroek
PPLO Coene
E van der Harst



Digestive Surgery 2006; 23(4): 255-258. Epub 2006 Aug 28.

# Abstract

Whether or not the skin can be primary closed after stoma closure is still debated in the existing literature. Therefore, this present study was undertaken to compare the complications and consequences between primary or delayed closure of the skin after stoma closure.

All consecutive stoma closures between January 2001 and August 2004 were included. In 25 patients (group I), the skin at stoma side was closed primarily. In 37 patients (group II), the skin was left open. Patient characteristics, comorbidity, medication use, hospital stay and long-term complications were recorded and retrospectively compared between the two groups.

In group I, wound infection rate was 36% vs. 5% in group II (p=0.005). Infected wounds were mostly found after ileostomy closure with primary closure of the skin (p=0.018). The occurrence of a wound infection was not related to the use of corticosteroids, diabetes mellitus, fistula formation, anastomotic leakage, or primary disease and did not lead to a prolonged hospital stay or an increased number of incisional hernias.

In our opinion, it is safe to close of the skin after stoma closure, but patients should be informed carefully about the advantages and disadvantages of this strategy, especially in case of ileostomy closure.

# Introduction

The construction of a temporary stoma is often integral to proper care of patients with complicated colorectal disease. Ideally, a temporary stoma lowers the operative risk, helps to prevent postoperative complications and mortality and is closed as soon as possible without complications.[1] Unfortunately, morbidity after ileostomy or colostomy closure is rather high, with wound infection as one of the most commonly reported complications, ranging in the literature from 2%-40%.[2-5] Although most infections pass without complications, a severer wound infection may result in increased morbidity, increased costs, prolonged hospital stay[2,6,7] and frequent outpatient follow-up, but also longer-term complications, such as incisional hernia.[8]
As it is considered a contaminated operation, it is important to determine the severity and frequency of wound infections after stoma closure. Besides, it is important to oversee the direct and long-term effects of a wound infection. The present study was undertaken to analyse the rate of wound infection and its (late) consequences in case of stoma closure and primary closure of the skin at the stoma side, compared to stoma closure and leaving the skin at the stoma side open for secondary healing.

# Patients and methods

All consecutive patients who had undergone bowel reconstruction and closure of their (loop) ileostomy or colostomy between January 2001 and August 2004 were included in this study. During this period, 22 colostomies and 40 ileostomies were closed. A handsewn anastomosis was performed in all cases.
Patients were divided into two groups, according to the operative management of choice, which was different between two participating surgeons. Group I contains patients in whom the skin was closed primarily after bowel reconstruction, as was the standard procedure for surgeon I. Group II contains patients in whom skin was left open for secondary healing (surgeon II). All patients received antibiotic prophylaxis during surgery. Preoperative bowel lavage was not performed in any patient.
Postoperative complications, wound infection in particular, in relation to primary closure of the skin, were documented both in the postoperative period and in outpatient follow-up and analysed retrospectively. Wound infection was defined as the presence of cellulitis, induration of the skin and/or purulent

discharge. Patient characteristics, comorbidity, medication use, hospital stay and long term complications were recorded. The postoperative results of procedures performed with or without primary closure of the skin after bowel reconstruction were compared.
Statistical analysis was made with the Fisher's exact test and the Mann-Whitney test. Differences were considered significant at $p<0.05$.

# Results

## Patients' characteristics

A total of 60 patients, in whom 62 stomas were closed, were included in this study. In 25 patients (group I), the skin was closed primarily, and in the remaining 37 cases (group II), the skin was left open. No differences were found between the two groups in age, male/female ratio, comorbidity and corticosteroids use (table 1).

**Table 1.** Patients' characteristics

| | Closure of skin (Group I) | Skin left open (Group II) |
|---|---|---|
| Number of stomas | 25 | 37 |
| Age[1] (years) | 57.3 ± 14.0 | 63.5 ± 11.4 |
| Male/female | 12/13 | 17/20 |
| Diabetes Mellitus | 6 | 2 |
| Cardiac/pulmonary comorbidity | 5 | 11 |
| Corticosteroids use | 3 | 4 |

*[1]Mean age ± SD.*

In 19 of 22 colostomy closures the skin was closed primarily. Of 40 ileostomy closures, primary closure of the skin was performed in 6 cases. Indications for primary surgery and the construction of a diverting stoma are presented in table 2.

**Table 2.** Indications for the construction of a stoma

| | Closure of skin (Group I) | Skin left open (Group II) |
|---|---|---|
| Cancer | 7 | 22 |
| Diverticular disease | 11 | 11 |
| Trauma | 2 | 1 |
| Ileus | 1 | 1 |
| Crohn's disease | 2 | 1 |
| Other | 2 | 1 |

## Wound infection

After bowel reconstruction, 9 patients of group I developed a wound infection, whereas in group II wound infection was found only twice (group I 36% vs. group II 5%; p=0.005 (table 3)). All wound infections in both groups occurred during hospital stay within 5 days (range 2-5). There were no differences in length of hospital stay (group I: 14±16 days vs. group II: 15±19 days; p= 0.20). Similar results were found when the patients with wound infection of group I were excluded.

The occurrence of a wound infection was not related to primary disease (diverticulitis, n=3; cancer, n=5; ileus, n=2; ischemia, n=1) or the use of corticosteroids (p= 0.76), diabetes mellitus (p= 0.81), fistula formation (p= 0.08), anastomotic leakage (p= 0.33) (table 3).

**Table 3.** Occurrence of wound infection after bowel reconstruction

| | Wound infection | No infection |
|---|---|---|
| Skin closed (group I) | 9 (36) | 16 (74) |
| Skin left open (group II) | 2 (5) | 35 (95) |
| Corticosteroids use | 1 (9) | 7 (14) |
| Diabetes mellitus | 1 (9) | 6 (12) |
| Anastomotic leakage | 1 (9) | 1 (2) |
| Fistula formation | 2 (18) | 1 (2) |
| Incisional hernia | 2 (18) | 4 (8) |

*Values in parentheses are percentages.*

Wound infections were managed by partial opening and drainage of the wound (n=8), conservative treatment with antibiotics (n=2) or both (n=1). Only 5 wounds in group I had some purulent discharge after opening it (20%). Wound infections did not lead to an increased number of incisional hernias, as shown in table 3 (p= 0.29).

### Type of Stoma

Group I contained significantly more colostomy closures compared to group II (19/25 vs. 3/37; p<0.001). Closure of a colostomy resulted in a wound infection in 6 cases. Wound infection after ileostomy closure was seen 5 times (27 vs. 13%; p=0.18). There were no significant differences in number of infected wounds after primary or delayed skin closure between colostomy or ileostomy closures.

Ileostomy closure and primary closure of the skin resulted in significantly more wound infections, as compared to delayed closure of skin in case of ileostomy closure (3/6 vs. 2/34; p=0.018). After colostomy closure there was no difference in infection rate whether or not the skin was closed primarily (6/19 vs. 0/3; p=0.53).

## Discussion

The management of the stoma side wound remains controversial. Multiple factors influencing the morbidity of stoma closure have been described, such as surgeon's experience, type of perioperative treatment and timing, obesity of the patient, smoking, corticosteroid use, primary disease and the operative technique.[2,9-12]

As closure of a stoma is considered a contaminated operation, it is suggested to leave the skin of the stoma wound open for secondary healing. It is believed that closure of the skin will lead to more wound infections,[2-5] which can lead to more late complications, such as incisional hernia. On the other hand, experienced technical skills and adequate antibiotic bowel preparation have lead to lower infection rates[9] and therefore primary closure of the skin could be safely performed, resulting in a decreased hospital stay.[2] A prospective study of Lahat et al.[5] comparing primary closure and delayed closure showed no advantages of the delayed closure of stoma side wounds concerning wound infection or hospital stay.

In our hospital, all patients received perioperative antibiotic prophylaxis. Bowel lavage was not performed. There was a significant difference in the

number of wound infections between primary closure of the skin and leaving the skin open for secondary healing after bowel reconstruction (36 vs. 5%). This complication rate is rather high, but comparable with those of other reports.[2-5] All infections occurred within five days and could be easily managed by partially opening the wound for controlled drainage and secondary healing and/or antibiotic treatment. Only 5 patients of group I had purulent discharge after treating the wound infection by opening the wound for drainage. The remainder were superficial infections without abscess formation. Antibiotics probably could have treated the latter, as occurred in 3 cases, instead of opening the wound for drainage. In other words, only 20% of the wounds that were closed primarily needed to be opened in order to treat postoperative wound infection with abscess formation.

The advantage of a noncomplicated procedure in which the skin at the stoma side is closed after bowel reconstruction is the presumed short outpatient follow-up for wound inspection. When the wound is left open for secondary healing, frequent wound inspection and professional supportive wound care at home is needed in some cases. It can take months for the skin at the stoma side to close and frequently an ugly scar is left that needs to be corrected sometimes. This was the mean reason why the closed skin was only partly opened in case of a wound infection. Besides this, the healed skin of the stoma closure side should be suitable to be reused in the future.

According to the existing literature, it is expected that colostomy closure is more likely to be associated with infected wounds than ileostomy closure.[13,14] In this study, colostomy closure indeed resulted in more postoperative wound infections, compared to ileostomy closure (27 vs. 13%), but this difference was not statistically significant. In contrast with Lahat et al.,[5] ileostomy closure with primary closure of the skin at the stoma side resulted in significant more wound infections compared to delayed closure of the skin. This difference was not found in case of colostomy closure. Although not proven, this phenomenon could probably be the result of micro leakage of small bowel contents in the wound before skin closure, as small bowel contents is thought to leak more easily compared to the more thickened large bowel contents.

The occurrence of a wound infection is suggested to be associated with longer hospital stay and therefore increased costs.[5,6] In our study, hospital stay between the two groups did not differ significantly. Besides, it seems that the presence of a wound infection did not lead to a longer hospital stay. Hospital stay in this study was rather long. This may be due to the fact that preventive stomas are usually selected for older patients. However, even among older patients, with the increasing emphasis on limiting the duration of admission and with the promotion of fast-track colorectal surgery, hospital stay will

certainly decrease within the nearby future. If the fast-track strategy is the strategy of choice in a hospital, early discharge and leaving the skin open could well be defended as proper treatment, since late-onset of abscess formation after discharge might be prevented in this case. It is presumed that in this case long-term outpatient follow-up for wound control is needed, especially in older patients. Primary closure of the skin might prevent this outpatient follow-up and hence patients can be relieved of intensive wound care. Therefore, patients should be informed carefully about the advantages and disadvantages of primary closure of the skin after stoma closure.

