

**TREATMENT STRATEGIES IN RECURRENT AND  
ONGOING DIVERTICULITIS**

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## TREATMENT STRATEGIES IN RECURRENT AND ONGOING DIVERTICULITIS

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## **CHAPTER 3**

DIVERTICULITIS-STATE OF THE ART.

Drs. M.A.W. Stam

dr. E.C.J. Consten

dr. W.A. Draaisma

dr. W.E. Hueting

*Published in Modern Medicine October 2014*

*NO ABSTRACT AVAILABLE*

## **CHAPTER 4**

### **RISK FACTORS FOR RECURRENT DIVERTICULITIS: A SYSTEMATIC REVIEW**

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Ç Ünlü

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E.C.J. Consten

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*Submitted*

## **Abstract**

### **Background**

An initial episode of diverticulitis has an uncomplicated course in the majority of patients. Up to 42% of patients, however, develops recurrent diverticulitis within two years. The aim of this systematic review is to identify patients with a higher risk of developing recurrent diverticulitis.

### **Method**

MEDLINE, EMBASE, CINAHL and Cochrane databases were searched for papers published between January 1966 and December 2015. Studies assessing the risk factors for recurrent diverticulitis were eligible for inclusion in the review. Studies included in the review were judged on methodological quality and subsequently assessed according to the risk factors related to recurrent diverticulitis.

### **Results**

Nine articles met the inclusion criteria. The majority of studies suffered from serious methodological flaws. Follow-up after conservative treatment of the primary episode ranged from 0-16.6 years and a recurrence rate of between 13% and 36% was found. Younger age, obesity, affected colon length of over 5cm, and complicated diverticulitis with abscesses or covered perforation were identified as risk factors for recurrence by some of the authors, however they were contradicted by others.

### **Conclusions**

This systematic review identified several potential risk factors for recurrent disease. However due to the low quality of the included studies and contradicting results no recommendations can be made.

## **CHAPTER 5**

### **RECURRENT LEFT-SIDED DIVERTICULITIS: ALWAYS THE SAME LOCATION?**

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## **Abstract**

### **Purpose**

Recurrent episodes of diverticulitis occur in about 33% of patients with uncomplicated diverticulitis. The exact location of these recurrent episodes has scarcely been subject of interest. Our aim was to investigate if recurrent episodes always occur in the same location as the initial episode.

### **Methods**

Medical charts of all patients suffering from an episode of diverticulitis between 2008 and 2012 were reviewed. Patients with a minimum of two CT-proven episodes of uncomplicated diverticulitis were eligible for inclusion. Patients with fistulas or stenosis, concomitant colonic cancer or inflammatory bowel disease were excluded. CT scans were reviewed in terms of disease severity and location of disease by two independent blinded radiologists.

### **Results**

90 Patients had two or more CT proven episodes of diverticulitis between 2008 and 2012. Eventually 34 patients were eligible for inclusion, 22 women (65%) and 12 men (35%). The main reason for exclusion was the presence of ongoing complaints and therefore the absence of two clinically distinguished episodes of diverticulitis. The average age at onset of disease was 57 years. Median follow-up was 51.5 months (range 16-107). Diverticulitis was mainly localized in the horizontal part of the sigmoid. Recurrent episodes occurred in the same location as the initial episode in the majority of patients (67%,  $p < 0,05$ ).

### **Conclusions**

Recurrent episodes of diverticulitis occur at the same location as an initial episode in the majority of patients. This may support the choice for a more limited resection of the originally affected segment in case of recurrent diverticulitis or persistent complaints.



## **CHAPTER 6**

SIGMOID RESECTION FOR DIVERTICULITIS IS MORE DIFFICULT THAN FOR MALIGNANCIES.

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*Submitted*

## **Abstract**

### **Objective**

Sigmoid resection for diverticulitis is usually the first procedure performed when starting the learning process for laparoscopic colorectal surgery. The aim of this study is to evaluate the difficulty of laparoscopic sigmoid resection for diverticulitis in comparison to sigmoid malignancy in order to assess its role in the residents training program.

