Laparoscopic Adhesiolysis, Technique and Clinic

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Laparoscopic adhesiolysis, technique and clinic

Laparoscopisch uitgevoerde adhesiolyse,
techniek en kliniek

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Slechts drie keuzes in het leven zijn belangrijk:

- keuze van levenspartner
- keuze van beroep
- keuze van wel of geen kinderen

Er komt een vierde bij:

- keuze van wel of niet promoveren

Aan Sonja

Aan Michiel, Elmar en Hilko

Aan mijn ouders (vader overleden 19 september 1969)

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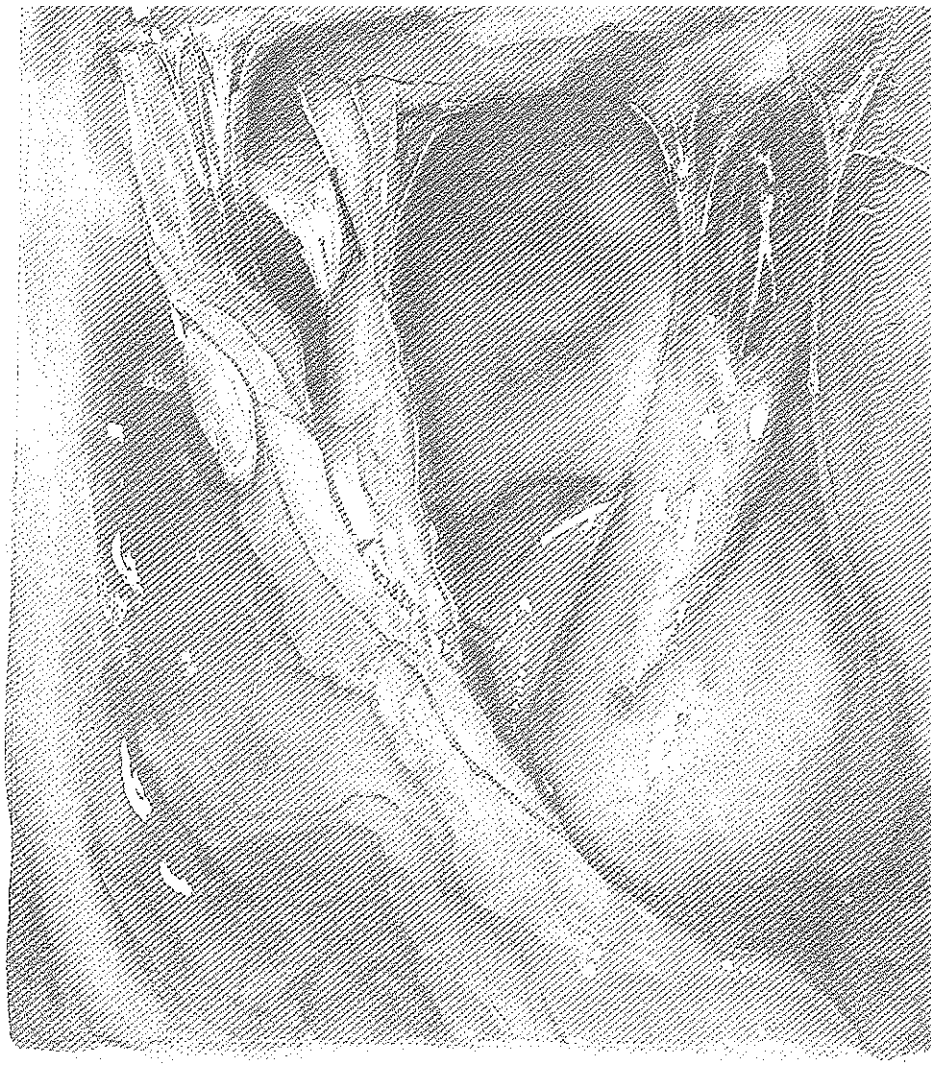


Chapter 1

General introduction, scope and aim of the thesis

History of laparoscopy

Laparoscopy is a combined word, and has its origin in the Greek word "laparo" (the flank) and in the word "skopein" (to examine). It was Georg Kelling, who was the first surgeon performing laparoscopy with a cystoscope in a living dog. This first "Kölioskopie" has been reported one century ago in 1902 in the Münchener Medizinische Wochenschrift.[52] It was also Kelling who successfully used celioscopy in two humans for diagnostic procedures between 1902 and 1910. A Swedish professor of medicine, Hans Christian Jacobaeus, working at the Karolinska Institute in Stockholm, must be mentioned as the progenitor of therapeutic laparoscopy and thoracoscopy. In 1910 he reported his experiences with laparoscopy in 17 patients suffering from ascites, and with thoracoscopy in two patients with suppurative pleura exsudates. For introduction of the cystoscope into the cavities he used a trocar he designed himself.[49] One year later the results of 115 laparoscopies and 72 thoracoscopies were reported. Only one bleeding occurred.[50] Minimal invasive laparo- and thoracoscopic surgery had started. However, it would last half a century before new developments encouraged new therapeutic modalities. From 1970 on professor Kurt Semm, a gynaecologist, performed advanced laparoscopic techniques such as biopsies, sterilisation, myoma enucleation and resection of salpinx and ovaries. In 1980 suturing of the bowel was technically feasible, and in 1983 the first laparoscopic appendectomy was a fact.[88] The latter indicates that the gynaecologists were the pioneers in this therapeutic laparoscopic field.

In 1987, Mouret, a general surgeon, removed a gallbladder laparoscopically for the first time.[26] Since 1986 a revolution has taken place in general surgery because of the development and application of the computer chip video camera and the acceptance of the laparoscopic technique for therapeutic interventions. The media accepted this new technique, and patients demanded this type of surgery and found surgeons with a strong desire for further innovation.[70] In 1992, Soper stated that laparoscopic cholecystectomy was the new gold standard. Soper also published a comparison between early postoperative results of laparoscopic versus standard open cholecystectomy.[90, 92] A randomised trial between the old and new gold standards of cholecystectomy has not been made before accepting the new hype as the enjoyed preference. All over the world more than 20.000 surgeons were trained to operate with new instruments and to handle with indirect control over their surgical hands. The medical industries developed the needed instruments, and the laparoscopic towers were positioned inside the hospitals. A new surgical era had begun.

History of adhesiolysis

In 1910, Kelling considered intra-abdominal adhesions as a contra-indication for laparoscopy.[52] Jacobaeus indicated thoracoscopy for lysis of pleural adhesions as treatment of tuberculosis.[50] This was 10 years before thoracotomy was performed. In 1933, the first report about lysis of intra-abdominal adhesions was written by C. Fervers, a German general surgeon. He used a cystoscope to visualise the peritoneal cavity and cauterised the adhesions. The oxygen he used for insufflation in combination with electrocautery caused an intra-abdominal explosion. The

doctor was shocked, but the patient recovered with a few minor complaints during a couple of days. After that incident, filtered air was used.
After introduction of the computer chip video camera and safe CO_2 pneumoperitoneum new enthusiasm for laparoscopic adhesiolysis was growing. In the first years of laparoscopic cholecystectomy previous abdominal surgery was considered a contra-indication for laparoscopic surgery due to possible intra-abdominal adhesions. Adhesions were considered as nasty bands, bothering an adequate visualisation of the anatomy and leading to bleeding. In these cases a traditional open operation was the treatment of choice. Adhesions around the gallbladder during laparoscopic cholecystectomy has led to 40% conversions to an open laparotomy. This figure shows the relevancy of adhesions and the problems to deal with. Ten years later the conversion rate for laparoscopic adhesiolysis was less than 8%, and a previous operation in the upper half of the abdomen was no longer reason for primary open cholecystectomy.[26] Surgeons had learned to deal with adhesions showing the progress of their experience.
Adhesions themselves were thought to be the cause of infertility and acute or chronic abdominal pain. In a review article by Soper about the laparoscopic progress till 1995, diagnostic laparoscopy was an accepted procedure for invasive investigation of the abdomen in patients with acute and chronic abdominal pain.[91] The results of laparoscopic adhesiolysis for chronic abdominal pain were reported in 1985 by Chan.[12] Since 1995, more than 20 articles described results of laparoscopic adhesiolysis for chronic abdominal pain.[102] The learning curve of laparoscopic adhesiolysis has ended.

Anatomy

Adhesions of the abdominal cavity can be congenital or acquired. Congenital adhesions account for 4.7% of the present adhesions found at laparotomy.[63] Patients without previous operations have their adhesions (2.3%) because of (un)known inflammatory processes in their abdomen. Ninety-three percent of the acquired adhesions are due to surgical peritoneal trauma.[56] Weibel and Mayo found adhesions in 21% of patients, who did not undergo abdominal surgery in an autopsy study.[103] Colo-rectal surgery, appendectomy and gynaecological procedures are most prone to adhesion formation.[68] In gynaecological reconstructive surgery with laparoscopic and microsurgical techniques 55% to 100% of patients have pelvic adhesions at second look one week to three years after the initial procedure.[15,17,19,20,97] Menzies reviewed the distribution of obstructing adhesions and observed the majority site of the occlusion to be located between loops of small bowel or between the small bowel with the site of previous surgery (84%).[68] In case of non obstructing adhesions, the small bowel was involved in a minority of 33%, and in the majority of these patients the omentum was involved. Although adhesions with the small intestine occur less frequently than those with the omentum, they are more likely to become obstructive.[68]

Classification of adhesions

Classification of adhesions can be based on etiology, topography, morphology, histological differentiation or on clinical importance.[61,89,101,104] Siegler and Luciano classified the adhesions into three clinical categories: from no adhesions (category 1) to category 3, defined as fully developed thick vascularised adhesions.[61,89] Knightly fulfilled the classification with a fourth category comprising organs with their serosal surfaces adhesive with themselves or with the parietal peritoneum of the abdominal wall.[53] With more criteria more objective judgement of the adhesions was possible with comparison between different studies.

