New Approaches To The Surgical Treatment Of Intra-abdominal Infection

Irene M. Mulder

Promotores: Prof.dr. J.F. Lange
Prof.dr. W.A. Bemelman

Contents

Chapter 2

Preoperative staging of perforated diverticulitis by computed tomography scanning

M Gielens
IM Mulder
E van de Harst
MP Gosselink
KJ Kraal
HT Teng
JF Lange
J Vermeulen

Techniques in Coloprocotology. 2012 Oct; 16(5): 363-8

Abstract

Background
Treatment of perforated diverticulitis depends on disease severity classified according to Hinchey's preoperative classification. This study assessed the accuracy of preoperative staging of perforated diverticulitis by computerized tomography (CT) scanning.

Methods
All patients were included who presented with perforated diverticulitis between 1999 and 2009 in two teaching hospitals of Rotterdam, the Netherlands, and in addition had a preoperative CT scan within 24 h before emergency surgery. Two radiologists reviewed all CT scans and were asked to classify the severity of the disease according to the Hinchey classification. The CT classification was compared to Hinchey's classification at surgery.

Results
Seventy-five patients were included, 48 of whom (64%) were classified Hinchey 3 or 4 perforated diverticulitis during surgery. The positive predictive value of preoperative CT scanning for different stages of perforated diverticulitis ranged from 45 to 89%, and accuracy was between 71 and 92%. The combination of a large amount of free intra-abdominal air and fluid was strongly associated with Hinchey 3 or 4 and therefore represented a reliable indicator for required surgical treatment.

Conclusions
The accuracy of predicting Hinchey's classification by preoperative CT scanning is not very high. Nonetheless, free intra-abdominal air in combination with diffuse fluid is a reliable indication for surgery as it is strongly associated with perforated diverticulitis with generalized peritonitis. In 42% of cases, Hinchey 3 perforated diverticulitis is falsely classified as Hinchey 1 or 2 by CT scanning.

Chapter 3

Treatment options for perforated colonic diverticular disease

IM Mulder
J Vermeulen

CML – Gastroenterology 2011; 30(3): 77-84

No abstract available

Chapter 4

Early experience with laparoscopic lavage for perforated diverticulitis

HA Swank
IM Mulder
AGM Hoofwijk
SW Nienhuijs
JF Lange
WA Bemelman

On behalf of the Dutch Diverticular Disease Collaborative Study Group

British Journal of Surgery 2013 Apr; 100(5): 704-10

Abstract

Background
Laparoscopic lavage has recently emerged as a promising alternative to sigmoid resection in the treatment of perforated diverticulitis. This study examined an early experience with this technique.

Methods
The files of all patients with complicated diverticulitis were searched in 34 teaching hospitals of the Netherlands. Patients with perforated diverticulitis treated with laparoscopic lavage between 1 January 2008 and 31 December 2010 were included.

Results
Treatment with laparoscopic lavage was performed in only 38 patients in ten hospitals. Lavage was successful in controlling sepsis in 31 of the 38 included patients, with 32% morbidity (10 of 31 patients) and fast recovery. Overall, 17 of 38 patients developed complications, of whom two had a missed overt sigmoid perforation. Two patients died from multiple organ failure and one from aspiration pneumonia; one other patient died after palliative management of inoperable lung carcinoma. Three patients in whom lavage was successful underwent subsequent sigmoid resection for recurrent diverticulitis. Patients in whom lavage was unsuccessful tended to have more co-morbidities, a higher preoperative C-reactive protein concentration and a higher Mannheim Peritonitis Index.

Conclusion
Laparoscopic lavage for perforated diverticulitis was feasible in the majority of patients, but identification of an overt sigmoid perforation and patient selection are of critical importance.