Mileski et al.[2] found a strong association between the use of corticosteroids and the number of complications after stoma closure. In our study, patients who were steroid dependent did not have more wound infections (or other complications) compared to the other patients. Closure of the skin was not associated with a higher number of other complications, such as incisional hernia, anastomotic leakage and fistula formation.

In conclusion, in our opinion, it is safe to close the skin after stoma closure, especially if the duration of admission is long enough to encounter its main complication, e.g. wound infection. Although the rate of wound infection is rather high, especially in case of ileostomy closure, management of this complication is easy without (long-term) complications.

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# Henri Albert Charles Antoine Hartmann

(16-6-1860 – 1-1-1952)

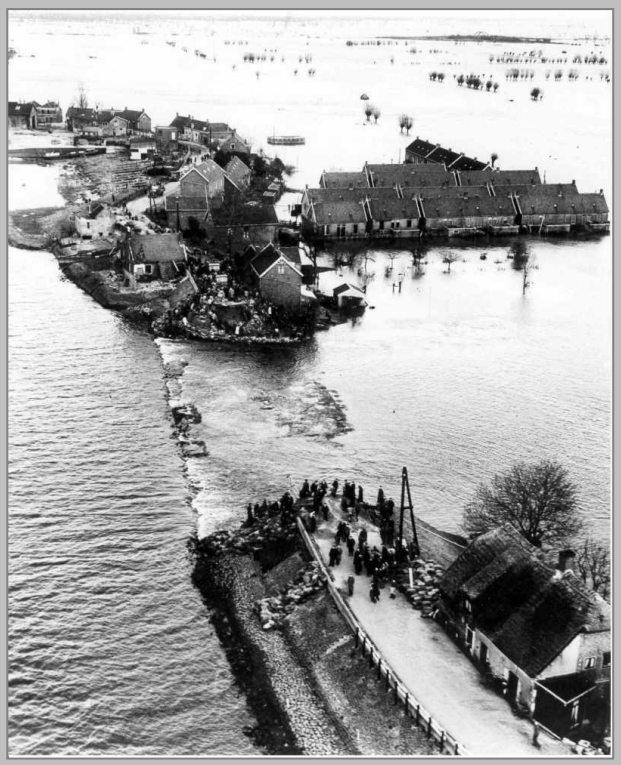
*Henri Albert Hartmann devised the two-stage colectomy, in which resection of the sigmoid in combination with an end-colostomy is performed.*

Henri Albert Hartmann studied medicine at the University of Paris, where he graduated in 1882. He worked at l'Hôpital Lariboisière and later at Hôpital Bichat as an assistant professor, assistant director and finally professor and chairman of surgery. He became chief of surgery at l'Hôtel-Dieu in 1914.
He was a member and later president of the Académie de Médecine. He was president of the Congress of Surgery, grand officer of the Legion d'Honneur and was elected to the Academie des Sciences. He was one of the founders of the French League against Cancer.

# 12

# Reversal of Hartmann's procedure through the stomal side: a new even more minimal invasive technique

*with*
W Vrijland
GHH Mannaerts



Surgical Endoscopy 2008; 22(10): 2319-2322. Epub 2008 Jul 12.

Presented at:
Annual meeting of the Dutch Society for Endoscopic Surgery 2008, Rotterdam (27-28 mar 2008)

# Abstract

Several minimal invasive, mainly laparoscopic-assisted, techniques for reversal of Hartmann's procedure (HP) have been published. The purpose of this pilot study was to assess a minimal invasive procedure through the stomal site that may compare favourably with open of laparoscopic-assisted procedures in terms of operative time, hospital stay and postoperative complications.

HP reversal through the stomal side was attempted in 13 consecutive patients. Lysis of intra-abdominal adhesions was done manually through an incision at the formal stoma side, without direct vision, between thumb and index finger. The rectal stump was identified intra-abdominally using a transanal rigid cub. A manually controlled stapled end-to-end colorectal anastomosis was created.

Mean duration of operation was 81 min (range 58-109 min); mean hospital stay was 4.2 days (range 2-7 days). In two patients the procedure was converted because of strong adhesions in the lower pelvic cavity around the rectal stump that could not be lysed manually safely. No complications occurred in the patients, in whom reversal was completely done through the stomal side,

In our opinion, restoration of intestinal continuity through the stomal side after HP is a feasible operation, without need for additional incisions. In the hands of a specialist gastrointestinal surgeon, this technique can be attempted in all patients, as conversion to a laparoscopic-assisted or an open procedure can be performed when necessary.

# Introduction

Restoration of bowel continuity after Hartmann's procedure (HP) is a technically challenging operation, associated with significant morbidity, with reported anastomotic leak rates of 4-16% and a mortality of up to 4%.[1] These rates can be as high as 30% and 14%, respectively, after stoma reversal in patients who had undergone HP for complicated diverticulitis.[2,3] This is the main reason why approximately 40% of the patients after HP will never undergo restoration of digestive continuity.[1] Besides risk factors such as the patients characteristic's[4,5] and disease aetiology[1,2] that cannot be altered, the most important risk factor for morbidity is the technique used for restoration of bowel continuity.[6-8]

Although many technical variations are described for reversal of HP, the optimal technique is still a matter of debate. Minimal invasive techniques (laparoscopic- or endoscopic-assisted), although lasting longer and technically challenging, seem to have advantages regarding less postoperative pain and disability, shorter hospital stay, and better cosmetics.[8-11] However, also in laparoscopic HP reversal all adhesions in the midline and pelvis need to be loosened. This may increase morbidity, i.e., postoperative paralytic ileus and small bowel lacerations.

This study describes a new even less invasive technique for reversal of HP through the stomal site, without the need for laparoscopic (or endoscopic) assistance. The feasibility of this technique and its outcome in terms of operative time and morbidity was assessed in a consecutive series of 13 patients.

# Patients and methods

Since August 2005 a total of 13 consecutive patients underwent reversal of HP through the stomal side at the Sint Franciscus Gasthuis Rotterdam, The Netherlands. All procedures were performed by one consultant surgeon (G.H.H.M.). Patients' data and results were recorded prospectively. The only exclusion criterion for trans-stomal restoration of bowel continuity was an accompanying abdominal wall hernia that needed correction with a mesh.

## Surgical technique

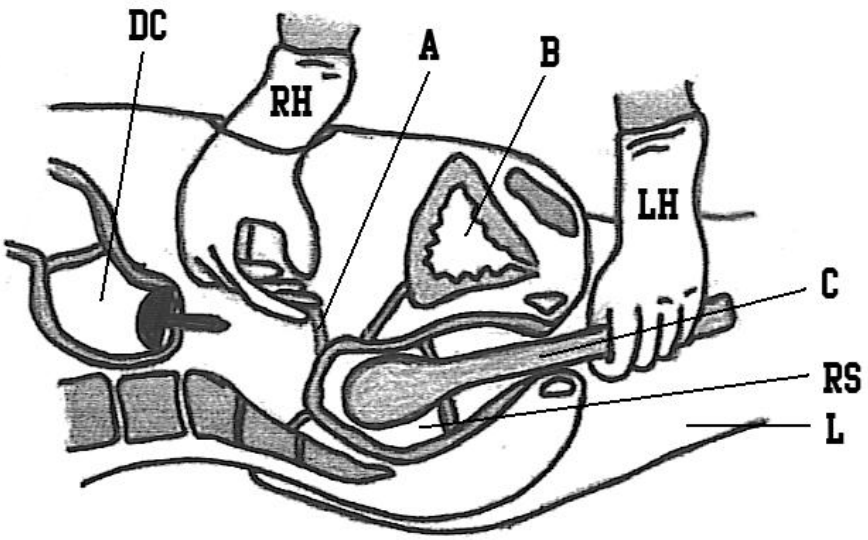
Preoperative bowel preparation consists out of an anal clysma. Broad-spectrum antibiotic prophylaxes (1000 mg Kefzol®/500 mg Flagyl®) are administered before surgery. Patients are placed in the lithotomy position and the first surgeon stands at the left of the patient throughout the operation.

First the colostomy is closed with a running suture in order to continue with a clean operation. Then the patient is scrubbed with Povidon® and the surgeon switches gloves. The stoma is released, taking a small amount of surrounding skin with it. The length of the incision at the stomal side must be just large enough for the surgeon to put his right hand intra-abdominally. The descending colon stump is brought outside the abdomen and adhesions to the left colon are carefully loosened by sharp dissection as long as it is visible. Further loosening of adhesions of the left colon is performed manually with index finger or between thumb and index finger in order to create enough length of the descending colon to reach the pelvic cavity. To achieve this, mobilization of the splenic flexure is seldom necessary, even if this has not been performed at primary surgery. If enough bowel length is created, clamps are placed at the end. The very distal part of the bowel with its attached skin is removed. An anvil of a circular stapler (31 mm) is placed intraluminal. The stump is closed using a linear stapler. The tip of the stapler anvil is brought through the colon wall just near the staple line and tied by a purse-string suture. This bowel segment including anvil is brought intra-abdominally.

Next the surgeon's right hand is placed intra-abdominally through the former stoma defect. Adhesions in the pathway to the distal (rectosigmoid) stump are gently loosened in a careful digital blind fashion. The left hand is used to introduce a rigid club transanally to identify the rectal stump. The rectal stump is gently manually lysed from small bowel adhesions by the surgeon's right hand (figure 1). Consecutively the circular stapler is introduced into the rectal stump. The pin of the circular stapler is passed through the rectal wall and then removed under digital control. Then the anvil is attached to the tip of the circular stapler. Before firing the circular stapler the proximal bowel segment is manually checked for rotation and interposition of small bowel, abdominal fat or the vagina wall. After firing the stapler, the integrity of the doughnuts of the functional end-to-end anastomosis is inspected. The stoma opening is closed with resorbable sutures (Vicryl 3.0) as well as the skin (Monocryl 3.0).

In case of firm adhesions that cannot be lysed manually the operation is converted to a laparoscopic-assisted procedure. However, when the adhesions are very firm, direct conversion to an open (laparotomy) procedure is executed.