Many new experiments were performed to investigate the results of different medications, fluids, or barriers for adhesion prevention. Multiple biopsies from many animal and human experiments were taken out for microscopic analysis. The need for a combination of clinical (macroscopic) and microscopic assessment has led to the Zühlke classification with four categories:[107]

1. filmy fibrin fibres, easy to separate by blunt dissection; connective tissue with many cells but few reticulin fibres
2. stronger adhesion, blunt dissection possible, partly sharp dissection necessary; beginning of vascularisation, more reticulin collagen fibres
3. strong adhesion, lysis possible by sharp dissection only; clear vascularisation, elastic and muscle fibres
4. very strong adhesion, lysis possible by sharp dissection only, organs strongly attached with severe adhesions, damage of organs hardly preventable, integration of serosal surfaces.

In all studies of this thesis the Zühlke classification has been used. This clinical and microscopical classification can be applied to every adhesion, irrespective of their location or origin and allows comparison between different studies and between assessments at different times in the same patient.

Histology

In adults the peritoneum has a surface of 10.000 cm^2, almost equal to the surface of the skin. The inner layer consists of connective tissue with an abundant vascular system for transport of oxygen and nutrients. Inside this connective tissue are poorly differentiated fibroblasts, which can differentiate into new mesothelial cells or into mast cells. The surface lining of the peritoneum is composed of highly differentiated mesothelial cells. The cells of this outer mesothelial layer of the peritoneum are loosely interconnected and make the peritoneum very vulnerable. During surgery this surface layer is easily injured. Running a finger along the outer layer is enough to damage the loose mesothelial cells resulting in denuding of the surface.

Pathophysiology

The peritoneal damage by surgical trauma is the result of the surgery itself, ischaemia, reaction to foreign materials, toxins, and many other factors. Re-epithelialization of the peritoneum takes 5 days, irrespective of the size of the defect. The repair starts with a coagulation process, that

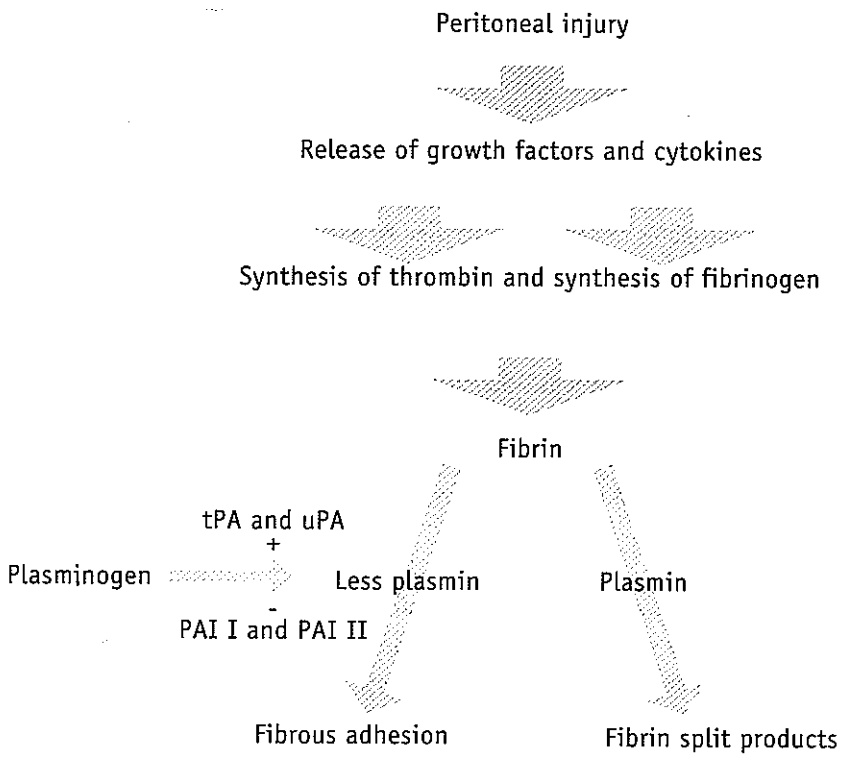
initiates a tournament with leukocytes, mesothelial cells and fibrin from the inner layer beneath the surface and not like skin growing from the edges.[24, 83, 84] Surgery increases the amount of abdominal fluid and the number of polymorphonuclear neutrophils and the quantity of plasma protein, and an inflammatory exsudate develops. The leukocyte population changes after 5 days, and macrophages become more prominent. These macrophages produce a lot of growth factors and cytokines, such as cyclooxygenase, lipoxygenase, plasminogen activator, plasminogen activator inhibitor, collagenase, elastase, interleukine 1 and interleukine 6, tumour necrosis factor and many more.[4, 84] These factors reach their highest levels during the first week after surgery. The postsurgical macrophages recruit in response to these growth factors and cytokines new mesothelial cells onto the surface of the injured peritoneum proliferating to islands of cells leading to a complete re-epithelisation.[24]

Pathophysiology of adhesions

Peritoneal injury initiates inflammation. Inflammation triggers the release of fibrinogen, a protein from blood and tissues. This fibrinogen reacts with thrombin to form fibrin monomers. With assistance of certain coagulation factors, for instance Factor XIIIa this fibrin monomers becomes insoluble. Further reaction with large proteins produces the fibrin gel matrix.[24] This cascade can happen within no more than three hours. The making of this fibrin gel matrix, sticky white material on the surface of injured peritoneum, happens in the first five days after surgery. Apposition of two damaged areas nearly always results in adhesion formation.[29,30,63] It is the contact between two injured surfaces coated with this sticky fibrin gel matrix that leads to the formation of a bridge between organs and is the base of further organisation of a primary adhesion.[24]

Later on it assimilates blood cells like leukocytes, erythrocytes and platelets, but also other cells like endothelium and epithelium and mast cells and debris; either cellular or surgical debris such as gauze particles, hair and talk. These primary adhesions will probably be degraded by fibrinolytic activity within the first weeks after surgery.[20, 43] However surgical trauma and several factors used during surgery cause impairment of local fibrinolytic activity. This inhibition will be responsible for failure of normal healing resulting in development of an irreversible pathological adhesion.[14, 28, 71]

The balance between fibrin formation and fibrinolysis decides whether or not an adhesion will be made. The activity of the enzyme tPA (tissue plasminogen activator) is reduced by plasminogen activator inhibitors I and II (PAI I and PAI II). The synthesis of PAI I and PAI II is induced by trauma or infection.[34, 82] Plasmin is the corner stone of fibrinolysis and the battle between activators and inhibitors of plasminogen determines the quantity of active plasmin. Decreased fibrinolytic activity will result in the formation of more adhesions. This was confirmed in a rat study. Fifteen rats treated with a fibrinolytic inhibitor (tranexamic acid) showed significantly more, and 15 other rats treated with a fibrinolytic stimulator (recombinant tPA) showed significantly fewer adhesions between the parietal peritoneum and the bowel compared with control rats. For clinical application this recombinant tPA can compensate the reduced fibrinolytic activity after surgical trauma of the peritoneum.[43]



Surgical consequences

Surgery causes peritoneal injury. Tissue manipulation, retraction of the bowel, use of gauze sponges and other instruments cause mesothelial abrasion, and can even strip the outer mesothelial layer, which provide the main supply of tPA intraperitoneally. The serosal fluid, containing this active tPA is usually removed during operation by swabs, suction or wound drains. It would be better if this fluid was replaced in the abdominal cavity at the end of surgery to support adhesion prevention.[48, 105]

Surgical trauma, the reduction of tissue oxygenation during surgery and the inflammatory reaction at the site of surgery, especially combined with peritonitis induce cytokines. These factors release plasminogen inhibitors PAI I and PAI 2 from the mesothelial cells and thereby reducing fibrinolysis. Activated plasmin is decreased during surgery due to either reduced synthesis of tPA or due to increased synthesis of the inhibitors PAI I and PAI 2.

Suturing of the peritoneum causes tension of the wound edges leading to local ischaemia and elimination of fibrinolytic activity, resulting in almost 100% adhesion formation. Ischaemia triggers a decreased production of active plasminogen and thereby diminishing fibrinolysis and

therefore stimulating adhesion formation. If the peritoneum is sutured after ischaemic bowel surgery, the fibrinolytic activity is eliminated after 24 hours, and will results in 100% adhesion formation.[76] Raftery showed in an animal study the effect of the formation of adhesions, and measured local fibrinolytic activity after minor and major damage of the oxygenation of a peritoneal defect. If the peritoneal defect was not sutured, the fibrinolytic activity was only slightly reduced with a low incidence of adhesions (5%).[76] Suturing of the peritoneum should be avoided routinely.
The use of retractors contributes to adhesion formation by damaging the local peritoneum and by inducing local ischaemia by local pressure. In a clinical study the activity of tPA was found reduced predominantly in those parts of the peritoneum where retractors had been placed during surgery.
Starch from gloves also induces adhesions.[31] Starch powder induces release of inflammatory mediators but also a reduction of the fibrinolysis and of mesothelial cells.[81] In a randomised study in rats significantly more adhesions were formed in those animals which were operated on with powdered gloves.[44] The use of powdered gloves should be abandoned.