Chapter 5

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

HA Swank
J Vermeulen
JF Lange
IM Mulder
JAB van der Hoeven
LPS Stassen
RMPH Crolla
MN Sosef
SW Nienhuijs
RJI Bosker
MJ Boom
PhM Kruyt
DJ Swank
WH Steup
EJR de Graaf
WF Weidema
REGJM Pierik
HA Prins
HBAC Stockmann
RAEM Tollenaar
BA van Wagensveld
PPLO Coene
GD Slooter
ECJ Consten
EB van Duijn
MF Gerhards
AGM Hoofwijk
TM Karsten
PA Neijenhuis
CFJ Blanken-Peeters
HA Cense
GHH Mannaerts
SC Bruin
QAJ Eijsbouts
MJ Wiezer
EJ Hazebroek
AAW van Geloven
JK Maring
AJL D'Hoore
A Kartheuser
C Remue
HMU van Grevenstein
J Konsten
DL van der Peet
MJPM Govaert
AF Engel
JB Reitsma
WA Bemelman

Dutch Diverticular Disease (3D) Collaborative Study Group

BMC Surgery 2010 Oct 18;10:29

Abstract

Background
Recently, excellent results are reported on laparoscopic lavage in patients with purulent perforated diverticulitis as an alternative for sigmoidectomy and ostomy.
The objective of this study 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: perforated DIVerticulitis: sigmoid resection with or without Anastomosis).

Methods
In this multicentre randomised trial all patients with perforated diverticulitis are included. Upon laparoscopy, patients with purulent peritonitis are treated with laparoscopic lavage and drainage, Hartmann's procedure or sigmoidectomy with primary anastomosis in a ratio of 2:1:1 (LOLA-arm). Patients with faecal peritonitis will be randomised 1:1 between Hartmann's procedure and resection with primary anastomosis (DIVA-arm). The primary combined endpoint of the LOLA-arm is major morbidity and mortality. A sample size of 132:66:66 patients will be able to detect a difference in the primary endpoint from 25% in resectional groups compared to 10% in the laparoscopic lavage 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 resection with primary anastomosis. Secondary endpoints for both arms are the number of days alive and outside the hospital, health related quality of life, health care utilisation and associated costs.

Discussion
The Ladies trial is a nationwide multicentre 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.

Trial registration
Nederlands Trial Register NTR2037

Chapter 6

Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial

S Vennix
GD Musters
IM Mulder
HA Swank
EC Consten
EH Belgers
AA van Geloven
MF Gerhards
MJ Govaert
WM van Grevenstein
AG Hoofwijk
PM Kruyt
SW Nienhuijs
MA Boermeester
J Vermeulen
S van Dieren
JF Lange
WA Bemelman

On behalf of the Ladies trial collaborators

Lancet 2015 Sep 26; 386: 1269-77

Abstract

Background
Case series suggest that laparoscopic peritoneal lavage might be a promising alternative to sigmoidectomy in patients with perforated diverticulitis. We aimed to assess the superiority of laparoscopic lavage compared with sigmoidectomy in patients with purulent perforated diverticulitis, with respect to overall long-term morbidity and mortality.

Methods
We did a multicentre, parallel-group, randomised, open-label trial in 34 teaching hospitals and eight academic hospitals in Belgium, Italy, and the Netherlands (the Ladies trial). The Ladies trial is split into two groups: the LOLA group comparing laparoscopic lavage with sigmoidectomy and the DIVA group comparing Hartmann's procedure with sigmoidectomy plus primary anastomosis. The DIVA section of this trial is still underway but here we report the results of the LOLA section. Patients with purulent perforated diverticulitis were enrolled for LOLA, excluding patients with faecal peritonitis, aged older than 85 years, with high-dose steroid use (≥20 mg daily), and haemodynamic instability. Patients were randomly assigned (2:1:1; stratified by age [<60 years *vs* ≥60 years]) using secure online computer randomisation to laparoscopic lavage, Hartmann's procedure, or primary anastomosis in a parallel design after diagnostic laparoscopy. Patients were analysed according to a modified intention-to-treat principle and were followed up after the index operation at least once in the outpatient setting and after sigmoidoscopy and stoma reversal, according to local protocols. The primary endpoint was a composite endpoint of major morbidity and mortality within 12 months. This trial is registered with ClinicalTrials.gov, number NCT01317485.

Findings
Between July 1, 2010, and Feb 22, 2013, 90 patients were randomly assigned in the LOLA section of the Ladies trial when the study was terminated by the data and safety monitoring board because of an increased event rate in the lavage group. Two patients were excluded for protocol violations. The primary endpoint occurred in 30 (67%) of 45 patients in the lavage group and 25 (60%) of 42 patients in the sigmoidectomy group (odds ratio 1.28, 95% CI 0.54–3.03, P=0.58). By 12 months, four patients had died after lavage and six patients had died after sigmoidectomy (P=0.43).