**Figure 1.** Manual lysis of adhesions at the tip of the rectal stump, which was identified using a rigid club. Previously the anvil of a circular stapler was placed intraluminal of the descending colon.




*DC, descending colon with anvil; RH, right hand; A, adhesions; B, bladder; LH, left hand; C, rigid club; RS, rectal stump; L, left leg.*

# Results

Patient characteristics are listed in table 1. Of the 13 patients that were assigned for reversal of Hartmann's procedure through the stomal site, two needed direct conversion to an open procedure (laparotomy) due to very firm adhesions in the pelvis that were not even tried to be loosened manually (15% conversion rate). One patient who underwent direct conversion to an open procedure because of firm adhesions not suitable for manual lysis developed an anastomotic leakage.

In one patient the anastomosis was inspected using a 30º telescope via the incision at the stomal side. No additional incisions were necessary in the 11 patients in whom reversal was accomplished through the stomal side. They all were without postoperative complications and could leave the hospital within 1 week (table 2).

In long-term follow-up one patient developed an incisional hernia at the stomal site 12 months postoperatively, which did not need surgical correction. Overall the patients showed quick recovery and were very content with the aesthetic outcome.

**Table 1.** Patients' characteristics (n=13)

| Parameter | |
|---|---|
| Sex, n (%) | |
| Male | 5 (38) |
| Female | 8 (62) |
| Mean age, years (range) | 56 (35-81) |
| Male | 55 (35-81) |
| Female | 56 (36-81) |
| Body mass index (kg/m²) | 27.2 (21.8-36.6) |
| American Society of Anesthesiologists score, n | |
| I | 3 |
| II | 5 |
| >II | 5 |
| Indication for initial surgery, n | |
| Iatrogenic bowel perforation | 3 |
| Intestinal obstruction due to complicated diverticulitis | 3 |
| Perforated diverticulitis | |
| Without peritonitis (Hinchey 1+2) | 3 |
| With generalized peritonitis (Hinchey 3+4) | 4 |
| Median delay of reversal, months (range) | 7.1 (3.5-11.0) |

**Table 2.** Results after reversal of Hartmann's procedure through the stomal side

| Number of transstomal completed patients | Mean operation time, minutes (range) | Mean hospital stay, days (range) | Length of incision, cm (range) | Number of anastomo-tic leaks, n |
|---|---|---|---|---|
| (n=11) | 81 (58-109) | 4.2 (2-7) | 9.2 (7.5-11) | 0 |

# Discussion

The standard surgical approach to the restoration of continuity has been by laparotomy. Minimally invasive surgery has gained popularity, because of less

postoperative pain and disability, shorter postoperative hospital stay, better cosmetics, and a faster return to work.[9-11] By significantly reducing the operative trauma, reports have shown decreased postoperative recovery time and surgically related stress.[8]

Our even more minimal invasive blind manual trans-stomal technique is a feasible technique and supposed to have several advantages, such as shorter operation time, less need for adhesiolysis, and faster recovery, compared with open and even with laparoscopic-assisted procedures. Moreover, HP reversal through the stomal side has the advantage over laparoscopic-assisted HP reversal that no additional incisions have to be made to place the trocars, which is supposed to improve aesthetics.

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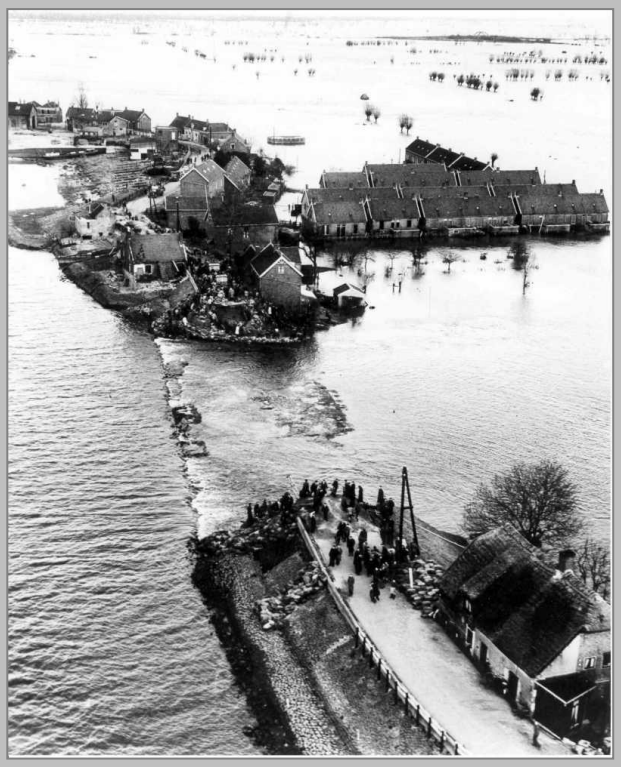
# 13

# Reversal of Hartmann's procedure after perforated diverticulitis through the stomal side without additional incisions: the SIR-procedure

*with*
JWA Leijtens
GHH Mannaerts



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# Abstract

Reversal of Hartmann's procedure (HP) is a complex operation and only performed in 50-60% of the patients. Stomal incision reversal (SIR), a new minimally invasive procedure for HP reversal, was assessed and compared to the standard surgical approach.

Sixteen patients who had undergone HP for perforated diverticulitis underwent HP reversal by SIR. The only incision in SIR is the one to release the end colostomy. Intra-abdominal adhesiolysis is done manually. A stapled end-to-end colorectal anastomosis is created. The 16 patients who underwent SIR were compared with 32 control patients who were matched according gender, age, American Society of Anesthesiologist (ASA) classification and Hinchey stage.

The operation time was shorter after SIR than after reversal by laparotomy (75 min (58-208) vs. 141 min (85-276); $p<0.001$). Patients after SIR had a shorter hospital stay than patients after laparotomy (4 days (2-22) vs. 9 days (4-64); $p<0.001$). Numbers of total postoperative surgical complications (early and late) were not different ($p=0.13$). Anastomotic leakage rate was similar in both groups (6%). Conversion rate in the SIR group was 19% (n=3).

SIR compared favourably towards HP reversal by laparotomy in terms of operation time and hospital stay, without increasing the number of postoperative complications.

# Introduction

In 1923, Henri Albert Hartmann[1] described a new surgical procedure for the treatment of rectosigmoid carcinoma. Hartmann's procedure (HP) consists of a colonic resection with an end colostomy and closed rectal pouch. The procedure was designed to reduce haemorrhage during the perineal stage of the operation. He advocated that patients should not undergo restoration of bowel continuity, because of the difficulty of this procedure.

Today, the HP is considered a two-stage procedure and often used in the treatment of perforated diverticulitis.[2] Nevertheless, the second stage (reversal of the end colostomy) is only performed in 50-60% of the cases,[3] since restoration of bowel continuity after HP is still considered as a technically challenging operation, associated with significant morbidity, with reported anastomotic leak rates of 4-16% and a mortality of up to 4%.[4,5] These rates can be as high as 30% and 14%, respectively, after stoma reversal in patients who had undergone HP for complicated diverticulitis.[6,7]

The standard surgical approach to the restoration of continuity has been by laparotomy. In this procedure a large midline incision is used, next to an incision for releasing the end colostomy. Minimally invasive surgery has gained popularity, because of less postoperative pain and disability, a shorter postoperative hospital stay, better cosmetics and a more rapid return to work.[8-10] However, also in laparoscopic HP reversal all adhesions in the midline and pelvis need to be dissected. This may increase morbidity: i.e. postoperative paralytic ileus and small bowel lacerations.

Previously we described a new minimally invasive method of Hartmann's reversal performed through the stomal site.[11] As no additional incisions have to be made besides the one at the stomal side, we have called this procedure 'stomal incision reversal'(SIR). SIR of HP has the advantage that the amount of adhesiolysis is limited to the paracolic pathway to the rectal stump. By significantly reducing the operative trauma, reports have shown decreased postoperative recovery time and surgically related stress.[12]

The object of this study was to assess outcome after restoration of bowel continuity after HP in terms of operative time, hospital stay and morbidity. The outcome was prospectively assessed in a consecutive series of 16 patients that underwent SIR and was compared to an historic age-, sex-, American Society of Anesthesiologist (ASA)- and Hinchey stage-matched control group of 32 patients that underwent HP reversal by laparotomy. The results are discussed in the context of primary surgery for acute perforated diverticulitis.

## Patients and methods

Between August 2005 and June 2009 a total of 22 consecutive patients underwent SIR at the Sint Franciscus Hospital of Rotterdam and the Laurentius Hospital of Roermond, The Netherlands. Of these patients, 16 had undergone prior HP because of perforated diverticulitis. Data of these 16 patients and results of the procedure were recorded prospectively and compared with 32 well-matched controls (1:2). Selecting two patients who had undergone HP reversal by laparotomy for every single SIR patient formed the control group. These patients were selected from a historic group of patients treated for perforated diverticulitis and who had subsequently undergone HP reversal by laparotomy. Data of this group was analyzed retrospectively. The control group was matched in terms of the following matching criteria: gender, age, ASA classification and severity of primary disease (Hinchey stage[13]). HP reversal in the patients of the control group was performed between February 1995 and October 2006. All 48 patients had undergone emergency HP to treat complicated perforated diverticulitis.

All SIRs were performed by two consultant surgeons (G.M. and J.L.), both experienced in colorectal and minimally invasive surgery. Prior to surgery the patients underwent colonoscopy to evaluate the descending colon and rectal stump. The indication for restoration of bowel continuity was set by a specialist colorectal surgeon. The only exclusion criterion for SIR was an accompanying symptomatic abdominal wall hernia that needed (open) correction. A brief description of the surgical procedure of SIR is stated below.[11]

After the stoma is released, adhesions to the left colon are loosened through the stoma side by sharp dissection to create enough length of the descending colon to reach the pelvic cavity. In a similar manner adhesions in the pathway to the distal (rectosigmoid) stump are loosened. Next, the surgeon's right hand placed intra-abdominally through the former stoma defect. The rectal stump is identified using an anal rigid club and gently cleared from adhesions. In case of firm adhesions that cannot be lysed manually in a safe manner the operation is converted to an open (laparotomy) procedure. An anvil of the circular stapler is placed intraluminally in the descending colon, consecutively the circular stapler is introduced into the rectal stump. Finally a manually controlled, stapled end-to-end colorectal anastomosis is performed and the stapler doughnuts are checked. Finally, to make sure, a laparoscope is introduced through the stoma side to exclude iatrogenic small bowel lesions.