Social economics

Nearly all patients, who underwent at least one abdominal operation develop at least one adhesion.[63] Follow up of more than 2000 laparotomies demonstrated that 1% of these patients develop adhesive obstruction within one year after surgery, and half of these occur within the first postoperative month. In a 10 years period this percentage will rise to 3%.[32] At Westminster Hospital during 24 years assessment obstructive intestinal adhesions accounted for 0.9% of all hospital admissions and for 3.3% of all major laparotomies. Thirty percent of all cases of obstructive bowel diseases were operated.[66] In 1992, a British survey reported an annual total of 12.000 to 14.400 cases of adhesive intestinal obstruction. In Western World postoperative adhesions are the most important cause of bowel obstruction (40%),[68] and even 60% to 70% of those obstructions involving the small bowel.[67]
An Australian study showed 45% to 80% reformation of adhesions after adhesiolysis.[72] Recurrent obstruction is common. The recurrence rate of adhesive obstruction after conservative treatment seems 12.5%,[8] while others found higher percentages up to 32% in different studies.[10]
Every abdominal reoperation has increased risk because of adhesions. More bowel perforations and more postoperative bleeding in these patients lead to increased morbidity and even mortality.[13,16,33,68] For doctors, adhesions create considerable workload and for the community more utilisation of hospital resources and high social costs and more expenditures for healthcare resources.
In the US admissions for treatment of adhesions accounted for almost 950.000 days of inpatient care with estimated $1.180 million expenditures in 1988.[77] Six years later the adhesiolysis hospitalisation rate has remained constant with a 10% reduction of expenditures because of decreased hospital length of stay.[78]

Clinical presentation

If a patient complains of abdominal pain and has a medical history and an abdominal scar predicting the presence of adhesions, it is uncertain whether these adhesions are responsible for the pain, and other causes must be searched for. Intra-abdominal adhesions cannot be shown with non-invasive investigations. Only laparoscopy or laparotomy can confirm adhesions, and can exclude other pathology.

Adhesions will be present in 68–100% of patients after previous abdominal surgery.[32,59,63,66] Fortunately the majority of patients with intra-abdominal adhesions have no complaints. However, Ellis found that after open abdominal surgery 35% of almost 30.000 patients were readmitted due to adhesion related disorders.[33] This percentage was confirmed in gynaecological surgery with an average of 2 re-admissions per involved patient.[60] Three to five percent of all patients after abdominal surgery will ever suffer from the consequences of these abdominal adhesions,[22,42,51] which include bowel obstructions,[1, 5, 33, 66] chronic abdominal pain,[58] and infertility.[24, 72, 64]

Intestinal obstruction occurs predominantly in the small bowel and develops in 1 to 12% of patiens after prior laparotomy,[1, 66] especially after colorectal surgery.[5] Strangulation of the bowel has a mortality risk between 5 and 30%.[32] Recurrent small bowel obstruction after adhesiolysis happens in 28% of patients.[55]

Reconstructive surgery for tubal infertility is frustrated by regrowth of adhesions. New techniques, re-laparoscopies for adhesiolysis and preventive measures have been applied to diminish adhesion formation. After laparotomic adhesiolysis pregnancy rates increase up to almost 50% among previously infertile women.[18, 37]

The indication of laparoscopic adhesiolysis for chronic pain is doubtful. A few authors deny that adhesions can cause chronic abdominal pain,[46,47] while many others believe and show good results after laparoscopic adhesiolysis.[27,36,38,56, 86] These studies were either retrospective or prospective, but not randomised. In 2001 Sulaiman found sensory nerve fibres in adhesions, supporting their own pain origin.[94] Relapse of chronic abdominal pain is as high as 26%,[85] and seems more frequent the longer the follow-up.[57] This relapse can be explained with reformation of adhesions after lysis,[72] increased severity of adhesions,[99] and even with denovo adhesions.[19, 72, 97]

Surgical technique

Adhesiolysis can be performed by laparotomy or laparoscopy. Laparoscopic adhesiolysis has the theoretical advantage of less adhesion reformation. This has been confirmed in animal models,[80, 96] but also after operations in humans.[74, 87]

Different techniques for adhesiolysis have been applied. Sutton used laser technique with good results,[95] but Luciano showed more tissue damage with laser therapy compared with electrosurgery.[61] Sharp dissection has the disadvantage of multiple small bleedings bothering a clear view for further dissection. Recently we preferred ultrasonic dissection for laparoscopic adhesiolysis as a safe and feasible technique.

Complications

Bleeding during laparoscopic adhesiolysis is usually a minor problem for the patient. Less than 1% of patients needs a blood transfusion.[79]

The incidence of bowel perforations, which occur during laparoscopic procedures for symptomatic adhesions varies from 5% to more than 25%.[16,35,36,79,98] The mortality after laparotomy for mechanical adhesive small bowel obstruction was 10% as described by Jeekel.[51] At secondary laparotomies through the same incision an iatrogenous bowel perforation occurred in 21% of patients. The number of previous laparotomies and the age of the patient appeared to be independent risk factors for these injuries.[100]

Bowel injuries are not always recognised during the time of surgery, and can result from needle puncture, trocar introduction or due to the adhesiolysis. In case of an unrecognised bowel perforation, the symptoms of peritonitis will usually be clear within 1 or 2 days. Postoperative signs of bowel perforation may be due to thermal bowel damage during the procedure. In these cases the bowel will perforate later and the clinical signs of the perforation are usually seen after 4 days.[79]

Developments

Critical in the procedure of laparoscopic adhesiolysis is the needle insertion, trocar placement and the adhesiolysis itself. Patients with previous abdominal operations pose a greater risk for perforations due to adhesive organs against the abdominal wall.

Several safety measures for laparoscopic adhesiolysis have been proposed, like subcostal insertion of the Veress needle.[79] In patients with multiple scars and prior upper abdominal surgery the needle was introduced in the left ninth or even eight intercostal space in the midclavicular line.

Open introduction of the initial trocar looks safer than the blind one, but is time consuming and has possibly more cicatricial hernias.[9,11,65] Radially dilating trocars make a smaller cut in the abdominal wall and create their introduction by pushing away the surrounding tissues. This smaller diameter possibly causes fewer hernias.[3] The Optiview® optical trocar (Optiview®, Ethicon, Endosurgery, Cincinnati, Ohio) is a blunt optical trocar, which is guided through the abdominal wall with the camera inside and controlled by the monitor. This device might combine the advantages of a safe and a fast penetration of the abdominal cavity.[41]

Laparoscopic adhesiolysis with scissors is inconvenient due to bleeding. Electrodissection causes charring of tissue and delayed thermal bowel perforations because of its excessive heat production.[35,42,69,93] Bipolar electrosurgery has the advantage of reducing the electrosurgical complications but still has delayed thermal lesions.[93] The ultrasonic device for laparoscopic cholecystectomy was introduced by Amaral in 1995.[2] Several different laparoscopic procedures have been performed successfully with this device.[40,93] The ultrasonically activated scalpel causes less heat production compared with that from electrocautery dissection and thereby theoretically diminishing the risk of delayed perforations.

Prevention

Surgical peritoneal inflammation is caused by surgical trauma such as abrasion, desiccation, overheating by lamps, irrigation fluids, exposure to foreign materials such as starch and sutures, or to intestinal contents and infection. The repair of the surgical damage with the deposition of fibrin is the same process as the formation of adhesions and starts at the same time.
With a disturbed balance between fibrin formation and fibrinolysis and if surgical traumatised surfaces are in contact, the fibrin gel matrix will form permanent adhesions.
Preventive measures might be divided in three categories:

- Surgical measures
- Drugs
- Barriers

Surgical measures

Minimal invasive surgery

Laparoscopes may cause as much or even more peritoneal trauma as the surgeons fingers.[82] Surgeons, however, always use one laparoscope in laparoscopic surgery and seldom use only one finger during laparotomic procedures. Gauzes are seldomly used in laparoscopic surgery. Staples are more inert than suture material, and entrance of glove powder is reduced to a minimum. Several studies suggest that minimal invasive surgery causes less trauma and therefore less adhesions (see: surgical techniques).

Minimal surgical trauma

Desiccation and irrigation of the abdominal cavity with overheated solutions should be avoided. The use of cautery for haemostasis should be limited to reduce necrosis. Minimise ischaemia by limiting the use of retractors and omitting suturing of the peritoneum. Multiple studies show subsequent adhesion formation due to ischaemia induced by suturing of the peritoneum.[23, 30]

Minimal foreign materials

Starch from the gloves can cause granulomas and peritonitis. Holmdahl et al. demonstrated 30% reduction in the number of adhesions in rats operated with starch free gloves.[44] Luijendijk et al. found starch granulomas in 5% of patients after prior surgery by surgeons using starch containing gloves.[63] Ellis demonstrated that washing gloves, even thoroughly, did not remove the starch.[31]
Improvement of the surgical techniques and surgical measures can only contribute to less formation of adhesions, but will not prevent them completely. Adjuvant treatment with drugs or barriers will be necessary.