Interpretation
Laparoscopic lavage is not superior to sigmoidectomy for the treatment of purulent perforated diverticulitis.

Chapter 7

Guidelines of diagnostics and treatment of acute left-sided colonic diverticulitis

C Andeweg
IM Mulder
RJF Felt-Bersma
A Verbon
GJ van der Wilt
H van Goor
JF Lange
J Stoker
MA Boermeester
RP Bleichrodt

Digestive Surgery 2013 ;30:278-292

Abstract

Background
The incidence of acute left-sided colonic diverticulitis (ACD) is increasing in the Western world. To improve the quality of patient care, a guideline for diagnosis and treatment of diverticulitis is needed.

Methods
A multidisciplinary working group, representing experts of relevant specialties,
was involved in the guideline development. A systematic literature search was conducted to collect scientific evidence on epidemiology, classification, diagnostics and treatment of diverticulitis. Literature was assessed using the classification system according to an evidence-based guideline development method, and levels of evidence of the conclusions were assigned to each topic. Final recommendations were given, taking into account the level of evidence of the conclusions and other relevant considerations such as patient preferences, costs and availability of facilities.

Results
The natural history of diverticulitis is usually mild and treatment is mostly conservative. Although younger patients have a higher risk of recurrent disease, a higher risk of complications compared to older patients was not found. In general, the clinical diagnosis of ACD is not accurate enough and therefore imaging is indicated. The triad of pain in the lower left abdomen on physical examination, the absence of vomiting and a C-reactive protein >50 mg/l has a high predictive value to diagnose ACD. If this triad is present and there are no signs of complicated disease, patients may be withheld from further imaging. If imaging is indicated, conditional computed tomography, only after a negative or inconclusive ultrasound, gives the best results. There is no indication for routine endoscopic examination after an episode of diverticulitis. There is no evidence for the routine administration of antibiotics in patients with clinically mild uncomplicated diverticulitis. Treatment of pericolic or pelvic abscesses can initially be treated with antibiotic therapy or combined with percutaneous drainage. If this treatment fails, surgical drainage is required. Patients with a perforated ACD resulting in peritonitis should undergo an emergency operation. There is an ongoing debate about the optimal surgical strategy.

Conclusion
Scientific evidence is scarce for some aspects of ACD treatment (e.g. natural history of ACD, ACD in special patient groups, prevention of ACD, treatment of uncomplicated ACD and medical treatment of recurrent ACD), leading to treatment being guided by the surgeon's personal preference. Other aspects of the management of patients with ACD have been more thoroughly researched (e.g. imaging techniques, treatment of complicated ACD and elective surgery of ACD). This guideline of the diagnostics and treatment of ACD can be used as a reference for clinicians who treat patients with ACD.

Chapter 8

Experimental study on synthetic and biologic mesh implantation in a contaminated environment

IM Mulder
EB Deerenberg
N Grotenhuis
M Ditzel
J Jeekel
JF Lange

British Journal of Surgery, 2012 Dec; 99(12): 1734-41

Abstract

Background
Implantation of meshes in a contaminated environment can be complicated by mesh infection and adhesion formation.

Methods
The caecal ligation and puncture model was used to induce peritonitis in 144 rats. Seven commercially available meshes were implanted intraperitoneally: six non-absorbable meshes, of which three had an absorbable coating, and one biological mesh. Mesh infection, intra-abdominal abscess formation, adhesion formation, incorporation and shrinkage were evaluated after 28 and 90 days. Histological examination with haematoxylin and eosin and picrosirius red staining was performed.

Results
No mesh infections occurred in Sepramesh, Omyramesh and Strattice . One mesh infection occurred in Parietene and Parietene Composite . Significantly more mesh infections were found in C-Qur (15 of 16; P≤0.006) and Dualmesh (7 of 15; P≤0.035). Sepramesh showed a significant increase in adhesion coverage from 12.5% at 28 days to 60.0% at 90 days (P=0.010). At 90 days there was no significant difference between median adhesion coverage of Parietene Composite (35.0%), Omyramesh (42.5%), Sepramesh (60.0%) and Parietene (72.5%). After 90 days the adhesion coverage of Strattice was 5.0%, and incorporation (13.4%) was significantly poorer than for other non-infected meshes (P≤0.009). Dualmesh showed shrinkage of 63% after 90 days.