The outcomes of patients that underwent SIR and HP reversal by laparotomy were compared. Primary endpoints were operation time and hospital stay.

Secondary endpoints were the incidence of postoperative complications and the time period between primary procedure and HP reversal. Some data of 8 patients who underwent SIR has been used in a feasibility study before.[11] Data are represented as median (range) unless indicated otherwise. Comparisons between the two groups were made with Mann-Whitney U test for quantitative variables or graded outcomes and the [chi]² test for categorical data. Differences were considered significant at a 2-tailed p value less than 0.05.

# Results

Of the 22 patients that had undergone SIR, the procedure was successfully performed in 16 cases (72%). Of the 22 patients 5 patients underwent conversion to an open procedure (because of firm adhesions (n=2), doubt about the quality of doughnuts (n=2) or iatrogenic small bowel laceration during stomal release (n=1)) and 1 patient, who had undergone HP because of a colovesical fistula, developed a recurrent fistula after HP reversal by SIR. One patient, who underwent conversion to an open HP reversal procedure, developed an anastomotic leakage. None of the patients in which SIR was successfully performed without conversion developed an anastomotic leakage.
Of the 22 patients, 16 had undergone HP because of perforated diverticulitis in the past. These 16 patients were included in this study. Characteristics of the patients after HP for perforated diverticulitis, who underwent restoration of bowel continuity by SIR (n=16) and by laparotomy (n=32) are listed in table 1. Both groups were matched and hence not different concerning gender, age, ASA classification and Hinchey stage during initial surgery for perforated diverticulitis.
Delay between HP for complicated perforated diverticulitis and its reversal was also not different between both groups. Postoperative follow up of the laparotomy group was significantly longer than follow up of the SIR group ($p<0.001$), as the first form an older cohort.
The median operation time was significantly shorter when performing SIR compared to HP reversal by laparotomy (table 1). Besides, patients after SIR had a shorter hospital stay than patients after laparotomy.

**Table 1.** Patients' characteristics, severity of previous disease and surgical procedure in patients who underwent restoration of bowel continuity

| | Type of HP reversal | | |
|---|---|---|---|
| | SIR | laparotomy | p |
| *Patient characteristics* | | | |
| Male/female | 8/8 | 16/16 | 1 |
| Age, years (range) | 54 (35-81) | 57 (32-85) | 0.72 |
| ASA classification | | | 0.67 |
| I/II | 11 (69) | 26 (81) | |
| III/IV | 5 (31) | 6 (19) | |
| Hinchey classification | | | 0.20 |
| I/II | 7 (44) | 11 (34) | |
| III/IV | 9 (56) | 21 (66) | |
| *Surgical procedure* | | | |
| Conversion to laparotomy | 3 (19) | -- | -- |
| Operation time, minutes (range) | 75 (58-208) | 141 (85-276) | <0.001 |
| Postoperative surgical complications | 4 (25) | 16 (50) | 0.13 |
| *Follow-up* | | | |
| Delay between procedures, months (range) | 5.7 (2.9-18.3) | 8.7 (0.4-19.9) | 0.18 |
| Postoperative hospital stay, days (range) | 4 (2-22) | 9 (4-64) | <0.001 |
| Postoperative follow up, months (range) | 18 (1.6-48) | 69 (2.1-136) | <0.001 |

*Values in parentheses are percentages unless indicated otherwise. HP = Hartmann's procedure; SIR = Stomal incision reversal; ASA = American Society of Anaesthesiologist.*

The numbers of total postoperative surgical complications (early and late) were not different between both groups (table 2; SIR 25 vs. laparotomy 50%; p=0.13). Midline incisional hernia as a long-term surgical complication was observed in 8 patients after laparotomy. Correction took place in 6 patients using a prosthetic mesh. The other two patients could be treated conservatively without surgical correction. Only one patient after SIR developed an incisional hernia at the former stoma defect 12 months postoperatively, which did not need surgical correction.

Of the 16 patients that were assigned for HP reversal by SIR, 3 needed conversion to an open procedure (laparotomy) due to very firm adhesions at the pelvic side (n=1) and doubt about the quality of doughnuts after performing a colorectal anastomosis using the circular stapler device (n=2). The postoperative course of these 2 patients was uncomplicated. The patient who underwent direct conversion to an open procedure because of firm

adhesions not suitable for manual lysis developed an anastomotic leakage. This patient underwent a reoperation with abdominal lavage of the abdominal cavity, placement of drains in the pelvic cavity and the performance of a diverting loop transversostomy. The anastomotic leakage rate was similar in both groups (6%). All patients with anastomotic leakage underwent reoperations. One patient died after HP reversal by laparotomy due to ongoing abdominal sepsis after anastomotic leakage.
For completeness' sake, the results of the remainder 6 patients who had undergone SIR were comparable to the 16 patients after perforated diverticulitis that underwent SIR and were described in this study.

**Table 2.** Postoperative complications after restoration of bowel continuity

| | **Type of HP reversal** | | |
|---|---|---|---|
| | **SIR** | **laparotomy** | **p** |
| Total surgical complications | 4 (25) | 16 (50) | 0.13 |
| Early surgical complications | 3 (19) | 8 (25) | 0.73 |
| Anastomotic leakage/abscess | 1 (6) | 2 (6) | 1 |
| Ileus | -- | 1 (3) | 1 |
| Wound infection | 1 (6) | 5 (16) | 0.65 |
| Acute urine retention | 1 (6) | -- | 0.33 |
| Late surgical complications | 1 (6) | 8(25) | 0.24 |
| Incisional Hernia | 1 (6) | 8 (25) | 0.24 |
| Medical complications | 0 | 2 (6) | 0.55 |
| Pulmonary infection | -- | 1 (3) | 1 |
| Cardiac decompensation | -- | 1 (3) | 1 |
| Mortality | 0 | 1 (3) | 1 |

*Values in parentheses are percentages.*
*HP = Hartmann's procedure; SIR = Stomal incision reversal.*

## Discussion

There is growing evidence that patients with perforated diverticulitis can be treated with a single-stage procedure, but HP is still performed most frequently in this category of patients.[2,7,14,15] Although HP is considered a two-

stage procedure, the second stage (reversal of colostomy) will never be performed in a large number of patients.[3,6] The main reason for this is that restoration of bowel continuity after HP is a technically challenging operation in this group with predominantly older patients: The higher the complexity of Hartmann's reversal, the higher the risk on peri- and postoperative complications. HP reversal in patients after perforated diverticulitis is known to be a very complex operation.[6,7]

Although minimally invasive surgery has shown to be related with less postoperative pain, better cosmetics, a decreased postoperative recovery time, a shorter postoperative hospital stay and a more rapid return to work,[8,10,12] the standard surgical approach to the restoration of continuity after HP still remains by midline laparotomy. In the present study, the results of a new minimally invasive HP reversal procedure, SIR, was found to have better results compared to the standard in patients after perforated diverticulitis.

A similar technique like SIR, but laparoscopically-assisted, has been published before.[11,16] In contrast with other laparoscopic HP reversal procedures, SIR was found to have a shorter operation time compared to HP reversal by laparotomy. The postoperative hospital stay was comparable with those reported after laparoscopic-assisted reversals of HP,[8,10,17] but much shorter than after HP reversal by laparotomy (this study). Besides, as no additional incisions had to be made in order to place trocars, the SIR supposes to improve aesthetics.

With all new procedures, but especially in SIR in which a part of the procedure is done without direct vision, the main question is if it is a safe procedure. Intra-abdominal adhesions are manually lysed by crushing them between the thumb en the index finger. In extensive adhesiolysis there is a theoretical risk of small bowel lacerations and postoperative paralytic ileus, due to contusion of the small bowel and intra-abdominal blood loss. The amount of adhesions that needs to be lysed during SIR is limited compared to HP reversal by laparotomy, because only adhesiolysis within the paracolic pathway to the rectal stump is needed. These adhesions are generally found to be very loose as prior resection has been performed in this area. Only the adhesions at the rectal stump, that needs to be lysed, can be firm. As the need for adhesiolysis is limited, the chance of small bowel lacerations is lowered. Nevertheless, it remains a delicate manoeuvre, preferably performed by a specialist gastrointestinal surgeon, especially in patients after perforated diverticulitis wherein HP reversal can be very difficult.[6,7] In the present study no small bowel laceration, major bleeding or postoperative ileus was observed after SIR.

The smaller extent of the surgical procedure is probably the main reason why hospital stay was shorter after SIR than after HP reversal by laparotomy. The

surgical wound after SIR is relatively small and intra-abdominal adhesiolysis is limited, resulting in less postoperative discomfort en probably a faster discharge from the hospital. But when assessing the difference in hospital stay, one must keep in mind that the post operative management has been changed radically during the last years which might also influence hospital stay. For instance, half of the HP reversals of the control group were performed before 2002.

Other postoperative complications, including anastomotic leaks (6%), were not different between both groups and are in comparison with the existing literature.[4-7,18,19] In the long term, more incisional hernias were observed after HP reversal by laparotomy. All incisional hernias after laparotomy were situated in the midline. Obviously, this was not observed after SIR, as in this procedure a laparotomy is withheld. This was the reason why an accompanying symptomatic abdominal wall hernia was seen as a relative contraindication for SIR. In case of HP reversal with accompanying abdominal wall correction surgery by laparoscopy or laparotomy is advised. Nevertheless, the difference in number of incisional hernias was not significant and probably related with the longer follow-up of the laparotomy group. This longer follow-up is a result of the used long time period in which the patients underwent HP reversal by laparotomy. It is know that the reversal rate of patients after perforated diverticulitis is low.[3,6] Therefore, it was necessary to use such a long time period in order to be able to form an appropriate case-matched control group.

In HP reversal SIR seemed to be a fast and safe procedure compared to the standard surgical approach by laparotomy. Nevertheless, one must always be cautious and gentle during manual adhesiolysis. To be sure the operative area is checked by laparoscopic view through the stoma side at the end of the procedure. When in doubt, one must not hesitate to convert towards open surgery or laparoscopic assistance.