### **Methods**

A cohort of patients was selected who suffered either from malignancy or recurrent diverticulitis in the sigmoid colon. Laparoscopic sigmoid resection was performed. The degree of difficulty was assessed by intraoperative complications and intraoperative technical hitches. Furthermore take-overs from assistant to surgeon, surgeon to surgeon and conversion were reported.

### **Results**

A total of 224 patients were included, 119 (53,1%) men and 105 (46,9%) women. Patients suffering from diverticulitis had significantly less co-morbidities than those with a malignancy. In the diverticulitis group there were significantly more technical hitches. There was a higher rate in take-overs from residents ( $p=0.02$ ) as well as surgeon to surgeon ( $p=0.04$ ). The rate of conversions was also significantly higher in the diverticulitis group ( $p=0.03$ ) when compared to the malignancy group.

### **Conclusion**

The outcomes of our study show that diverticulitis may not be the ideal condition to start the learning process for laparoscopic colorectal surgery.

## **CHAPTER 7**

THE RELATION BETWEEN QUALITY OF LIFE AND HISTOPATHOLOGY IN  
DIVERTICULITIS; CAN WE PREDICT SPECIMEN RELATED OUTCOME?

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*Published Int J Colorectal Dis (2015) 30:665-671*

## **Abstract**

### **Purpose**

An important factor in the decision to perform laparoscopic sigmoid resection for patient suffering from recurrent and ongoing diverticulitis is quality of (QoL). It is unknown whether quality of life relates to the severity of diverticulitis as seen in the resected colonic segment. The aim of this study is to analyze histopathological findings of patients suffering from recurrent or ongoing diverticulitis and their QoL before and after surgery in order to improve patient outcome prediction.

### **Methods**

A cohort of consecutive patients with diverticulitis between January 2010 and April 2014 was analyzed. All patients were scheduled for surgery and had at least 3 episodes of diverticulitis or more within the last 2 years, or experienced ongoing complaints for at least 3 months or more and confirmation by a radiologist. We compared QoL questionnaires, to known histopathological entities.

### **Results**

For this study 54 consecutive patients were included, 15 (27,8%) men and 39 (72,2%) women. A marked difference in quality of life before and after surgery for patients having a more severe histopathological entity was not found ( $p=0,83$ ). However, a clinically relevant higher VAS score 6 months after surgery was shown in patients with peritonitis. Furthermore, these patients had more fibrosis in the histopathological samples.

### **Conclusion**

In conclusion, even though a relation between the different pathological entities and QoL could not be determined, patients with diverticulitis and concomitant microscopic

peritonitis had significantly more fibrosis and suffered from a higher VAS scores 6 months after surgery.

## **CHAPTER 8**

RECURRENCES AND ONGOING COMPLAINTS OF DIVERTICULITIS; RESULTS OF A SURVEY AMONG GASTROENTEROLOGISTS AND SURGEONS.

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## Abstract

### Objective

This study aims to investigate the current opinion of gastroenterologists and surgeons on treatment strategies for patients, with recurrences or ongoing complaints of diverticulitis.

### Background

Treatment of recurrences and ongoing complaints remains a point of debate. No randomized trials have been published yet and guidelines are not uniform in their advice.

### Design

A web-based survey was conducted among gastroenterologists and GE-surgeons. Questions were aimed at the treatment options for recurrent diverticulitis and ongoing complaints.

### Results

In total of 123 surveys were filled out. The number of patients with recurrent or ongoing diverticulitis were seen at the outpatient clinic each year was respectively 7 (0-30) and 5 (0-115). Surgeons see significantly more patients on an annual basis 20% versus 15% ( $p=0.00$ ). Both surgeons and gastroenterologists preferred to treat patients in a conservative manner using pain medication and lifestyle advice (64.4 vs 54.0,  $p=0.27$ ), however gastroenterologists would treat patients with mesalazine medication, which is significantly more (28%,  $p=0.04$ ) than in the surgical group. Surgeons tend more towards surgery (31.5%,  $p=0.02$ ).

### Conclusions

Both surgeons and gastroenterologists prefer to treat recurrent diverticulitis and ongoing complaints in a conservative manner. Quality of life, the risk of complications and the viewpoint of the patient are considered important factors in the decision to resect the affected colon.