Conclusion
Parietene Composite and Omyramesh performed well in a contaminated environment. Strattice had little adhesion formation and no mesh infection, but poor incorporation. Some synthetic meshes can be as resistant to infection as biological meshes.

Surgical relevance
Surgeons are reluctant to use synthetic materials in contaminated environments owing to the risk of mesh infection. Mesh infection often necessitates removal of the mesh, leaving an abdominal wall deficit larger than the original hernia. Recently developed biological meshes are suggested to allow implantation in a contaminated environment.
This experiment shows promising results regarding infection rate, incorporation and adhesion formation of certain synthetic meshes in a contaminated environment. Biological meshes showed no mesh infection and little adhesion formation. However, incorporation of biological meshes was poor, making the biomechanical strength of the repair questionable. In contaminated abdominal wall surgery one-stage repair might be performed with implantation of certain types of synthetic mesh.

Chapter 9

Infection susceptibility of crosslinked and non-crosslinked biological meshes in an experimental contaminated environment

IM Mulder
EB Deerenberg
WA Bemelman
J Jeekel
JF Lange

American Journal of Surgery, 2015: 210; 159-166

Abstract

Background
This experimental study investigates infectious complications and functional outcome of biological meshes in a contaminated environment.

Methods
In 90 rats peritonitis was induced, and after 24 hours, a biological mesh was implanted intraperitoneally including 2 non-crosslinked mesh groups (Strattice and Surgisis) and 2 crosslinked mesh groups (CollaMendFM and Permacol). Sacrifice was after 90 and 180 days.

Results
More mesh infections occurred in crosslinked meshes compared with non-crosslinked meshes (70% vs 4%; P<0.001). Mesh infection was the highest in crosslinked CollaMendFM (81.2%) and lowest in non-crosslinked Strattice groups (0%). Incorporation into the abdominal wall was poor in all meshes (0% to 39%). After 180 days no residue of non-crosslinked Surgisis mesh was found. After 180 days, shrinkage was 0.8% in crosslinked Permacol and 20% in Strattice groups. Strattice showed the least adhesion formation (median 5%).

Conclusions
Infection rate of biological meshes in a contaminated field was the highest in crosslinked meshes. All biological meshes showed poor incorporation, which makes long-term abdominal wall repair questionable.

Chapter 10

Problematic incorporation of biological meshes in ventral hernia repair during long-term follow-up

IM Mulder
EB Deerenberg
WA Bemelman
JF Lange

Submitted

Abstract

Background
This study investigates long-term incorporation, adhesion formation, mesh infection and shrinkage after implantation of biological meshes in non-contaminated environment.

Methods
In 64 rats a mesh-model was used to implant various meshes intraperitoneally: 2 non-crosslinked mesh groups (Strattice and Surgisis) and 2 crosslinked mesh groups (CollaMendFM and Permacol). Sacrifice was after 90 and 180 days.

Results
High numbers of infectious complications were observed (12.5% transcutaneous prosthesis migration and 23.4% macroscopic mesh infection). Incorporation of meshes was poor (0% to 36.8%) on POD 180. Mesh shrinkage was highest in Surgisis (POD 90 57%, $P<0.01$). On POD 180, shrinkage did not differ between the meshes. Surgisis had the highest adhesion score on POD 90 (90%, $P<0.023$). Adhesions covering the mesh was least in Strattice (5%, $P<0.029$).

Conclusions
Experimental intraperitoneal implantation of biological meshes is accompanied by various infectious complications with little incorporation and will most likely not adequately prevent the formation of recurrent incisional hernia.

Chapter 11

Polyvinyl alcohol hydrogel decreases formation of adhesions in a rat model of peritonitis

IM Mulder
EB Deerenberg
M Ditzel
JC Slieker
WA Bemelman
J Jeekel
JF Lange

Surgical Infections 2012 Oct; 13(5):321-5

Abstract

Background
Adhesion formation after surgery for peritonitis-related conditions, with such associated complications as intestinal obstruction, pain, and infertility, remains an important problem. Applying a liquid barrier intra-peritoneally might reduce initial adhesion formation.