In our experience, when adhesions are very firm it is better to convert directly to an open procedure instead of a laparoscopically attempt. In the present study conversion was performed in 3 patients. In two of them the consulting surgeon had his doubts about the integrity of the anastomotic doughnuts after firing the circular stapler device. After inspection during mini-laparotomy the anastomosis was found to be sufficient in both patients. The third patient needed conversion to laparotomy because of firm adhesions that could not be lysed manually without direct vision. The conversion rate of 19% in this small series is comparable to the reported 9-22% conversion rate after laparoscopic-assisted reversal of HP.[8,10,17] Besides, it is likely that a learning curve is involved and the conversion rate will be lowered with more experience in SIR.

In conclusion, in patients who underwent HP for perforated diverticulitis, restoration of bowel continuity by SIR compared favourably towards HP reversal by laparotomy in terms of operation time and hospital stay, without increasing the number of postoperative complications. SIR can be considered a good and safe alternative in all patients, as conversion to laparotomy can be easily performed when necessary.

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# Johan Frederik Lange

(22-7-1953 – present)

*Johan Frederik Lange is the initiator and promoter of the research that has led to this thesis.*

Johan Lange studied medicine at the Rotterdam Medical School, which became later the Erasmus University of Rotterdam, where he graduated in 1979. He completed his traineeship in surgery at the St. Clara Hospital in 1985. He worked as an assistant surgeon for two years in Hôpital Paul Brousse of Paris, before he returned to the St. Clara Hospital of Rotterdam to work as a specialised gastrointestinal and laparoscopic surgeon. From 1999 he participated at the research department of the Rotterdam Erasmus Medical Center. In 2005 he became professor in surgery and training director of the Erasmus University Medical Center. He is the chairman of the commission of patient safety of the Dutch Society of Surgery and one of the founders of the Dutch Diverticular Disease Collaborative Study Group.

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## Summary and general discussion

# Summary

Diverticular disease is one of the most common diseases related to the gastro-intestinal tract requiring in-hospital treatment in Western countries. Nevertheless, controversies persist about the optimal treatment strategies of the different stages of diverticulitis. To elucidate this problem three randomized clinical trials that have evolved under the auspices of the Dutch Diverticular Disease Collaborative Study Group (3D-study group) have started in 2010. The controversies in current treatment strategies of diverticular disease of the colon and the importance of the clinical trials are discussed in **chapter 2**.

In every disease it is at least preferably to understand the aetiology of the disease in order to develop its optimal treatment. For prevention strategies knowledge about its aetiology is a must. The pathophysiology of diverticular disease and its complications, like perforation, seems to be a result of a complex interaction between colonic structure, motility and diet, possible genetic influences, the coexistence of other bowel diseases and the impact of medicine use. All this is discussed in **chapter 3**. Unfortunately, hard evidence in the pathophysiology of diverticulitis and perforation is conflicting in present literature or lacking at all. The lack of knowledge makes it difficult to develop prevention strategies of this disease. Hence there is a need for further good quality epidemiological research to identify risk factors in the development of diverticulosis and diverticulitis. The question remains if it is feasible to evolve such an observational study, as it probably requires a large population and many years of follow up.

Perforated diverticulitis, as the most severe stage of diverticular disease, is only observed in about 2% of cases. The importance of this stage of disease is represented by its high morbidity and mortality rates. Regardless of selected surgical strategy perforated diverticulitis is the most common benign cause of mortality in surgery after ruptured abdominal aortic aneurysm. The most commonly performed surgical procedure in perforated diverticulitis is Hartmann's procedure (HP), originally developed for rectal carcinoma, in which the affected sigmoid is removed with the establishment of end colostomy. Sigmoid resection with primary anastomosis (PA), in which end colostomy is avoided, is an alternative to HP. Fear for anastomotic leakage often deters surgeons to perform PA. **Chapters 4 and 5** discuss the factors related to postoperative short-term outcome after perforated diverticulitis. Outcome was mainly influenced by the severity of the disease, indicated by the Mannheim Peritonitis Index and Hinchey's classification, the condition of the patient, indicated by the age and American Society of Anesthesiologist

classification (ASA), and the attendance of a surgeon specialized in gastrointestinal or colorectal surgery during the operation. The mean postoperative mortality was almost 29% (83 of 291 patients), ranging from 23% in Hinchey I patients up to 50% in Hinchey IV patients. Patients younger than 50 years of age had a mortality rate of 7%, whereas 38% of the patients older than 70 year died. The same mortality rates were found in patients with ASA I and ASA≥ 3 (6 and 40%, respectively). The type of surgery was not significantly related to postoperative mortality, but it seemed that patients after HP required more often additional interventions or operations to treat postoperative complications. In general, patients with acute perforated diverticulitis can be managed well by PA, but this decision should be made while taking into account patient's comorbidity, response on preoperative resuscitation and the availability of a surgeon experienced in colorectal surgery and intensive care medicine.

Long-term survival after perforated diverticulitis is discussed in **chapter 6**. The overall 5-years survival after perforated diverticulitis was only 53%. Long-term survival was significantly impaired compared to the general Dutch population, with a 5-years survival of 72% in the 250 patients who had survived initial emergency surgery for perforated diverticulitis. The limited long-term survival was mainly caused by the poor general condition of the patients. Neither the severity of primary disease nor the selected primary surgical strategy did influence long-term survival. For selecting optimal surgical strategies in perforated diverticulitis it is important to take short- and long-term outcome in relation to patient's characteristics into account. HP should no longer be considered as preferred treatment for perforated diverticulitis in all patients. In younger healthy patients, PA may be the procedure of choice for all stages of severity of perforated diverticulitis when all short- and long-term outcomes are considered.

As survival outcomes for patients after HP and PA seems to be similar, quality of life (QOL) might be a crucial factor when assessing the optimal surgical strategy for perforated diverticulitis. QOL after perforated diverticulitis was assessed in 131 patients and discussed in **chapter 7**. Patients after HP showed a significant lower QOL than patients after PA and also compared to the general Dutch population. The main reason for this low QOL was the presence of end colostomy. Patients who had their stoma reversed in a second operation showed similar QOL outcomes compared to the general population. In conclusion, when an end colostomy can be avoided, like in patients who undergo PA, or reversed, QOL in patients who have survived emergency surgery for perforated diverticulitis may improve. Besides short- and long-term survival, QOL outcomes must therefore be regarded as an important factor in decision making for initial (surgical) treatment.

The optimal surgical strategy in patients with perforated diverticulitis is still a matter of debate. Currently, it is generally accepted that Hinchey I and II diverticulitis can be treated conservatively with antibiotics, with or without percutaneous abscess drainage. Failure of this conservative treatment still necessitates surgical treatment. In most of these cases PA can be safely performed. Thoughts about the optimal treatment of perforated diverticulitis with generalized peritonitis are diverse. This has been the case since the first therapeutic guidelines for this stage of the disease were postulated. The evolution of changing patterns in surgical strategies in perforated diverticulitis complicated by generalized peritonitis is described in **chapter 8**. In the beginning of the twentieth century a three-staged and initially nonresectional strategy was advocated as the safest surgical approach. The classic three-stage operation includes an initial diverting colostomy and drainage followed by resection of the involved colon and, finally, colostomy closure as the third stage. With the development of antibiotics, primary resectional surgery gained popularity. Since the 1980s and 1990s HP had become the preferred surgical strategy in perforated diverticulitis. At present, HP is still the most frequently performed operation in perforated diverticulitis, although improvements in surgical and radiological intervention techniques and progress in the management of peritoneal sepsis led to an increasing interest in PA. In addition, in 2008 the results of a new minimal invasive, nonresectional technique to treat perforated diverticulitis with purulent peritonitis were presented with excellent results compared to HP. It is therefore not very likely that HP will remain the advocated surgical strategy for treatment of perforated diverticulitis with generalized purulent peritonitis in the near future. Whether this is the same for treating patients with faecal peritonitis remains to be seen.

To assess which surgical strategy is superior in the treatment of perforated diverticulitis with generalized purulent and faecal peritonitis a nationwide multicenter randomized trial has started in 2010. Patients with purulent peritonitis will be randomized between laparoscopic lavage and drainage without resection of the affected sigmoid, HP and PA with or without diverting loop ileostomy (DI). Patients with faecal peritonitis will be randomized between HP and PA. The study protocol is presented in **chapter 9**.

HP leaves the patient with end colostomy. Restoration of bowel continuity can eventually take place in a second operation. In PA an end colostomy is avoided. Adding DI after PA decreases the rate of symptomatic anastomotic leakage, which is the most feared complication after PA. **Chapter 10** describes the results of stoma reversal after HP and PA with DI. HP was reversed in only 45% of patients, whereas 74% of DIs were reversed with significantly fewer postreversal complications. HP reversal is a more complex

surgical procedure and hence results in more postoperative complications, with an anastomotic leakage rate of 16% and a mortality rate of 5%. The complexity of surgical procedure and related postoperative complications is the main reason why many patients will never have their stoma reversed. When treating a patient with acute perforated diverticulitis it is essential to decide on optimal operative strategy. This involves not only the type of primary surgery, but other aspects must also be taken into consideration. Before primary surgery a balance must be made between morbidity and mortality of the primary operation, stoma reversal operation, the risk of a permanent stoma and the quality of life. All these should take into account the individual characteristics of the patient and the severity of the disease. As HP reversal is a difficult operation with a high postoperative morbidity and even mortality, reversal when indicated should be performed by a specialist colorectal surgeon or not be performed at all. Previously, PA with or without DI seemed not to be inferior compared to HP in the treatment of perforated diverticulitis and should be the preferred strategy in most patients. In patients of older age and with ASA classification III or higher, HP must seriously be considered the surgical procedure of choice, because long-term survival is limited and restoration of bowel continuity is therefore not an issue.

**Chapter 11** discusses what to do with the skin at the formal stoma side during stoma reversal. As stoma reversal is considered a contaminated operation, it is important to determine the severity and frequency of wound infection after stoma closure and the consequences on the short- and long-term. A comparison was made between 25 patients in whom the skin at the formal stoma side was primary closed and 37 patients in whom the skin was left open. Although the rate of wound infection is rather high (27% after primary skin closure), especially in case of DI reversal, management of this complication is easy without (long-term) complications. Closure of the skin was not associated with a higher number of other complications, such as incisional hernia, anastomotic leakage and fistula formation.