## **CHAPTER 9**

A LIBERAL DIET FOR UNCOMPLICATED DIVERTICULITIS IS SAFE; RESULTS OF THE  
DIVERTICULITIS DIET STUDY.

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*Accepted for publication in Colorectal Disease.*



## **ABSTRACT**

### **Aim**

The optimal diet for uncomplicated diverticulitis remains unclear. Guidelines refrain from recommendation due to lack of objective information. The objective of this study is to prove that a liberal diet in a first, acute, uncomplicated episode of diverticulitis is safe.

### **Methods**

A prospective cohort study of patients with diverticulitis between 2012 and 2014 was performed. Requirements for inclusion were a first radiological proven modified Hinchey 1a/b episode of diverticulitis, ASA I-III and ability to endure a liberal diet. Exclusion criteria were use of antibiotics and suspicion of underlying inflammatory bowel disease or malignancies. All included patients were advised to use a liberal diet. Primary outcome parameter was complications. Secondary outcome measures were the development of recurrences and ongoing complaints.

### **Results**

Eighty-six patients were included, 37 (43,0%) were men. At the outpatient clinic all patients confirmed to have used a liberal diet. There were a total of 9 adverse events in 7 patients (8.1%). These consisted of re-admissions due to pain or recurrences and surgery (n=3,3.5%). Two patients needed surgery due to ongoing complaints (n=2) and one developed a Hinchey stage 3 (n=1) 5 days after initial presentation. The number of patients that experienced ongoing complaints at six months after their initial episode was 17 (19.8%), 4 (4.7%) patients suffered from recurrences.

### **Conclusion**

The incidence of complications of a liberal diet in a first, acute, uncomplicated episode of diverticulitis are in line with current literature, therefore a liberal diet can be safely advised in Hinchey 1a/b diverticulitis.

## CHAPTER 10

SURGERY VERSUS CONSERVATIVE MANAGEMENT FOR RECURRENT AND ONGOING DIVERTICULITIS; RESULTS OF A MULTICENTER RANDOMIZED CONTROLLED TRIAL (DIRECT-TRIAL).

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*Accepted the Lancet Gastroenterology and Hepatology*

## **Abstract**

**Background** Patients with recurrent or persisting complaints following an episode of left sided diverticulitis are managed with either conservative measures or elective sigmoidectomy. To date randomized data are lacking. We aimed to determine which treatment leads to a better quality of life.

**Methods** An open-label, multicenter, randomized clinical trial was performed in 24 teaching and 2 academic hospitals in the Netherlands (DIRECT trial). Patients presenting with either recurrent or persistent abdominal complaints after an objectified episode of left sided diverticulitis were included. Recurrent diverticulitis was defined as a total of three or more presentations with clinical signs of acute diverticulitis within a period of two years. Persistent abdominal complaints were defined as patients with ongoing lower left abdominal pain and, or persistent change in bowel habits for a period of more than three months after an episode of diverticulitis. Patients were randomly assigned to either conservative management or elective (laparoscopic) sigmoidectomy using a stratified digital en-block randomization system. Primary endpoint was quality of life measured by the Gastro-intestinal Quality of life Index (GIQLI) six months after inclusion or surgery depending on randomization group. This trial is registered with trialregister.nl (NTR1478).

**Findings** Between July 1, 2010 and April 1, 2014, 109 patients were randomized when the data safety and monitoring board prematurely terminated the trial because of increasing difficulties in recruitment. Fifty-three patients were randomized to resection and 56 to conservative management. The GIQLI score was significantly higher among patients randomized to resection (mean difference 14.2, CI 7.2-21.1) ( $p < 0.0001$ ). Seven (13.2%) patients in the resection arm developed anastomotic leakage. Among patients treated conservatively, 13 (23.2%) ultimately underwent elective resection due to ongoing abdominal complaints, with no anastomotic leakage. There was no mortality.

**Interpretation** Elective sigmoidectomy despite its inherent complication risk is superior to conservative management in terms of quality of life in patients with recurrent and persisting abdominal complaints after an episode of diverticulitis.