Drugs

Research has been done with several kinds of drugs acting in several steps in the adhesion formation. Non-steroid anti-inflammatory drugs and corticosteroid drugs have been applied to reduce the inflammatory reaction. Anticoagulant drugs (heparin, coumarines) were used counteracting the effect of fibrin formation; even 5-fluorouracil has been tried to minimise

cell proliferation.[23,67,105] All these drugs have the disadvantage of interference with the normal wound healing process and may lead to delayed wound healing e.g. infection, incisional hernia and wound dehiscence.[23,67] Fibrin disposition is the main step of adhesion formation and fibrinolytic therapy would be a logic solution for practical purposes. However, several fibrinolytic drugs (tPA, streptokinase, urokinase) have shown not only contradictory results,[67] but haemorrhagic complications were to be expected.[106]
Methylene blue has been investigated as a powerful agent reducing adhesion formation. Probably its effect is due to inhibition of free radicals. In an experimental group of 120 rats the adjustment of intra-abdominal methylene blue resulted in 90% reduction of the severity of the adhesions.[39] It has hardly any side-effects, but in high concentrations it might induce adhesions.[75]

Barriers
Adhesion formation takes about seven days and occurs only between two damaged surfaces. Separating the two damaged surfaces with a barrier during the first postoperative week should prevent or reduce the adhesions formation. Dextran 70 as a macromolecular solution has been administered intraperitoneally as a barrier in a lot of studies with different results and has not resulted in routine application. Hyskon (low dose of 32% dextran 70 in dextrose) inhibits the formation of primary adhesions, but not the reformation after adhesiolysis.[45] Sepracoat™ (Genzyme Corporation, Cambridge, MA, USA) is a hyaluronic acid phosphate buffered saline solution intra-peritoneally applied to coat the peritoneal surfaces to make them less vulnerable for abrasion and desiccation. Diamond et al. demonstrated in a randomised study with Sepracoat significant reduction of the incidence, extent and severity of adhesions after gynaecological laparotomic operations.[21] A real mechanical barrier Seprafilm™ (Genzyme Corporation, Cambridge, MA, USA) can be placed between the compromised surgical surfaces. It reduces the extent and the severity of adhesions in humans.[6, 7, 102]

Not only the consequences of adhesions but also the possibilities of the prevention of these complications are underestimated. Today surgeons can do more than ever to reduce the incidence, extent and severity of adhesions.[82]

The aim

This study has to give answers on many questions patients asking me when they come for treatment of longstanding abdominal pain, and think that their abdominal adhesions have to be lysed to relief their pain. I have selected seven most relevant questions as subject for clinical studies in order to be able to give evidence-based answers to my patients.

1. *Is diagnostic laparoscopy indicated in patients with chronic abdominal pain?*
2. *Is laparoscopic adhesiolysis feasible? Is it wise trying to obtain a complete adhesiolysis?*
3. *Is laparoscopic adhesiolysis a safe procedure?*
4. *Are new and safer techniques available to perform laparoscopic adhesiolysis?*
5. *What is the recurrence rate of adhesions after laparoscopic adhesiolysis?*
6. *Which clinical measures can be taken to prevent postoperative adhesions, and what is the value of preventive measures?*
7. *Is laparoscopic adhesiolysis really beneficial in patients with chronic abdominal pain?*

van Wanrooy

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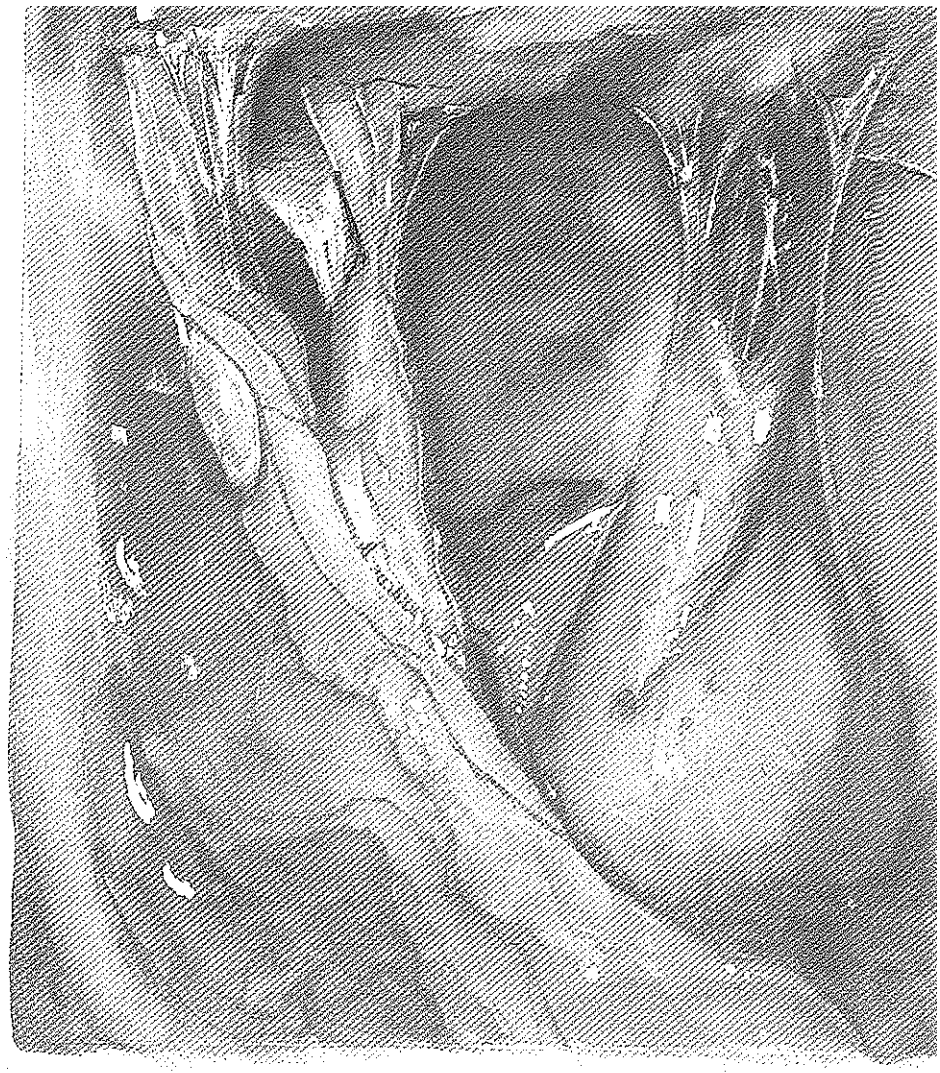

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Chapter 2

Complications and feasibility of laparoscopic adhesiolysis in patients with chronic abdominal pain A retrospective study

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Abstract

Background: A retrospective study was done to determine whether laparoscopic adhesiolysis benefits patients with chronic abdominal pain. Factors that influence complications and feasibility of laparoscopic adhesiolysis were evaluated.
Methods: 174 consecutive operations in 157 patients were retrospectively analysed for factors which might influence the complication rate and the feasibility of laparoscopic adhesiolysis.
Results: In 128 out of 174 procedures a complete adhesiolysis was performed. We had to accept an incomplete adhesiolysis in 39 other patients and in 7 patients a primary conversion was needed. We noticed 16 major complications. Two patients died. Relief of pain was recorded in 80% of patients after short follow-up. The number of previous abdominal operations and patient age significantly affected the outcome of surgery.
Conclusion: Laparoscopic adhesiolysis in patients with chronic abdominal pain seems to be a feasible and effective operation with considerable risk.

Introduction

Is it wise to perform adhesiolysis in patients with chronic abdominal pain? An analysis of the risk and feasibility of laparoscopic adhesiolysis in patients with chronic abdominal pain is necessary to answer this question.

Although the formation of adhesions is the most frequent complication of abdominal surgery, some consider adhesions as a physiological consequence, even as a friend.[6, 13] Others describe adhesions as postoperative adhesive peritoneal disease.[7] Nearly all patients of both sexes develop intra-abdominal adhesions after surgery in the abdominal cavity.[14] About 5% of all patients after abdominal surgery will ever suffer from the consequences of these adhesions which include (sub)total bowel obstruction, strangulation, intermittent acute or chronic pain, and infertility.[9]
Adhesions are also considered to cause chronic abdominal pain. Although an explorative laparotomy is an option in patients with this condition, the open procedure for chronic abdominal pain without complete bowel obstruction has never gained wide acceptance. Laparotomy bears the risk of inducing new adhesions and the morbidity and mortality of such an open procedure is supposed to be too high to justify it. However, after the introduction of the laparoscopic techniques, there is renewed interest in surgical treatment of adhesions causing chronic pain. Although Cook warned of the dangers of laparoscopy in patients with suspected bowel adhesions in 1977,[3] laparoscopic adhesiolysis was recommended as an attractive surgical procedure for intestinal obstruction and chronic abdominal pain 10 years later.[8,15] Every year many patients with chronic abdominal pain undergo laparoscopic adhesiolysis in Dutch hospitals despite the lack of evidence that this procedure is effective in an era of evidence-based surgery. This retrospective study was done to identify factors that determine the outcome of complications and the technical performance of laparoscopic adhesiolysis.

Patients and methods

Patients

We analysed retrospectively 157 patients who underwent primary laparoscopic adhesiolysis between October 1991 and September 1997 in two district hospitals (Máxima Medical Center Eindhoven and Groene Hart Hospital Gouda). Thirteen underwent a second adhesiolysis and four patients a third procedure accounting for a total of 174 operations. All patients had a history of chronic abdominal pain, defined as continuous or intermittent abdominal pain for at least 1 month. All but 5 patients had previous abdominal surgery. Most patients were referred by internists and a few by general practitioners. Fifty-seven were male and 100 female. Their ages ranged from 13 to 73 years, with a mean age of 45 years. Three authors (DS, WvE, ORvD)

performed the operations and all have extensive experience in laparoscopic surgery (>500 operations).
Abdominal pathology other than adhesions was excluded by a variety of preoperative investigations including ultrasound, radiographic studies of the small bowel and colon, or colonoscopy. Patients with other pathology that could be the cause of chronic abdominal pain and patients with acute or inflammatory diseases were excluded from the analysis. Patients were also excluded on account of increased anaesthesiological risk (ASA classification 3 and 4) and for general laparoscopic contraindications such as pregnancy (first trimester) and ventriculoperitoneal shunt.