Restoration of bowel continuity after HP for perforated diverticulitis is a technically challenging operation associated with significant morbidity, with reported anastomotic leak rates as high as 30% and a mortality of up to 16% in present literature. Besides risk factors such as patient's characteristics and disease aetiology that cannot be altered, the most important risk factor for morbidity is the technique used for restoration of bowel continuity. In **chapter 12** a new minimal invasive technique for HP reversal is described. In this new technique HP reversal is performed through the formal stoma side without the need for additional incisions. This so called stomal incision reversal (SIR) has the advantage over the standard surgical approach by laparotomy that the amount of adhesiolysis is limited to the paracolic pathway to the rectal stump.

During HP reversal by laparotomy all adhesions in the midline and pelvis need to be released. This may increase morbidity, i.e., postoperative paralytic ileus and small bowel lacerations.
The feasibility of this new minimal invasive technique of HP reversal was determined in 16 patients after complicated perforated diverticulitis. The results are discussed in **chapter 13**. The outcome was prospectively assessed in a consecutive series of 16 patients that underwent SIR and was compared to an historic age-, sex-, ASA- and Hinchey stage-matched control group of 32 patients that underwent HP reversal by laparotomy. Of the 16 patients that were assigned for HP reversal by SIR, three needed conversion to an open procedure (laparotomy) due to very firm adhesions at the pelvic side or doubt about the quality of doughnuts after performing a colorectal anastomosis using the circular stapler-device. Anastomotic leakage rate was similar in both groups (6%). Overall, restoration of bowel continuity by SIR compared favourably towards HP reversal by laparotomy in terms of operation time and hospital stay, without giving rise to the number of postoperative complications. SIR can be considered a good and safe alternative in all patients, as conversion to laparotomy can be easily performed when necessary.

# Discussion and future perspectives

In our present healthcare system with guidelines and evidence-based medicine the care for diverticular disease has to follow suit. Despite the high incidence, its pathophysiology and its optimal treatment and prevention strategies remain poorly understood and inadequately investigated, especially in case of perforated diverticulitis. There are several reasons for this. First, the pathogenesis of diverticular disease, diverticulitis and perforation seems to be multifactorial including lifelong dietary habits, medicine use, coexistence of other bowel or collagen-related diseases and genetic influences. This complex interaction of factors makes it very difficult to investigate. Nevertheless, fundamental epidemiological research is warranted to assess aetiology of this disease and subsequently develop prevention strategies. The first and relative straightforward step in observational research should be represented by the establishment of a nationwide database of all patients referred to hospital because of complaints related to diverticular disease. At present, such a database is already available for patients undergoing surgery for colorectal malignancies (Dutch Surgical Colorectal Audit; DSCA). In addition, for

(future) genetic research a tissue bank containing parts of resected bowel with (perforated) diverticula should be established.
Second, although uncomplicated diverticulitis is a common gastrointestinal disease, the incidence of perforated diverticulitis is relatively low (below 4 per 100.000). Due to its low incidence, it is difficult to design and successfully complete randomized controlled trials to assess optimal treatment strategies. The operations are classified as emergency and may be performed outside office hours, rendering it even more difficult to start such trials. It has already been tried in the past, but due to low study-enrolment no firm conclusions could be drawn.
Third, it is extremely difficult to gain any grants to establish a randomized trial to assess the optimal treatment for perforated diverticulitis. Although short and long term survival of patients with perforated diverticulitis is poor (not any better than in patients suffering from colon or rectum carcinoma), the disease is a benign disease and therefore probably less appealing to financially support clinical investigation.
Nevertheless, the consequences for general health care and especially for the patients are enormous, as it is accompanied by high morbidity and mortality rates and poor QOL after having survived the event. Healthcare costs are significant due to long intensive care and overall hospital stay, the high rate of additional interventions or operations to treat complications and outpatient stoma care.
Altogether this warrants good evidence-based treatment guidelines, conducted from randomized trials, resulting in better short- and long-term outcomes. Furthermore, there is evidence that the incidence of this complicated stage of disease has increased in parallel with the overall prevalence in the ever more aged population. Therefore an integrated nationwide incentive, the Dutch Diverticular Disease Collaborative Study Group has been established as a corporation of three multicenter randomized trials concerning the treatment of all different stages of diverticular disease. The primary goal of this 3D-study group is to finally solve the vast problem of diverticulitis and to combine efforts to promote the trials nationwide and internationally. In addition, patients' accrual in all three trials can be optimised in this joint effort by close corporation of the research groups, by utilization of a common website (www.diverticulitis.nl) and collaborating trial coordinators. The LADIES-trial is designed to provide evidence in optimal treatment strategies with regard to perforated diverticulitis complicated by generalized purulent or faecal peritonitis. The main questions of the underlying trial are whether laparoscopic lavage and drainage without resection of the affected sigmoid is superior over resectional surgical strategies in purulent peritonitis and whether PA is not inferior to HP in faecal peritonitis.

# Strategies in perforated diverticulitis

The optimal treatment strategy for perforated diverticulitis depends on the degree of peritonitis. The degree of peritonitis and hence the severity of disease can be represented during surgery by Hinchey's classification. Hinchey I and II represent localized peritonitis with phlegmon or abscess near the affected sigmoid and abscess elsewhere, respectively. Even localized perforated diverticulitis can present as acute abdomen frequently resulting in emergency surgery when preoperative CT-scan for diagnosis is withheld. Generally, Hinchey I and II perforated diverticulitis can be treated conservatively with antibiotics, with or without percutaneous drainage of abscesses. Abscesses up to five cm could probably be treated successfully with antibiotics alone. If conservative treatment fails, surgical intervention is indicated, in which resection with primary anastomosis is preferably above Hartmann's procedure. The performance of a DI to 'protect' the anastomosis can be considered.

Hinchey III and IV perforated diverticulitis are characterized by generalized purulent and faecal peritonitis, respectively. Both represent indications for emergency surgery. Several systematic reviews have concluded primary anastomosis to have better outcome than Hartmann's procedure for patients with generalized peritonitis due to perforated diverticulitis. Nevertheless, randomized controlled trials are lacking in present literature and selection bias could play a role, as such that sometimes the best patients (ASA I and II) had undergone primary anastomosis and otherwise around. Nonetheless, these reviews are the best available evidence.

In case of Hinchey III peritonitis laparoscopic treatment by lavage and drainage, without resection has shown such excellent results that this new approach cannot be ignored. The problem is that Hinchey's classification represents the severity of disease during surgery. Preoperative CT scanning is essential to differentiate between Hinchey I, II and generalized peritonitis (Hinchey III and IV), but exact differentiation between purulent of faecal peritonitis is not possible until today. It is therefore advised that all patients with perforated diverticulitis with generalized peritonitis will undergo diagnostic laparoscopy. In case of purulent peritonitis laparoscopic lavage and drainage can be performed subsequently. Alternatively, resectional surgery can be considered in which primary anastomosis is preferred. In case of faecal peritonitis, conversion to laparotomy is advised to perform sigmoid resection with primary anastomosis (or Hartmann's procedure), as laparoscopic lavage and drainage have shown not to be successful in Hinchey IV perforated diverticulitis.

These statements still need to be confirmed by the randomized controlled trial (LADIES-trial) that is currently running in The Netherlands under the auspices of the Dutch Diverticular Disease (3D) Collaborative Study Group.

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## Samenvatting en discussie

# Samenvatting

Klachten gerelateerd aan diverticulose van het colon zijn één van de meest voorkomende indicaties voor ziekenhuisopname. Toch bestaat er nog steeds onduidelijkheid over de optimale behandeling van de verschillende stadia van dit ziektebeeld. Om het probleem aan te pakken zijn begin 2010 drie klinische gerandomiseerde studies onder de auspiciën van de Dutch Diverticular Disease Collaborative Study Group (3D-study Group) van start gegaan. De controversen binnen de huidige behandelingstrategieën van divertikelziekte en het belang van de gestarte klinische studies worden in **hoofdstuk 2** besproken.
Om tot een optimale behandelingstrategie te komen, zou bij voorkeur de etiologie van de ziekte bekend moeten zijn. Bij preventie van de ziekte is kennis betreffende de etiologie zelfs essentieel. Het ontstaan van diverticulose en daaraan gerelateerde complicaties, zoals diverticulitis en perforatie, lijkt een gevolg te zijn van een complexe interactie tussen darmwandstructuur en intestinale motoriek, dieetgewoonten, genetische invloeden, voorkomen van andere darmaandoeningen en medicijngebruik. Dit alles wordt besproken in **hoofdstuk 3**. Helaas is er tot op heden geen overtuigend bewijs voor de precieze ontstaanswijze van divertikelziekte. Hierdoor is het vrijwel onmogelijk strategieën ter preventie van dit ziektebeeld te bedenken. Kwalitatief goed epidemiologisch onderzoek naar risicofactoren voor diverticulose en diverticulitis is dan ook zeer gewenst. Het is echter maar de vraag of een dergelijk onderzoek haalbaar is, aangezien dit zeer grote groepen patiënten, die voor meerdere jaren gevolgd moeten worden, vereist.
Geperforeerde diverticulitis is het meest ernstige stadium van divertikelziekte, maar wordt slechts in twee procent van de gevallen gezien. De enorme impact van de ziekte ligt vooral in het hoge aantal complicaties en sterfte waarmee deze gepaard gaat. Na het geruptureerde aneurysma kent geperforeerde diverticulitis van alle benigne aandoeningen de hoogste postoperatieve sterfte, ongeacht de gekozen behandelingstrategie. De meest uitgevoerde chirurgische behandeling is de Hartmann procedure (HP), die oorspronkelijk ontwikkeld is om rectumcarcinoom te behandelen. Tijdens HP wordt het aangedane sigmoid gereseceerd en een eindstandig colostoma aangelegd. Een alternatief voor HP is de operatie waarbij de darmuiteinden primair geanastomoseerd worden en dus een eindstandig colostoma voorkomen wordt. Angst voor naadlekkage kan de chirurg ervan weerhouden om een primaire anastomose (PA) aan te leggen. **Hoofdstuk 4 en 5** beschrijven de korte termijn postoperatieve resultaten van patiënten met geperforeerde diverticulitis en de factoren die daarop van invloed zijn. De resultaten van de chirurgische behandeling bleken vooral beïnvloed te worden door de ernst van de ziekte (Mannheim Peritonitis Index

en Hinchey classificatie), de conditie van de patiënt (leeftijd en American Society of Anesthesiologist (ASA) classificatie) en de aanwezigheid van een gastrointestinaal of colorectaal gespecialiseerd chirurg gedurende de operatie. De postoperatieve mortaliteit was gemiddeld 29% (83 van 291 patiënten overleden tijdens ziekenhuisverblijf), variërend van 23% in geval van Hinchey stadium I diverticulitis tot 50% in geval van Hinchey stadium IV. Patiënten die jonger waren dan 50 jaar hadden een mortaliteit 7%, terwijl ruim 38% van de oudere patiënten (>70 jaar) kwam te overlijden. Dit bleek in dezelfde mate voor patiënten met ASA I vergeleken met patiënten met ASA ≥3 (respectievelijk 6 en 40%). De postoperatieve mortaliteit bleek niet gerelateerd te zijn aan de gekozen chirurgische procedure, hoewel patiënten die HP ondergingen vaker complicaties hadden waarvoor een aanvullende radiologische of operatieve behandeling noodzakelijk was. In het algemeen kan gesteld worden dat PA een verantwoorde keuze is voor behandeling van patiënten met geperforeerde diverticulitis, maar dat bij deze keuze rekening gehouden moet worden met de conditie van de patiënt, de reactie op reeds ingestelde behandeling (op de intensive care afdeling) en de beschikbaarheid van een colorectaal gespecialiseerd chirurg.