Methods
A combination of the cecal ligation and puncture model of peritonitis with the side-wall defect (SWD) model of adhesion formation was performed. Forty rats were assigned randomly to receive no barrier or 1mL or 2mL of the cross-linked polyvinyl alcohol and carboxymethylcellulose (PVA/CMC) hydrogel A-Part Gel (B. Braun Aesculap AG, Tuttlingen, Germany). After 14 days, the animals were sacrificed, and adhesion formation and abscess formation were scored.

Results
Thirty animals survived, distributed equally among the groups. There were significantly fewer adhesions to the SWD in the PVA/CMC groups (median 0) than in the control group (median 26%–50%) ($p < 0.05$). The median tenacity of the adhesions was significantly higher in the control group (Zühlke score 2) than in the PVA/CMC groups (Zühlke score 0) ($p < 0.05$). The amount and size of intra-abdominal abscesses were not significantly different in the three groups.

Conclusion
In this experiment, PVA/CMC hydrogel reduced the amount of adhesions to the SWD and between viscera significantly with equal risk of abscess formation.

Chapter 13

Summary

This thesis focussed on intra-abdominal infection, its treatment and complications following treatment of intra-abdominal infections.

In **Chapter 2** the accuracy of preoperative staging of perforated diverticulitis with computed tomography (CT) scanning was assessed in a retrospective study. The CT findings were compared with the clinical findings during surgery and classified according to the Hinchey classification. This study showed that the positive predictive value of preoperative CT scanning for different stages of diverticulitis ranged from 45 to 89%. Accuracy was between 71 and 92%. There was a clear understaging of disease in patients with Hinchey 3 diverticulitis, 42% of patients were falsely classified as Hinchey 1 or 2. The presence of a large amount of free intra-abdominal air and fluid was strongly associated with Hinchey 3 and 4.
Therefore, we concluded that current CT scanning does not seem to suffice to accurately predict the severity of perforated diverticulitis according to Hinchey's classification. A new scoring system is needed to guide treatment in patients with diverticulitis.

In **Chapter 3** an overview of treatment options for perforated diverticulitis was given. Historically the most performed surgical treatment is sigmoidectomy with subsequent colostomy, also referred to as Hartmann's procedure. However, this treatment strategy leads to high rates of permanent colostomies. Improvements in intensive care medicine and surgical technique has led to an increased number of patients treated with primary anastomosis instead of colostomy. Due to fear of anastomotic leakage this treatment is reserved mostly for young and healthy patients without faecal peritonitis. In this group of patients with purulent peritonitis, laparoscopic lavage of the abdomen with drainage could be an alternative treatment strategy.

In **Chapter 4** a retrospective study on the early experience with laparoscopic lavage in patients with purulent peritonitis was presented. Laparoscopic treatment was successfully performed in the majority of patients, conversion to laparotomy was performed in 3%. Laparoscopic lavage was associated with 32% morbidity, and a fast recovery if sepsis was successfully controlled which occurred in 81.5% of patients. Patients in whom lavage was unsuccessful tended to have more co-morbidities, a higher preoperative C-reactive protein concentration and a higher Mannheim Peritonitis Index. After successful laparoscopic lavage treatment 10% of patients required subsequent sigmoid resection for recurrent diverticulitis during follow-up. Treatment strategy for perforated diverticulitis with laparoscopic lavage was feasible in the majority of patients, but identification of an overt sigmoid perforation and patient selection are of critical importance for successful treatment.

In **Chapter 5** the protocol of a large randomized multicenter trial on the treatment of perforated diverticulitis was presented, the LADIES trial. This trial investigated the morbidity and mortality in patients with purulent and faecal generalised peritonitis following the three operative strategies; laparoscopic lavage and drainage, sigmoidectomy with primary anastomosis and Hartmann's procedure.
It was a five armed trial: patients with purulent peritonitis were randomised 2:1:1 to laparoscopic lavage, Hartmann's procedure or sigmoid resection with primary anastomosis. The aim of the LOLA trial was to show that laparoscopic lavage would lead to a 15% reduction in major morbidity and mortality compared to sigmoid resection. Patients with faecal peritonitis were to be randomised 1:1 into Hartmann's procedure or sigmoid resection with primary anastomosis. All patients who underwent sigmoid resection (both purulent and faecal peritonitis) were to be analysed in the DIVA trial. This analysis aimed to prove that Hartmann's procedure and sigmoid resection with primary anastomosis would lead to an equal 12 months mortality rate, yet sigmoid resection with primary anastomosis would lead to a 30% higher stoma-free survival.