Procedure

All procedures were done under general anaesthesia. A Veress needle to establish a pneumoperitoneum was inserted at a site devoid of scars. In a few cases the Hasson trocar or the Optiview trocar (Ethicon, Sommerville, NJ, USA) was used. In very difficult cases with multiple crossing scars or after multiple previous laparotomies, the ninth intercostal space in the midclavicular line on the left side was used as an entry for the Veress needle. A zero degree laparoscope was used. Two other 5 or 10 mm trocar sleeves were inserted under direct vision. In a few cases a fourth trocar was inserted. The entire abdominal cavity was examined laparoscopically.
A high flow CO_2 insufflator (Storz Tuttlingen, Germany) was employed, that allows suctioning when a bleeding was encountered. Smooth tipped atraumatic graspers were found to be essential for exposure by retracting abdominal organs. Unexpected pathology requiring treatment was addressed at the time of laparoscopy. In all procedures it was intended to lyse all adhesions between organs and the abdominal wall as well the adhesions between the organs themselves. Sharp dissection with scissors was the primary technique. Electrosurgery (Valleylab) and use of the argon beam laser (H.G.M. Inc. Lameris, Veenendaal, The Netherlands) as dissection technique have been used in a minority of cases. No profylactic measures were taken after the laparoscopic adhesiolysis in this group of patients. The follow-up period was at least 4 weeks. The patients were asked whether their pain had worsened, was unchanged, had lessened, or had disappeared.

Parameters

All factors that could possibly influence the occurrence of complications were analysed. Gender, age, duration of pain, number and type of previous abdominal operations, technique of adhesiolysis, and experience of the surgeon with the technique of adhesiolysis were recorded. Because of the wide range of duration of pain before the operation a subdivision in three groups was made: (1-6 months; 7-12 months and more than 12 months).
The kind of previous operation was allocated to one of three groups: appendectomy, gynaecological procedures (including sterilisation) and others. The surgical experience of each surgeon was analysed by comparing the outcome of the first 15 operations with the remaining

ones. Wound hematoma, hernia, and infection were defined as minor complications and bleeding in the abdominal cavity and perforation as major complications. Bleeding was recorded as a complication if more than simple local diathermy was necessary. Perforation was defined as a laceration of the wall of the bowel with a mucosal defect.
In addition a relation between the above-mentioned factors with the same subdivision in time and the feasibility of complete adhesiolysis was evaluated. Complete adhesiolysis was defined as full adhesiolysis between abdominal organs and the abdominal wall and between abdominal organs themselves. Almost complete adhesiolysis and enterolysis was defined as a complete adhesiolysis in the painful part of the abdomen as far as the instruments could reach, the remainder of the abdominal cavity being left untreated. The completeness of the adhesiolysis was divided in two groups: complete and incomplete. Almost complete adhesiolysis has been classified in the incomplete group. Laparoconversion immediately after the laparoscopy because of inability to introduce the other trocars safely was not defined as a complication but as a shortcoming of the technique. A conversion because of a perforation counts as a complication.
After a period of about 6 weeks we asked the patients during their visit to the outpatient department to rate their pain in 4 categories: worse, unchanged, less pain, and disappearance of pain. Less pain and disappearance of pain were classified as good results, unchanged and worse effect as bad results.
Percentages and continuous data were compared, respectively, with Fisher's exact test or the Mann-Whitney U-test. Multivariate analysis (logistic regression) was used to evaluate factors simultaneously which had a significant relation with outcome in univariate analysis. Two analyses were performed: one including all operations and one including only the first operation of each individual patient. As both analyses resulted in the same conclusions, only the first results are reported. P=0,05 (two-sided) was considered the limit of significance.

Results

Patients

Between 3 October 1991 and 3 September 1997, 157 patients underwent an attempted laparoscopic adhesiolysis (174 operations). There was no loss of short-term follow-up. All data for evaluation of the complications and the feasibility of the adhesiolysis were available. The mean follow-up time was 6 weeks.

Complications

No complications related to the introduction of the Veress needle or the Optiview trocar were seen. The Veress needle was introduced in the left ninth intercostal space in 20 patients with multiple scars on the abdominal wall without any difficulties. Only two minor trocar-related complications were seen, one bleeding at the trocar site leading to a hematoma and one infection of a trocar puncture site.

We noticed 16 major complications. Three patients suffered intra-abdominal blood loss. Two of them could be managed during the laparoscopy. In the other patient the bleeding was not recognised during the operation, but the patient recovered well after transfusion of 4 units of packed cells. In addition there were 11 visceral perforations, 3 of the colon and 8 of the small bowel. Four out of 11 perforations of the bowel (36%) were not recognised during the procedure. All four patients developed generalised peritonitis; half of them were recognised after two days and 2 others after four days. Another patient had bowel obstruction and was operated on the fourth postoperative day, which revealed a volvulus of the small bowel, which was treated by partial resection. Another patient had signs of peritonitis on the second postoperative day and had a second laparoscopy. No pathology was found and recovery was uneventful.

Table 1. *Factors associated with complications of laparoscopic adhesiolysis*

	Major complications:		
	No	*Yes*	*P value*
Number of operations:	158	16	
Factors:			
• Gender m. (%)	30	19	ns
• Age mean (years)	44 (SD 16)	55 (SD 18)	0,009
• Duration of pain (months) (median) (range)	17 9 (1– 150)	21 8 (1- 72)	ns
• Number of previous operations (median)	2 (0 - 21)	3 (1 - 23)	0,002
• Kind of previous operation (%) [1]			
- Appendectomy	41	31	ns
- Gynaecol. proc.[2]	44	69	ns
- Others	58	75	ns
• Instrument (%) [3]			
- Argon laser	20	25	ns
- Scissors	71	50	ns
- Electrodissection	25	19	ns
• Surgical experience			
- First 15 patients (%)	26	25	ns

[1] total percentage more than 100% because of more previous operations in many patients.
[2] among women.
[3] in some patients more than one technique was used.

Table 1 shows the influence of several factors on the major complication rate. The percentages of the complications in the three subgroups 1-6 months, 7-12 months, and more than 12 months were 8%, 11%, and 11%, respectively. Thus the conclusion was that the duration of preoperative pain had no effect on the risk of complications. The number of previous operations and the age of the patient significantly influenced the major complication rate.
Two of the above-mentioned patients died. One female had undergone a sigmoid resection for a malignant tumour 8 years before the adhesiolysis. Two months after the resection of the tumour she was operated upon for strangulation of the small bowel and a partial resection was performed. She returned on account of abdominal pain and underwent laparoscopic adhesiolysis. At laparoscopy a perforation of the small bowel occurred, which required minilaparotomy for closure. This patient died suddenly on the 12th postoperative day (autopsy was not permitted). The other patient died on the second postoperative day. Autopsy showed a fecal peritonitis due to a colon perforation, which had not been recognised during laparoscopic adhesiolysis.

TABLE 2. *Factors associated with the completeness of the adhesiolysis*

	Extent of adhesiolysis		
	Incomplete	Complete	P value
number of operations [1]	39	128	
Factors:			
• Gender m. (%)	21	32	ns
• Age mean (years)	45 (SD 16)	45 (SD 17)	ns
Duration of pain (months) (median)	12 (1-72)	9 (1-150)	ns
• Number of previous operations. (median)	2 (0-23)	1 (0-24)	0.004
• Kind of previous operation (%) [2]			
- Appendectomy	33	45	ns
- Gynaecol. proc.	45	49	ns
- Others	69	56	ns
• Instrument %			
- Argon laser	10	25	ns
- Scissors [3]	78	70	ns
- Electrocdissection'	46	18	0.001
• Surgeon`s experience			
- First 15 patients (%)	18	30	ns

[1] 7 patients were converted to laparotomy after laparoscopy without laparoscopic adhesiolysis.
[2] total percentage more than 100% because of more previous operations in many patients.
[3] more than one technique was used in some patients.

Completeness

In 128 out of 157 patients it was possible to perform a complete adhesiolysis of all abdominal organs. The adhesiolysis was incomplete in 39 instances. Twenty-seven of these had been classified as almost complete lysis. In 5 other patients we made a visceral perforation during the laparoscopic procedure which required laparotomy to suture the defect. We were not able to complete the adhesiolysis in 7 other patients (impaired view by light absorption because of diffuse blood clots on the peritoneal surface in 2 patients and no cleavage plane between the intestinal loops with too great perforation risk in 5 patients) and accepted the results. In one of them pain persisted and this patient developed an intestinal obstruction. After 3 weeks' conservative treatment a laparotomy was done and a small bowel resection performed (2 small bowel perforations and serosal tears during the laparotomic adhesiolysis).

In 7 patients we performed only a laparoscopy and were not able to start the adhesiolysis. Technical difficulties (insufficient light, too high pressure pneumoperitoneum) forced us to discontinue in 2 patients. In the other 5 patients (almost) the whole abdominal cavity was filled with adhesions. In these cases the other trocars could not be introduced at the same site as the camera. A laparoconversion was done in these 7 cases to perform a laparotomic adhesiolysis.

Table 2 shows the influence of factors that could interfere with the completeness of the adhesiolysis. The number of previous operations and the use of electrocoagulation technique were found to reduce significantly the success rate of complete laparoscopic adhesiolysis. The completeness of the adhesiolysis in the above-mentioned subgroups of the duration of the preoperative pain was 77%, 81%, and 74%, respectively. These figures demonstrate that the feasibility of adhesiolysis is not related to the duration of pain.