Lange termijn overleving na geperforeerde diverticulitis wordt in **hoofdstuk 6** beschreven. De totale 5-jaars overleving was slechts 53%. De lange termijn overleving was significant korter dan die van de algemene Nederlandse bevolking, met een 5-jaars overleving van 72% voor de 250 patiënten die het ziekenhuis konden verlaten na geperforeerde diverticulitis doorgemaakt te hebben. Deze slechte lange termijn overleving was vooral het gevolg van de slechte algemene conditie van de patiëntpopulatie, maar bleek niet door de ernst van de initiële ziekte of de primair gekozen chirurgische aanpak beïnvloed te zijn. Aangezien zowel korte termijn als lange termijn resultaten van belang zijn bij het selecteren van de meest optimale behandelingstrategie, kan HP niet langer beschouwd worden als de meest verantwoorde procedure voor alle patiënten met geperforeerde diverticulitis. Vooral in de jongere en conditioneel sterke patiënten geniet PA de voorkeur, ongeacht de ernst van de ziekte (Hinchey classificatie).

Kwaliteit van leven (QOL) na operatie is wellicht één van de meest belangrijke uitkomsten om de meest optimale behandelingstrategie voor geperforeerde diverticulitis te bepalen, vooral omdat overlevingsuitkomsten tussen HP en PA vergelijkbaar zijn. De QOL van 131 patiënten die een spoedoperatie vanwege geperforeerde diverticulitis ondergingen wordt in **hoofdstuk 7** beschreven. Patiënten die HP hadden ondergaan hadden lagere QOL scores ten opzichte van patiënten na PA en de algemene Nederlandse populatie. De belangrijkste reden hiervoor was de aanwezigheid van een eindstandig colostoma. De patiënten die hun HP stoma hadden laten opheffen

via een volgende operatie toonden gelijkwaardige QOL scores als de algemene bevolking. Concluderend zullen patiënten na geperforeerde diverticulitis een betere QOL hebben indien een eindstandig colostoma voorkomen wordt, zoals bij patiënten na PA, of indien het stoma in een later stadium opgeheven kan worden. Naast korte en lange termijn overleving, zou QOL een zwaarwegende factor moeten zijn voor het bepalen van de juiste behandelingstrategie bij patiënten met geperforeerde diverticulitis.

Tot op heden bestaat er discussie over de beste behandeling van de verschillende stadia van geperforeerde diverticulitis. Inmiddels lijkt een conservatieve behandeling voor Hinchey I en II (lokale peritonitis) diverticulitis echter algemeen geaccepteerd. De conservatieve behandeling bestaat uit het geven van antibiotica, eventueel aangevuld met percutane drainage van intra-abdominale abcessen. Indien deze conservatieve behandeling niet tot het gewenste resultaat leidt, is een operatieve behandeling alsnog geïndiceerd. Vrijwel altijd kan dan veilig voor PA gekozen worden.

De meeste discussie bestaat tegenwoordig nog over de behandeling van geperforeerde diverticulitis met gegeneraliseerde peritonitis. Deze discussie bestaat eigenlijk al sinds de eerste keer dat er therapeutische richtlijnen voor dit ziektebeeld werden opgesteld, ongeveer een eeuw geleden. De discussies over en veranderingen in de veronderstelde optimale behandeling voor geperforeerde diverticulitis met gegeneraliseerde peritonitis worden in **hoofdstuk 8** beschreven. In het begin van de twintigste eeuw werd de drie-fase strategie als de meest veilige benadering omschreven. De klassieke drie-fase strategie bestaat uit het primair aanleggen van een eindstandig colostoma met het plaatsten van drains ter hoogte van de perforatie, gevolgd door resectie van het aangedane colondeel (meestal sigmoid) in een tweede fase. Tenslotte kan door een derde operatie het stoma weer opgeheven worden. Met de ontwikkeling van antibiotica kreeg het primair reseceren van het aangedane colondeel (meestal sigmoid) steeds meer navolging en sinds de jaren tachtig werd HP als meest optimale chirurgische behandeling van geperforeerde diverticulitis geadviseerd. Tot op heden is HP de meest uitgevoerde operatie in geval van geperforeerde diverticulitis, hoewel door ontwikkelingen in chirurgische en radiologische technieken en verbetering in therapeutische mogelijkheden van sepsis PA steeds vaker als voorkeursoperatie gezien wordt. Voorts werden in 2008 uitstekende resultaten gepresenteerd van een nieuwe minimaal invasieve en niet-resectionele chirurgische behandeling voor geperforeerde diverticulitis met gegeneraliseerde purulente peritonitis. Het is dan ook niet waarschijnlijk dat HP de voorkeursbehandeling voor geperforeerde diverticulitis met purulente peritonitis zal blijven. Of dit ook zal veranderen voor fecale peritonitis is nog maar de vraag.

Begin 2010 is een landelijke gerandomiseerde multicenter studie van start gegaan om te bepalen welke chirurgische behandelingstrategie voor geperforeerde diverticulitis met gegeneraliseerde purulente en faecale peritonitis de voorkeur heeft. In deze studie (LADIES-trial) zullen patiënten met purulente peritonitis na randomisatie behandeld worden volgens drie strategieën: laparoscopische lavage en drainage zonder resectie van het aangedane sigmoid, HP of PA met of zonder dubbelloops ileostoma (DI). Patiënten met fecale peritonitis zullen gerandomiseerd worden tussen HP en PA. Het protocol van de LADIES-trial wordt in **hoofdstuk 9** beschreven.
Patiënten die HP ondergaan zullen een eindstandig colostoma krijgen. Eventueel kan door een volgende operatie het stoma weer opgeheven worden. Patiënten die PA ondergaan krijgen geen colostoma. Door het tegelijkertijd aanleggen van DI bij PA kan de anastomose 'beschermd' worden tegen naadlekkage die als meest gevreesde complicatie beschouwd wordt. Het aantal symptomatische naadlekkages is minder na PA met DI dan zonder DI. In **hoofdstuk 10** worden de resultaten besproken van patiënten die hun stoma (HP stoma of DI) hebben laten opheffen. HP werd slechts in 45% opgeheven, terwijl DI in 74% van de patiënten opgeheven werd en met minder postoperatieve complicaties. Het opheffen van HP is een veel complexere ingreep en gaat daardoor gepaard met meer complicaties, zoals een naadlekkage-percentage van 16% en een mortaliteit van 5%. Dit is dan ook de belangrijkste reden dat bij veel patiënten het eindstandig colostoma na HP nooit opgeheven wordt. Het is belangrijk om ook dit in acht te nemen tijdens de primaire operatie voor geperforeerde diverticulitis. Er dient dan ook een goede afweging gemaakt te worden tussen mogelijke complicaties en sterfte rondom de initiële operatie, maar ook gedurende een tweede hersteloperatie, het risico op een permanent colostoma en de QOL. Uiteraard moet hierbij ook rekening gehouden worden met de conditie van de patiënt en de ernst van de ziekte. Aangezien het opheffen van HP een zeer complexe operatie is, zal dit uitgevoerd moeten worden door een colorectaal gespecialiseerd chirurg, of anders misschien maar helemaal niet. Eerder is al beschreven dat PA minstens gelijkwaardig is aan HP en zou dus in de meeste patiënten de voorkeursbehandeling kunnen zijn. Bij patiënten met ASA III of hoger kan HP een gerechtvaardige keuze blijven, aangezien in deze patiëntcategorie de verwachte overleving beperkt is en in het algemeen een tweede operatie om het stoma op te heffen niet aan de orde is.
In **hoofdstuk 11** wordt besproken wat er met het huiddefect op de voormalige stoma plaats gedaan moet worden. Het opheffen van een stoma wordt namelijk als een gecontamineerde operatie gezien en daarom is het van belang om te onderzoeken hoe vaak postoperatieve wondinfecties voorkomen en wat de consequenties hiervan op de korte en lange termijn zijn. Vijfentwintig