**Funding** Netherlands Organisation for Health Research and Development.

## NEDERLANDSE SAMENVATTING PROEFSCHRIFT

Per jaar worden in Nederland zo'n 22.000 patiënten op de SEH gezien met verdenking op diverticulitis, waarvan voor 18.000 patiënten een opname noodzakelijk is. De kosten hiervan worden geschat op 40 tot 80 miljoen euro per jaar. Diverticulitis is hiermee een van de meest voorkomende, benigne gastro-intestinale aandoeningen in de westerse bevolking. Geschat wordt dat 70% van deze populatie van 70 jaar en ouder divertikels heeft in het colon. Van deze groep patiënten zal een geschatte 25% een of meerdere episodes van diverticulitis doormaken.

Bij de patiënten met recidiverende diverticulitis kan de frequentie van de recidieven verschillen van eens per drie maanden tot eenmaal per 10 jaar. Dit is per patiënt en episode verschillend. In de meeste gevallen zal echter een eerste recidief binnen vijf jaar na de initiële episode plaatsvinden. Bij aanhoudende klachten na een eerste of recidief diverticulitis - zoals pijn links onderin de buik, aanhoudende vermoeidheid, problemen met de stoelgang, verminderde eetlust en episoden van koorts- is verwijzing naar een specialist op zijn plaats.

Een aantal aspecten van zowel de etiologie als behandeling bij patiënten met diverticulitis staan open voor discussie. Enkelen hiervan zullen aan bod komen in dit proefschrift.

### Dieet en diverticulitis

Met betrekking tot voeding in de acute fase van diverticulitis is het te adviseren patiënten een vrij dieet te laten gebruiken. Het oude adagium dat patiënten een helder vloeibaar dieet moeten volgen in de acute fase om perforatie te voorkomen, is in de nieuwe richtlijnen verlaten. Deze nieuwe zienswijze wordt echter alleen ondersteund door retrospectief onderzoek. De DIDI-studie, heeft dit prospectief bevestigd. Het blijkt dat het geven van voeding geen verhoogd risico geeft op perforatie in de acute setting. Het continueren van voeding komt eveneens overeen met de Richtlijn Ondervoeding. Deze schrijft voor dat patiënten nooit meer dan drie dagen suboptimaal zouden moeten worden gevoed.

### Risico factoren en recidieven

In de literatuur zijn er aanwijzingen dat er risicofactoren bestaan voor het optreden van een recidief diverticulitis. Tot op heden is echter nooit onomstotelijk bewezen welke categorie patiënten een verhoogd risico loopt op het ontstaan van een recidief diverticulitis. Onderzoeken zijn retrospectief van aard en auteurs spreken elkaar tegen. Mogelijke risicofactoren voor het ontwikkelen van een recidief zijn jonge leeftijd, belaste familieanamnese voor diverticulitis, obesitas, de aanwezigheid van abscessen, een grote lengte van het ontstoken colon, recidieven in het verleden en relevante co-morbiditeit. Een algemeen geaccepteerde risicofactor is een immuun gecompromitteerde patiënt. Het aantonen van een recidief is met name gebaseerd op echo-, laboratorium- en lichamelijk onderzoek. Het vervaardigen van een CT-scan bij patiënten met een recidief is niet veel voorkomend. Het blijkt echter uit retrospectief onderzoek dat bij patiënten bij wie er wel een CT-scan gemaakt is het recidief vaak in hetzelfde dan wel een aangrenzend gebied binnen het sigmoïd plaatsvindt. Dit heeft mogelijk in de toekomst gevolgen voor de lengte van het te reseceren colon.