In **Chapter 6** we discussed the results of the LOLA arm of the LADIES trial. The main conclusion was that laparoscopic peritoneal lavage for purulent perforated diverticulitis does not reduce major morbidity and mortality compared to sigmoidectomy at 12 months follow-up. An increased acute reintervention rate was found in patients after laparoscopic lavage (39%) compared to sigmoidectomy (19%). However 76% of patients did not need further surgery during primary hospital stay. There was no difference between the treatment groups in stoma free rates in surviving patients after 12 months (78% lavage group, 71% sigmoidectomy groups), but in the lavage group 74% never had a stoma.

In **Chapter 7** an overview of the available evidence combined with expert opinion was presented in a guideline for diagnosis and treatment of diverticulitis. The guideline was written under the auspices of the Netherlands Society of Surgery. The working group consisted of four surgeons, a gastroenterologist, a radiologist, an internist, a dietician and an epidemiologist and statistician. The evidence on treatment on some parts of diverticular disease is still scarce, leading to treatment strategies mainly being guided by the doctors personal preference. Although younger patients have a higher risk of recurrent disease there is not an increased risk of complications compared to older patients.
The triad of pain in the lower left abdomen on physical examination, the absence of vomiting and a C-reactive protein >50 mg/l has a high predictive value to diagnose acute colonic diverticulitis. If this triad is present and there are no signs of complicated disease, patients may be withheld from further imaging. If imaging is indicated, ultrasound is the first modality of choice. Only after a negative or inconclusive ultrasound CT scan is advised.
The optimal treatment strategy depends on the degree of peritonitis. In general, patients with Hinchey 1 and 2 diverticulitis can be treated conservatively with fluids, analgesics, and antibiotics, with or without percutaneous drainage of abscesses. There is no indication for routine endoscopic examination after an episode of uncomplicated diverticulitis.
There is no evidence for the routine administration of antibiotics in patients with clinically mild uncomplicated diverticulitis. Pericolic or pelvic abscesses can initially be treated with antibiotic therapy or combined with percutaneous drainage. If conservative treatment fails, emergency surgical intervention is indicated, in which resection with primary anastomosis is preferred above Hartmann's procedure. The performance of a diverting loop-ileostomy to protect the anastomosis should be considered, especially in patients with a number of comorbidity factors.
In the last decades non-resectional treatment with laparoscopic lavage has increased in popularity for treating Hinchey 3 diverticulitis. Initial results showed morbidity and mortality rates <5%. The results of randomised controlled trials comparing laparoscopic lavage with resectional strategies were not included in this guideline because the trials were still recruiting patients.

In **Chapter 8** a rat model in a contaminated environment was presented. In 144 rats we compared seven intraperitoneally placed meshes on infectious complications, adhesion formation, incorporation and shrinkage after a follow-up of 28 or 90 days. Significantly more mesh infections were found after implantation of C-Qur (94%) and Dualmesh (47%). Sepramesh showed a significant increase in adhesion coverage from 12.5% at 28 days to 60% at 90 days. At 90 days there was no difference in adhesion formation between the synthetic meshes (35-73%). After 90 days the adhesion coverage of the biological Strattice mesh was 5%, and incorporation (13%) was significantly poorer than for other meshes. Dualmesh showed shrinkage of 63% after 90 days.
This experimental results of synthetic mesh implantation in a contaminated environment make strict contraindication in humans questionable. Although there are no meshes without disadvantages, certain synthetic meshes might be somewhat more infection-resistant and therefore useful for permanent hernia repair in a contaminated environment.