patiënten, waarbij de wond primair gesloten werd na het opheffen van het stoma, werden vergeleken met 37 patiënten waarbij de huid opengelaten werd. Hoewel het percentage wondinfecties hoog was (27% bij primair sluiten van de huid), vooral ingeval van DI, had dit nauwelijks gevolgen op de korte en lange termijn doordat deze complicatie eenvoudig te behandelen was. Het primair sluiten van de huid tijdens opheffen van het stoma was niet geassocieerd met een hoger aantal complicaties zoals littekenbreuk, naadlekkage of fistelvorming.
Herstel van darmcontinuïteit na HP vanwege geperforeerde diverticulitis is een complexe en technisch moeilijke operatie die gepaard kan gaan met significante comorbiditeit. In de literatuur wordt tot 30% kans op naadlekkage en 16% op postoperatieve mortaliteit beschreven. Naast factoren zoals de patiënt zelf en etiologie van de primaire ziekte, die beide niet te beïnvloeden zijn, is de gebruikte operatietechniek om het stoma op te heffen de belangrijkste risicofactor voor complicaties. In **hoofdstuk 12** wordt een nieuwe minimaal invasieve techniek beschreven voor het opheffen van HP. Bij deze nieuwe operatietechniek wordt het stoma opgeheven via het voormalige stomadefect, zonder dat er extra incisies nodig zijn. Deze zogenaamde ‘stomal incision reversal (SIR) techniek heeft ten opzichte van de standaard techniek via mediane laparotomie het voordeel, dat alleen de adhesies in de paracolische goot naar de rectumstomp toe los gemaakt moeten worden. Bij continuïteitsherstel na HP via mediane laparotomie dienen ook adhesies in de onderbuik en kleine bekken losgemaakt te worden. Dit kan extra morbiditeit met zich meebrengen, zoals darmletsel en postoperatieve ileus.
De uitvoerbaarheid en veiligheid van de SIR werd onderzocht in 16 patiënten die HP ondergaan hadden vanwege gecompliceerde en geperforeerde diverticulitis. De resultaten van dit onderzoek zijn in **hoofdstuk 13** beschreven. De uitkomst van SIR werd prospectief onderzocht bij 16 patiënten en vergeleken met een historische groep patiënten die HP herstel via een laparotomie hadden ondergaan en gematched werden voor leeftijd, geslacht, ASA classificatie en Hinchey stadium van de primaire ziekte. Bij alle 16 patiënten die SIR zouden ondergaan, werd drie maal naar laparotomie geconverteerd vanwege te straffe adhesies in het kleine bekken of vanwege twijfel over het intact zijn van de donuts nadat een circulair gestaplede anastomose gemaakt was. Het percentage naadlekkage was voor beide groepen gelijk (6%). Algemeen beschouwd waren de resultaten na SIR beter dan na HP herstel via laparotomie. SIR had een kortere operatieduur en korter ziekenhuisverblijf, zonder dat er meer complicaties rondom de operatie gevonden werden. Concluderend is SIR een goed en veilig alternatief voor patiënten na HP, waarbij, indien nodig geacht, te allen tijde alsnog naar een laparotomie geconverteerd kan worden.

# Discussie en toekomstperspectieven

In het huidige zorgsysteem met richtlijnen en evidence based medicine mag de kwaliteit van zorg met betrekking tot diverticulitis niet achterblijven. Hoewel de incidentie van diverticulose en diverticulitis zeer hoog is, zijn de etiologie en de optimale behandeling- en preventiestrategieën van dit ziektebeeld nauwelijks opgehelderd of onderzocht. Dit geldt in het bijzonder voor geperforeerde diverticulitis. Hiervoor zijn meerdere redenen aan te dragen.
Ten eerste lijkt de etiologie van diverticulose, diverticulitis en geperforeerde diverticulitis multifactorieel te zijn, onder andere afhankelijk van levenslange dieetgewoonten, medicijngebruik, genetische aanleg en de aanwezigheid van andere aandoeningen van de darmwand. Dit complexe samenspel maakt het zeer moeilijk om onderzoek te doen. Toch is goed fundamenteel epidemiologisch onderzoek om gericht preventieve maatregelen op te kunnen stellen tegen divertikelziekte van groot belang. Een eerste en relatief eenvoudige stap hiervoor zou het opzetten van een nationale databank kunnen zijn, waarin alle patiënten met diverticulitis opgenomen worden. Een dergelijke databank bestaat al voor patiënten geopereerd voor colorectaal carcinoom (Dutch Surgical Colorectal Audit; DSCA). Daarnaast zou het opstellen van een weefselbank met specimen colonwand met divertikels voor (toekomstig) genetisch onderzoek van nut kunnen zijn.
Ten tweede is de incidentie van geperforeerde diverticulitis relatief laag (minder dan 4 per 100.000), terwijl ongecompliceerde diverticulitis juist een zeer frequente aandoening aangaande de gastointestinale tractus is. De lage incidentie van geperforeerde diverticulitis maakt het zeer lastig om een gerandomiseerde studie op te zetten en tot een goed einde te brengen. De behandeling van geperforeerde diverticulitis betekent vaak een spoedoperatie en zal dus regelmatig tijdens diensturen plaatsvinden, hetgeen de studie er niet gemakkelijker op maakt. Eerdere studies zijn dan ook ten gevolge van lage inclusie-rates voortijdig gestaakt, waardoor er geen harde conclusies met betrekking tot de meest optimale behandelingstrategie van geperforeerde diverticulitis getrokken konden worden.
Ten derde is het lastig om voldoende financiële ondersteuning te krijgen om een gerandomiseerde studie naar de behandeling van geperforeerde diverticulitis op te zetten. Hoewel de korte en lange termijn overleving van deze patiëntenpopulatie zeer matig is (zeker niet beter dan patiënten met colon- of rectumcarcinoom), lijkt een benigne ziekte als deze voor grootschalig gesponsord wetenschappelijk onderzoek niet aantrekkelijk of interessant genoeg.

Desondanks is de impact van de ziekte op het huidige zorgsysteem, maar vooral op de patiënt zelf, enorm doordat deze met een hoge morbiditeit, mortaliteit en een slechte QOL gepaard gaat. De medische kosten zijn eveneens significant door een lang verblijf op de intensive care afdeling, totale opnameduur, de aanvullende radiologische en operatieve interventies om complicaties te behandelen en door stoma-gerelateerde kosten.
Duidelijke richtlijnen, gebaseerd op goed klinisch onderzoek, zijn dan ook van essentieel belang om de korte en lange termijn resultaten te kunnen verbeteren. Vooral ook omdat er aanwijzingen zijn dat de incidentie van geperforeerde diverticulitis toeneemt in de steeds ouder wordende bevolking. Om deze reden is de Dutch Diverticular Disease Collaborative Study Group opgericht; een samenwerkingsverband van drie nationale studies naar de behandeling van verschillende stadia van diverticulitis. Het doel van de 3D-study Group is het bevorderen van alle drie studies zodat uiteindelijk meer duidelijkheid ten aanzien van de optimale behandelingstrategie van diverticulitis verschaft kan worden. Met dit samenwerkingsverband wordt bovendien een hoger inclusiepercentage nagestreefd door gebruik te maken van één website (www.diverticulitis.nl). De LADIES-trial is, als één van de drie studies, opgezet om de optimale behandelingstrategie voor geperforeerde diverticulitis met gegeneraliseerde purulente en fecale peritonitis te onderzoeken. De twee belangrijkste onderzoeksvragen zijn: 1. Heeft laparoscopische lavage met drainage zonder resectie betere resultaten dan primaire resectie van het aangedane sigmoid bij patiënten met geperforeerde diverticulitis met purulente peritonitis? 2. Heeft PA de voorkeur boven HP bij de behandeling van patiënten met geperforeerde diverticulitis met fecale peritonitis?

## Strategieën bij geperforeerde diverticulitis

De optimale behandeling van geperforeerde diverticulitis is afhankelijk van het stadium van de ziekte. Het stadium van de ziekte en dus de ernst ervan kan perioperatief volgens de Hinchey classificatie bepaald en benoemd worden. Hinchey I en II worden gekenmerkt door lokale peritonitis ten gevolge van een flegmone dan wel abces nabij de perforatie of een abces elders in de buik. Zelfs Hinchey I en II geperforeerde diverticulitis kunnen zich presenteren met het beeld van acute buik. Niet zelden zal een spoedoperatie het gevolg zijn, vooral als een diagnostische CT-scan overgeslagen wordt. In het algemeen kunnen Hinchey I en II diverticulitis met antibiotica conservatief behandeld

worden, waarbij het intra-abdominaal gelegen abces eventueel percutaan gedraineerd kan worden. Abcessen tot vijf cm blijken overigens goed met antibiotica alleen te behandelen te zijn. Chirurgische interventie is geïndiceerd wanneer de conservatieve behandeling niet succesvol is. PA is dan de operatie van voorkeur, eventueel in combinatie met het aanleggen van een beschermend DI.

Hinchey III en IV geperforeerde diverticulitis wordt respectievelijk door gegeneraliseerde purulente en fecale peritonitis gekenmerkt. Beiden zijn indicaties voor spoedoperatie. Meerdere systematische reviews beschrijven dat PA betere postoperatieve uitkomsten dan HP heeft bij patiënten met geperforeerde diverticulitis met gegeneraliseerde peritonitis. Echter gerandomiseerde studies ontbreken in de huidige literatuur en selectiebias kan in deze reviews een misleidende rol spelen, waarbij de mogelijkheid bestaat dat de beste patiënten (ASA I en II) PA ondergingen en andersom. Niettemin leveren de systematische reviews tot op heden het best beschikbare bewijs.

De behandeling van geperforeerde diverticulitis met gegeneraliseerde purulente peritonitis (Hinchey III) door middel van laparoscopische lavage en drainage zonder resectie van het aangedane sigmoid heeft recent dusdanig goede resultaten opgeleverd, dat deze nieuwe behandelingstrategie niet genegeerd mag worden. Een probleem is echter dat het juiste stadium van de ziekte volgens de Hinchey classificatie pas tijdens de operatie bepaald kan worden. Tegenwoordig kan een preoperatieve CT-scan wel tussen Hinchey I en II differentiëren en bovendien het beeld van gegeneraliseerde peritonitis (Hichey III en IV) laten zien, maar differentiatie tussen purulente en fecale peritonitis is tot op heden niet mogelijk. In geval van een gegeneraliseerde peritonitis vanwege geperforeerde diverticulitis wordt daarom diagnostische laparoscopie geadviseerd. Indien er sprake is van purulente peritonitis kan volstaan worden met laparoscopische lavage en drainage. Als alternatief kan voor resectie van het aangedane sigmoid gekozen worden, waarbij PA boven HP de voorkeur heeft. In geval van fecale peritonitis zal naar een laparotomie om het aangedane sigmoid te reseceren geconverteerd moeten worden, aangezien laparoscopische lavage en drainage bij Hinchey IV geperforeerde diverticulitis niet effectief is gebleken. De relevantie van bovenstaande richtlijnen dienen bevestigd te worden door de gerandomiseerde studie (LADIES-trial) die onder de auspiciën van de Dutch Diverticular Disease Collaborative Study Group momenteel in Nederland wordt uitgevoerd.

# 16

## List of publications

# List of publications

1. Pathophysiology and prevention of diverticulitis and perforation; Vermeulen J, Van der Harst E, Lange JF: Neth J Med 2010 (accepted)
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