### Electieve resecties en consensus

Recente literatuur toont aan dat recidieven geen indicatie zijn voor het verrichten van

een sigmoïdresectie. Het idee dat met elk recidief de episode heftiger wordt is inmiddels verlaten. Uit een nationale enquête onder chirurgen en MDL-artsen blijkt dat bij het maken van de afweging met betrekking tot het wel of niet verrichten van een sigmoïdresectie is het belangrijk zowel patiëntgebonden, ziekte gebonden als operatie gebonden factoren mee te wegen. Indicaties tot het verrichten van een sigmoïdresectie bij deze patiënt populatie moeten dan echter ook meer worden gezocht in het kader van kwaliteit van leven. Sigmoidresecties bij patiënten met recidieven en aanhoudende klachten van diverticulitis hebben een positief effect op de kwaliteit van leven. Ondanks de risico's die verbonden zijn aan deze operatie. De moeilijkheidsgraad van deze operaties is eveneens onderzocht in dit proefschrift en blijkt hoger te liggen dan dat van operaties in hetzelfde gebied voor kanker. Dit heeft met diverse oorzaken te maken waaronder de anatomische veranderingen die optreden bij patiënten met aanhoudende ontstekingen. Patiënten moeten goed worden voorgelicht over de voor en nadelen van zowel de conservatieve als de operatieve behandelmethoden. Uit onderzoek naar de relatie tussen de pathologie en de kwaliteit van leven komt eveneens naar voren dat de ernst van de ontsteking verbazend genoeg niet gerelateerd is aan de ernst van afname in kwaliteit van leven.

## SUMMARY OF THESIS

Each year approximately 22,000 patients in the Netherlands are seen in the emergency department with suspected diverticulitis. This leads to an estimated 18,000 admissions a year with total estimated costs of 40 to 80 million euro per year. Diverticulitis is thus one of the most common and costly benign gastrointestinal diseases in the western population. It is estimated that 70% of the population aged 70 and older have diverticula in the colon. Of these patients approximately 25% will experience one or more episodes of diverticulitis. In patients with recurrent diverticulitis the frequency of relapses may vary from every three months to once every 10 years. In most cases the first relapse will take place within five years after the initial episode. If symptoms persist after a first or recurrent diverticulitis - such as left lower abdominal pain, persistent fatigue, difficulty with bowel movements, decreased appetite and episodes of fever, referral to a specialist is in place. Several aspects of both the etiology and treatment of patients with diverticulitis are subject of debate. Some of them will be discussed in this thesis.

### Diet and diverticulitis

With regard to nutrition in the acute phase of diverticulitis we advise patients a liberal diet. The old adage to follow a clear liquid diet in the acute phase has been abandoned in new guidelines and is supported by retrospective study from our group. The DIDI study a large prospective cohort study has confirmed this. This study demonstrates that the administration of a liberal diet does not increase the risk of perforation in the acute setting. Continuing a liberal diet and proper nutrition also corresponds to the directive malnutrition. This requires that patients should never exceed a three-day suboptimal diet.

### Risk factors and recurrences

In the literature, there is evidence that risk factors exist for recurrent diverticulitis. To date, however, it has never conclusively proven which category of patients is at increased risk of developing recurrent diverticulitis. Studies are retrospective of nature and contradict each other. Possible risk factors for the development of a recurrence are young age, family history of diverticulitis, obesity, the presence of abscesses, a large length of the inflamed colon, relapses in the past and related co-morbidity. However due to the low quality of the included studies no definite recommendations can be made. Knowledge on risk factors can be of help when informing patients with acute primary or recurrent diverticulitis.

Diagnosis of recurrent diverticulitis is often based on physical examination, laboratory findings and ultrasound results. Performing a CT-scan in patients with recurrences is not common practice in the Netherlands. In a retrospective study in patients who have had a CT scan, the recurrence often occurred within the same or an adjacent area within the sigmoid. This might have consequences for the length of the colon resection.

### Elective resections and consensus

Recent literature shows that relapses are no longer the main indication to perform a sigmoid resection in patients suffering from recurrences and ongoing complaints. The idea that each recurrence occurs more complicated has been abandoned. A national survey among surgeons and gastroenterologists shows that important factors in deciding whether or not to perform a resection are patient-related QoL and surgical complications. Surgical resection of the affected colon has a positive effect on QoL in this subgroup of patients, despite the potential risks associated with this operation.

Sigmoid resection for diverticulitis appears to be more challenging than for malignancies located in the sigmoid due to anatomical changes that occur in patients with persistent inflammation. Patients should be well informed about the pros and cons of both the conservative and operative treatment methods. Research into the relation of the pathological outcome and quality of life also shows that the severity of inflammation, surprisingly, is not related to the severity of decline in quality of life.