In **Chapter 9** infectious complications and functional outcome of four biological meshes were investigated in 90 rats. Meshes were implanted in a contaminated environment and outcomes were

measured after 90 or 180 days. More mesh infections occurred in crosslinked meshes compared with non-crosslinked meshes (70% vs 4%). Incorporation into the abdominal wall was poor in all meshes ranging from 0% to 39%. After 180 days no residue of non-crosslinked Surgisis mesh was found. After 180 days, shrinkage was 0.8% in crosslinked Permacol and 20% in non-crosslinked Strattice. Strattice showed the least adhesion formation (5%).
In conclusion, this experiment demonstrates a high infection rate and increased adhesion formation of crosslinked biological meshes. Resistance to infection of non-crosslinked Strattice could allow implantation in the contaminated environment. However, the poor incorporation of all biological meshes and complete degradation of Surgisis makes long-term biomechanical strength of hernia repair questionable. Implantation of biological prostheses could be a valid choice in staged contaminated abdominal wall repair. The high costs of a biological mesh can be justified by prevention of mesh infection which is associated with high costs for intensive care treatment, reoperation, and prolonged hospital stay.

In **Chapter 10** four biological meshes implanted in a non-contaminated environment were compared after 90 or 180 days. In 64 rats infectious complications, incorporation, shrinkage and adhesion formation were investigated. High numbers of infectious complications were observed: 13% transcutaneous prosthesis migration and 23% macroscopic mesh infection. Incorporation of meshes was poor (0% to 37%) after 180 days. Shrinkage did not differ between the meshes after 180 days. After 90 days Surgisis had the highest adhesion score (90%). Adhesions covering the mesh was least in Strattice (5%).
We advocate more caution with implantation of biological meshes for abdominal wall repair. There seems to be no evidence for previously purported hypothesis that biological material enables ingrowth of cells and vessels resulting in a sustainable hernia repair. Implantation of biological mesh does not seem to reduce infection rate which is a significant riskfactor for the recurrence of incisional hernia. Biological meshes might not have the required characteristics for implantation in clean environment with high infection rate and low incorporation of the mesh in the current experiment.

In **Chapter 11** the influence of a new adhesion barrier on adhesion formation was investigated in a peritonitis rat model in 40 rats. Application of the anti-adhesive barrier, polyvinyl alcohol and carboxymethylcellulose hydrogel, resulted in fewer adhesions than in the control group. Additionally the tenacity of the adhesions was lower when the barrier was applied. There was no difference in amount and size of intra-abdominal abscesses between the study groups.
Polyvinyl alcohol and carboxymethylcellulose hydrogel demonstrated promising efficacy in this experiment. Therefore further investigation of this product is needed focusing on its safety when applied around an intestinal anastomosis and in the presence of synthetic material such as intra-abdominally placed meshes.

Chapter 15

List of publications

Ladies Trial: laparoscopic peritoneal lavage or resection for purulent peritonitis and Hartmann's procedure or resection with anastomosis for purulent or faecal peritonitis in perforated diverticulitis. Dutch Diverticular Disease (3D) Collaborative Study Group.
BMC Surgery 2010 Oct 18;10:29

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CML – Gastroenterology 2011;30(3):77–84.

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Surgical Infections 2012; 13(5):321-5

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HA Swank, **IM Mulder**, AG Hoofwijk, SW Nienhuijs, JF Lange, WA Bemelman; Dutch Diverticular Disease (3D) Collaborative Study Group.
British Journal of Surgery 2013 Apr;100(5):704-710.

Guidelines of diagnostics and treatment of acute left-sided colonic diverticulitis.
CS Andeweg, **IM Mulder**, RJ Felt-Bersma, A Verbon, GJ van der Wilt, H van Goor, JF Lange, J Stoker, MA Boermeester, RP Bleichrodt.
Digestive Surgery 2013 Aug 20;30(4-5):278-292

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HA Swank, **IM Mulder**, WC Hop, MJ van de Vijver, JF Lange, WA Bemelman.
Surgical Endoscopy 2013 Dec;27(12):4439-48

In vitro model to study the biomaterial-dependent reaction of macrophages in an inflammatory environment.
N Grotenhuis, HF vd Toom, N Kops, Y Bayon, EB Deerenberg, **IM Mulder**, GJ van Osch, JF Lange, YM Bastiaansen-Jenniskens.
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