Table 3. *Laparoscopically confirmed concomitant pathology besides adhesions in the abdominal cavity and therapy in 6 out of 157 patients with chronic abdominal pain*

	Abnormality	Treatment
1.	Fecolith in appendix (palpable and visible)	Laparosc. appendectomy
2.	Neurinoma (confirmed by microscopy) around prolene suture	Laparosc. removal of neurinoma and prolene suture
3.	Inguinal hernia	Sec. hernioplasty
4.	Retained gallstones in omentum with inflammation after previous laparoscopic cholecystectomy	Laparosc. part. resection of omentum and extraction gallstones
5.	Adhesions around gallbladder and gallstones (missed cholecystitis)	Laparosc. cholecystectomy
6.	Liver cirrhosis with portal hypertension	Liver biopsy

Other pathology

In Table 3 concomitant abdominal pathology found during laparoscopy is recorded. Pathology other than adhesions was found in 4% of all patients.

Relief of pain

Table 4 shows the outcome of the responses of the patients with regard to the relief of pain. After laparoscopic adhesiolysis 80% of patients had good results, and 20% were classified as bad results. Incompleteness of the adhesiolysis did not affect this outcome.

Table 4. *Pain relief after laparoscopic adhesiolysis at the first follow-up visit, and the relation of relief with the completeness of the adhesiolysis*

	Good result		Bad result		Total
Incomplete adhesiolysis	31	(80%)	8	(20%)	39
Complete adhesiolysis	103	(80%)	25	(20%)	128
	134		33		167 *

* 7 patients with conversion after laparoscopy without laparoscopic adhesiolysis were not evaluated.

Discussion

In the past, treatment of extensive abdominal adhesions was considered to be too risky or too dangerous to undertake safely.[3] Ikard stated that critical analysis fails to extract the association of adhesions and intrinsic pain from the realm of myth. He considered bowel obstruction as the only indication for enterolysis and regarded a laparoscopic approach as inadequate and dangerous.[10] Recent data suggest that laparoscopy in patients with previous abdominal surgery is acceptable when performed by competent laparoscopists.[12] Others consider the outcome of adhesiolysis to be good or fairly good and therefore recommend laparoscopic adhesiolysis in cases of abdominal pain, provided other causes of abdominal discomfort have been eliminated. Roseff pleaded that pain in the abdomen should never be attributed to psychological or emotional causes unless the presence of organic pathology has been excluded by diagnostic laparoscopy.[18]

Safe establishment of a pneumoperitoneum in patients with previous abdominal surgery can be difficult. In those patients with multiple scars we inserted the Veress needle in the left ninth intercostal space and always obtained a satisfactory pneumoperitoneum. This unusual site was advised by Childers in patients at high risk for umbilical adhesions after a previous midline incision through the umbilicus.[2] Later during the study we sometimes used the Optiview trocar for introduction into the cavity under direct vision. Bonjer et al. reviewed the risks of introduction of the Veress needle and noticed 0,05% – 0,2% risk of visceral perforation. They

emphasised that often perforation was not recognised until postoperative peritonitis and proposed the use of an open technique with the Hasson trocar.[1]
In our series we noticed 9% major complications including 2 patients who died (1%). We were concerned by these results. The incidence of intestinal perforations which occurs during laparoscopic procedures for symptomatic adhesions is reported to occur in 5% to even more than 25% of patients.[4,7,8,17,20] The mortality with laparotomy in the treatment of mechanical adhesive bowel obstruction was 10% as described by Jeekel.[11] In a review article written by Tera and Aberg a 15,2% mortality was found for small gut laparotomic surgery.[19] At secondary laparotomies through the same incision 21% bowel perforations occurred. The number of previous laparotomies and the age of the patient appeared to be independent risk factors for bowel perforation.[21]
It must be remembered that in our series 4 out of 11 perforations of the bowel (36%) were not recognised during the procedure. Bowel injuries not recognised at the time of surgery can result from needle introduction, from trocar puncture, or from the adhesiolysis. The symptoms of peritonitis after a direct perforation are usually clear within 1 or 2 days. Thermal damage to the bowel may be another cause for bowel perforation. In these cases the clinical signs of perforation are usually seen after 4 days.[17]
We did not complete the adhesiolysis in 39 patients. In 27 of these patients we did not continue the procedure because we thought further adhesiolysis would not benefit the patient and the painful adhesion was supposed to be lysed. It is unclear whether nonobstructive adhesions between loops of bowel or adhesions between bowel and the parietal peritoneum can cause pain. The study of Mueller et al. indicated that not all abdominal adhesions do cause pain. They believe that only those adhesions which involve limitation of movement of the organs are likely to cause pain.[16] This supports the concept that even incomplete adhesiolysis can benefit the patient if the symptomatic bands are lysed. In our patient group we saw the same benefits, 80% relief or disappearance of pain, for those patients with incomplete adhesiolysis as for the patients with complete adhesiolysis. François reported 8.7% intestinal perforations due to trocar injuries and enterolysis. He stresses the importance of stopping enterolysis when the risk of perforation becomes too great because there is a reasonable chance that the responsible adhesion has already been lysed.[7,8] It is good to remember that multiple previous operations are an important reason for incomplete adhesiolysis and an important factor causing complications during laparoscopic adhesiolysis. We also believe that in difficult cases with progressive risk of complications it is better to accept an incomplete adhesiolysis and to wait for the possible relief of pain. If at all feasible we consider relaparoscopy to be indicated in those cases where pain persists. The aim of the operation should not be an abdominal cavity without adhesions but rather an asymptomatic patient.
Thirteen patients underwent a second adhesiolysis and four even a third procedure. The question arises whether this could have been prevented by using adhesion prevention medication. The literature shows controversial results of any preventive measures. De Iaco et al.[5] showed in a rabbit study a significant reduction in adhesion formation after the use

of a hyaluronic acid based gel as compared with oxidised regenerated cellulose and no treatment. Yarali et al., however, found in a rat study[23] that hyaluronic acid membrane was ineffective in reducing adhesion formation and reformation. In a study of West et al.[22] both hydrogel treatment and hyaluronic acid pretreatment reduced the mean extent of adhesion formation. However, after adhesiolysis only hydrogel could reduce the mean extent of adhesion reformation, while hyaluronic acid had no more effect than a control group with no treatment. There are drugs that can be used to prevent reformation of adhesions after (laparoscopic) adhesiolysis, but so far no prospective randomised study in patients has been done proving the benefit. The follow-up time is too short to allow final conclusions to be drawn about the benefit of laparoscopic adhesiolysis. A longer follow-up period is necessary.

In summary, laparoscopic adhesiolysis can be performed by surgeons skilled in the laparoscopic technique, but we were not able to complete the lysis in 23% of the patients. Nevertheless, the number of serious complications, often not noticed during the procedure, is substantial. This suggests the necessity for a careful postoperative follow-up of the patients. High-risk patients should not be discharged from the hospital the day after the operation. Greater age and a higher number of previous operations cause more complications, forcing the surgeon to a very careful selection of the patient for laparoscopic adhesiolysis. The morbidity and mortality are comparative with those of hemicolectomy, and that is a major operation.

We do know the risks, we do know the complications, we do know the technical difficulties, but we still do not know whether laparoscopic adhesiolysis will substantially benefit the patient. An editorial comment concerned with this difficult topic proposed that an ideal study would be a prospective trial randomising laparoscopic adhesiolysis and diagnostic laparoscopy.[14] Such a study was initiated in 1998.

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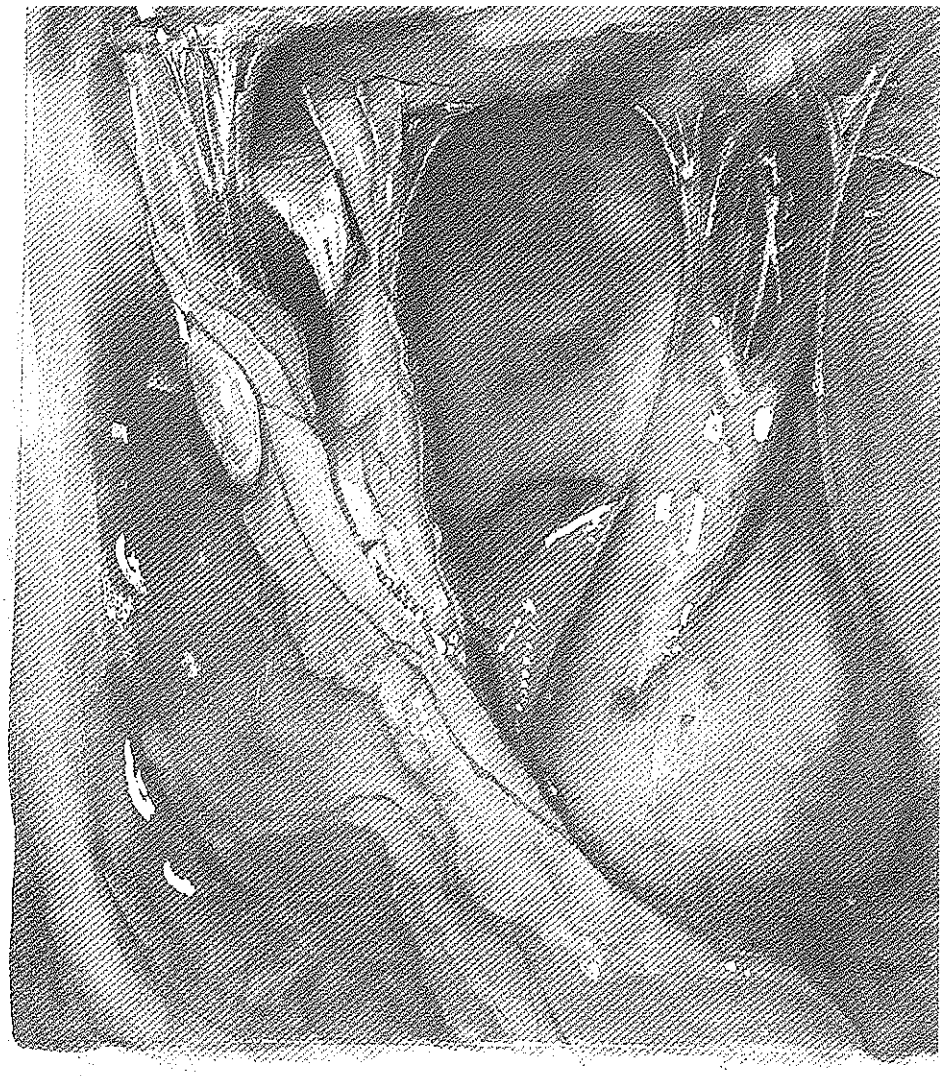

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Chapter 3

A prospective analysis of predictive factors on the results of laparoscopic adhesiolysis in patients with chronic abdominal pain

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Abstract

Purpose: Laparoscopic adhesiolysis for chronic abdominal pain is subject for criticism. In this prospective study we analyze factors which encourage or discourage the indication for therapeutic laparoscopic adhesiolysis.
Methods: Two hundred twenty-four consecutive patients with chronic abdominal pain underwent diagnostic laparoscopy, and in case of adhesions, adhesiolysis. Pain relief was assessed and the individual impact of variables on pain relief was determined.
Results: Laparoscopy was performed in 224 patients. Two hundred patients had only adhesions and underwent primary laparoscopic adhesiolysis. Three months after adhesiolysis 74% of patients were pain free or had less pain. The remaining 26% of the patients experienced no change (22%) or had more pain (4%). Female gender, older age and bowel perforation, leading to a laparotomy appear individual factors associated with less pain relief.
Conclusions: Laparoscopic adhesiolysis can be done (almost) completely in 92% of patients with adhesions. After laparoscopic adhesiolysis 74% of patients had good results and 4% had more pain. The complication rate is high.

Introduction

Laparoscopic surgery has been accepted as a technique for diagnostic and therapeutic procedures in general surgery. The value of diagnostic laparoscopy in patients with chronic abdominal pain has been documented.[1,2] The diagnosis could be established in 76% of 265 patients with chronic abdominal pain as described by Salky and Edye.[2] Chronic abdominal pain remains a continuing challenge and may be caused by the presence of intra-abdominal adhesions. The disturbed motility of the organs was held responsible for chronic abdominal pain caused by adhesions. Recently, Sulaiman et al. showed sensory nerve fibers in all peritoneal adhesions capable of conducting pain of their own.[3]

Almost all patients develop adhesions after an intra-abdominal procedure.[4] Ellis has classified intra-abdominal adhesions as normal physiology, except for those adhesions causing bowel obstruction.[5] Adhesions were responsible for 303,836 hospitalizations in the United States in 1994.[6] About 5% of all patients who have had an abdominal operation will suffer from the consequences of adhesions which include bowel obstruction, strangulation, intermittent acute or chronic pain and infertility.[7] There is no discussion about the indication for adhesiolysis in cases of obstruction or strangulation of the bowel, but adhesiolysis by laparotomy has never gained acceptance as a treatment modality for chronic abdominal pain. One of the reasons is the high complication rate during and after adhesiolysis. A postoperative mortality rate of 10% and more in adhesiolysis for acute bowel obstruction was found by Jeekel and by Tera.[8,9]

With growing experience in laparoscopic techniques, the field of laparoscopic adhesiolysis is being explored. A few articles have appeared, describing retrospectively the success rates and also the complications and the failures of laparoscopic adhesiolysis in patients with chronic abdominal pain.[1,10] So far, an analysis of several factors possibly influencing the outcomes has not been performed. Such an analysis can contribute to a better patient selection to improve the results or to diminish the failure rate. In this study, the impact of various variables on outcome of laparoscopic adhesiolysis has been assessed prospectively.

Patients and methods

Patients

Between October 1992 and January 2000, 224 patients underwent a diagnostic laparoscopy for evaluation of chronic abdominal pain at two district hospitals and one university hospital (Máxima Medical Center Eindhoven, Groene Hart Hospital Gouda and Erasmus Medical Center Rotterdam). Chronic abdominal pain has been defined as continuous or intermittent abdominal pain with daily intake of analgesics and a duration of at least three months. Most patients were referred by internists and few by general practitioners. All patients had been examined by a surgeon, and all women also by a gynecologist. Patient characteristics are summarized in Table 1.

Table 1. *Characteristics at baseline of 224 patients with chronic abdominal pain*

Age (years, mean)	46 [range: 6-81]	
Gender	f:	74%
	m:	26%
Pain factors	Duration of pain (months, median)	12 [range: 3-180]
	Site of pain	
	• Localized beneath a scar	85%
	• Localized in the same quadrant(s) as the previous operation	87%
	Presence of adhesions at the site of pain (quadrant of the abdominal wall)	
	• Adhesions between organs and the abdominal wall	98%
	• Adhesions between the organs themselves.	62%
Preoperative investigations	Blood tests	100%
	Urine analysis	100%
	Radiographic studies of small and large bowel	96%
	Colonoscopy	49%
	Ultrasound	91%
	CT scan	39%
	Ultrasound and CT scan	29%
Previous surgery (median)	2 [range: 0-23] SD: 2,23	213 patients
Kind of previous surgery	Appendectomy	47%
	Gynecological procedures: ovary surgery, hysterectomy (tube ligation excluded)	52%
	General surgery: bowel resection, stomach resection, splenectomy, cholecystectomy	57%

Patients with chronic abdominal pain were scheduled for a diagnostic laparoscopy if non-invasive investigation could not detect a cause for their pain. Except for 11 of these 224 patients, all had undergone previous abdominal surgery. In all these patients their pain was initiated after the previous surgery. Patients with an abdominal contusion were neither selected nor excluded.
If adhesions were present at laparoscopy, adhesiolysis was performed. Patients without adhesions and patients with adhesions with other pathology that could be the cause of chronic abdominal pain were excluded from this analysis of laparoscopic adhesiolysis.
All patients underwent laparoscopic adhesiolysis for the first time. The patients were informed that in case no other pathology than adhesions was found in the abdomen, the operation would be continued laparoscopically with the intent of a complete adhesiolysis. Four authors (DS, WvE, ORvD, HB) performed the operations; all have extensive experience in laparoscopic surgery.

Procedure

The diagnostic and therapeutic laparoscopy was done with the patient under general anesthesia. A urinary catheter and a nasogastric tube were not given routinely. To establish a pneumoperitoneum, the Veress needle was mostly used and inserted at a site devoid of scars. In very difficult cases with multiple crossing scars or after multiple previous laparotomies, the ninth intercostal space in the midclavicular line on the left side was used as an entry for the Veress needle. Sometimes the Hasson or the Optiview trocar (Ethicon Endo-Surgery, Cincinnati, OH, USA) was used. A two or three port approach with 5 or 10 mm trocar sleeves was established under direct vision. A fourth trocar was inserted in a few cases. A high flow CO_2 insufflator (Storz Tüttlingen, Germany) was employed, allowing suction when bleeding was encountered.

Smooth-tipped atraumatic graspers with a long bit were found to be essential for exposure of the abdominal organs (B. Braun Medical BV, Oss, The Netherlands). With this kind of graspers solid organs can be touched safely for further inspection. Their long bit enables the surgeon to grasp the bowel as much as possible in order to avoid pinpoint fixation of the bowel with its perforation risk. To identify all adhesions, the bowel was run through from Treitz ligament to the pelvic area. Sharp dissection with scissors was used in the vast majority of patients. Electrosurgery (Valleylab) as dissection technique has been used in a few cases. The argon beam laser (H.G.M. Inc. Lameris, Veenendaal, The Netherlands) was used in 10 patients in the beginning of the study but during the last few years ultrasonic dissection was preferred (Ethicon, Summerville, NJ, USA). Unexpected pathology requiring treatment has been addressed in the same procedure.

Data analysis

Gender, age, duration of pain, number and type of previous abdominal operations, technique, extent (completeness), complications of the adhesiolysis, and experience of the surgeon with the technique of adhesiolysis were considered as factors that might influence the results. The kind of previous operation was allocated to one of three groups: appendectomy, other general surgery and gynecological procedures (sterilization excluded). The extent of the adhesiolysis and enterolysis was divided in three groups: incomplete, almost complete and complete adhesiolysis. Complete adhesiolysis was defined as full adhesiolysis between abdominal organs and the abdominal wall and between abdominal organs themselves (enterolysis). Almost complete adhesiolysis and enterolysis was defined as a complete adhesiolysis in the painful part of the abdomen as far as the instruments could reach, the remainder of the abdominal cavity being left untreated. Incomplete adhesiolysis was defined as an inability to lyse the adhesions in the painful part of the abdomen. In the analysis, the extent of the adhesiolysis was allocated in two groups: complete and incomplete. Almost complete adhesiolysis was classified in the incomplete group.

Wound hematoma, hernia, and infection were defined as minor complications. Bleeding in the abdominal cavity and perforation of the bowel were classified as major complications.

Bleeding was recorded as a complication if transfusion was required. Perforation was defined as a laceration of the wall of the bowel with a mucosal defect. Conversion, because of inability to introduce safely the other trocars after the introduction of the optic trocar, was not considered as a complication nor as an incomplete result but as a shortcoming of the technique.
A conversion because of the necessity to close a bowel perforation was classified as a complication. The surgical experience of each surgeon was analyzed by comparing the outcome of the first 15 operations with that of the remaining ones.
At three months postoperatively, patients assessed their pain according to 4 categories: worse, unchanged, less pain and disappearance of pain. Less pain and disappearance of pain were classified as good results, unchanged and worse effect as bad results. A multivariate analysis was done to identify denominators of pain relief. This analysis was applied on two comparisons:

1: all good results (disappearance of pain and less pain) versus bad results (pain unchanged or worse)
2: disappearance of pain only versus the three other categories

Rates and continuous data were compared, respectively with Fisher's exact test or the Mann-Whitney U-test. Factors, that had a significant relation with outcome in univariate analysis were evaluated simultaneously using multivariate analysis (logistic regression). P=0.05 (two-sided) was considered the limit of significance.
The protocol was approved by all three Ethical Committees of the participating hospitals.

Results

Patients

A total number of 224 patients with chronic abdominal pain were scheduled for laparoscopy between 3 October 1992 and 3 January 2000. All these patients underwent a laparoscopic procedure without complications. Twenty-four patients were excluded for further analysis (Figure 1). Eight patients had no adhesions, although they were laparotomized before. Otherwise, 11 other patients were included having adhesions without previous abdominal surgery or trauma. All patients having other pathology underwent uneventful treatment of these disorders (Table 2).
In 6 patients only an incomplete diagnostic laparoscopy could be done without adhesiolysis because of shortcomings of the technique. In four of these patients, the whole abdominal cavity was occupied by adhesions in such a manner that adhesiolysis could not be initiated because of unreliable introduction of the other trocars under direct view of the camera (inaccessible abdomen). In another patient, the bowel was too dilated to deal with, and in the last patient, an internal hernia was the cause of impaired overview of the anatomy. A conversion to laparotomy was done in these six cases to perform an open adhesiolysis. All

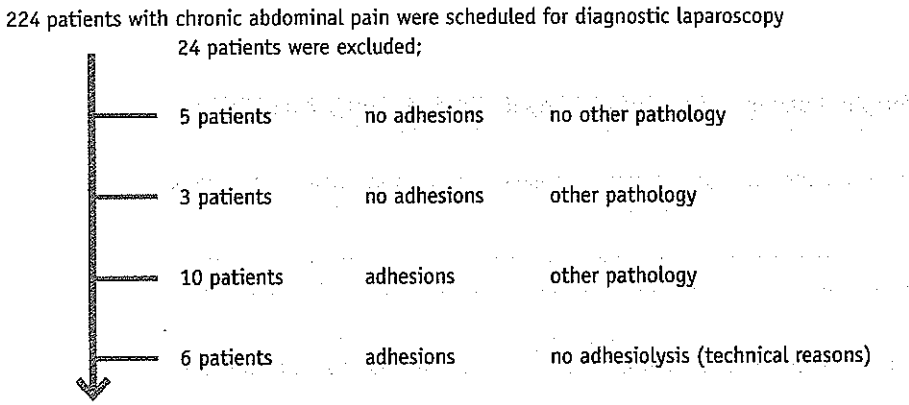

Figure 1. *patient selection*

Table 2. *Treatment of 13 patients (13/224) with other pathology besides adhesions*

Diagnosis	No. of patients	Therapy	Result
Faecolith appendix	1	Laparosc. appendectomy	No pain
Protruding prolene suture	1	Extirpation	No pain
Faecolith appendix and inguinal hernia	1	Laparosc. appendectomy and hernia repair. (t.e.p.)*	No pain
Liver cirrhosis	1	Liver biopsy	Unchanged
Malrotation asc. colon	1	Coecopexy	Unchanged
Inguinal hernia	1	T.e.p.*	No pain
Inflammatory mass around 2 dropped gallstones	1	Partial omentum resection	No pain
Chronic cholecystitis	3	Laparosc. cholecystectomy	No pain
Faecolith appendix	1	Laparosc. appendectomy	Less pain
Granuloma around suture	1	Excision	No pain
Para-umbilical hernia	1	Closure defect	No pain

* t.e.p.: total extraperitoneal endoscopic hernia repair

but one patient with an infection at a trocar site had an uneventful recovery. The patient with the dilated small bowel underwent a partial resection of the jejunum because of multiple serosal tears and an iatrogenic perforation of the small bowel. One year later this patient returned because of abdominal pain, and at laparoscopy numerous adhesions were found, which could be lysed laparoscopically. At the end of this procedure a bioresorbable membrane (Seprafilm™, Genzyme Corporation, Cambridge, MA, USA) was placed between the organs and the abdominal wall.

Adhesiolysis

A primary laparoscopic adhesiolysis was done in the remaining 200 patients. None of these patients had ever been operated upon before because of adhesions. Hundred forty-eight were female and fifty-two male. Their ages ranged from 6 to 81 years, with a mean age of 47 years. Introduction of the trocars was uneventful, and a complete adhesiolysis was attempted. The laparoscopic adhesiolysis was completed in 83%. An almost complete adhesiolysis was done in 9%, and an incomplete lysis in 8% of these patients.

All patients had previous abdominal surgery, except for 11 patients who had local adhesions of unknown origin. These 11 patients underwent complete adhesiolysis without complications. Six of them were free of symptoms after the adhesiolysis, and the other 5 experienced unchanged pain after two months follow-up.

Morbidity analysis shows 11 perforations of the bowel. In 7 of these patients a visceral perforation of the bowel was recognized during surgery. This forced us to do a conversion to close the defect. One of these 7 patients suddenly died 12 days after the operation. Autopsy was not allowed. Four of the 11 patients developed generalized peritonitis in the days after adhesiolysis. Two of them showed clinical signs after two days, and in the two other patients the signs of peritonitis were recognized after 4 days. These 4 patients were re-operated by laparotomy. The perforations were oversewn. Three of them had an uneventful recovery. One patient died. She was laparotomized because of septic shock two days after the laparoscopic procedure and died the same day. Laparotomy and autopsy showed a defect in the colon, which has caused a fecal peritonitis. All perforations were single per patient and were localized in the colon (3 times) and in the small bowel (8 times). Two of all patients died (2/224) resulting in a mortality rate of 1%.

Four patients had troublesome bleeding, but the bleeding could be managed during the laparoscopic procedure. Transfusion was not indicated. In one patient the bleeding was not recognized during the operation; this patient recovered well after transfusion of 4 units of packed cells. No trocar hernia but one trocar site infection was counted as a minor complication. No bladder complications occurred.

After a median follow-up of three months, laparoscopic adhesiolysis was found to benefit 74% of the treated patients. Their pain had disappeared (40%) or lessened (34%). The other 26% of the patients were dissatisfied, because they felt no change of their pain (22%) or had even more pain (4%) after the adhesiolysis.

In the first comparison a multivariate analysis was done to identify denominators of pain relief (disappearance or less pain) versus no relief (pain unchanged or worse). Table 3 lists these factors and their results. The 11 patients with a perforation had significantly worse results. No significant differences between the instrumental techniques were noticed. The use of the argon laser or the ultrasonic harmonic scalpel for dissection compared with sharp instrument dissection seems to have better results, but differences are not significant. The degree of experience with the technique of adhesiolysis of the separate surgeons also did not affect the

Table 3. *The influence of several factors on the results of laparoscopic adhesiolysis for chronic pain in 200 patients. Good result (disappearance or less pain) versus bad result (unchanged pain or worse). Data given are number of patients (percentage) or median (range)*

	Good result		Bad result		p-value
	Number	*(perc)*	*Number*	*(perc)*	
Patients	*148*	*(74%)*	*52*	*(26%)*	
Factors:					
• Gender (%)					0.46
male	41	(28%)	11	(21%)	
female	107	(72%)	41	(79%)	
• Age median (years)	46	(6-81)	45	(22-75)	0.47
• Duration of pain median (months)	12	(1-180)	14	(1-108)	0.54
• Number of previous operations (median)	2	(0-23)	2	(0-18)	0.77
• Type of previous operation (%)*					
- appendectomy	68	(46%)	27	(52%)	0.52
- gynaecological procedures **	52	(49%)	23	(56%)	0.46
- others	87	(59%)	28	(54%)	0.62
• Instrument (%)***					0.07
- argon laser	29	(20%)	5	(10%)	
- scissors	47	(32%)	24	(46%)	
- electrocoag.	33	(22%)	15	(29%)	
- ultracision	31	(21%)	6	(12%)	
• Completeness (%)					0.72
- complete	124	(84%)	41	(79%)	
- almost complete	13	(9%)	6	(11%)	
- incomplete	11	(7%)	5	(10%)	
• Major complications (%)					
- bleeding (number)	1		0		
- perforation (number)	5	(3%)	6	(12%)	0.03

* total percentage more than 100% because of more previous operations in many patients.
** percentages related to female patients only.
*** total number of patients is 190, treated with only one single technique.

outcome. No differences were found between the 3 surgeons. Neither (in)completeness of the adhesiolysis nor the kind of previous operations had significant effect on the relief of pain. In the second analysis (Table 4), comparisons were made between those patients who were *pain free* at evaluation and those who were not (less pain, unchanged or worse pain). This

Table 4. *The influence of several factors on the results of laparoscopic adhesiolysis for chronic pain in 200 patients. Pain free patients (disappearance of pain) versus not pain free patients (less pain, unchanged pain or worse). Data given are number of patients (percentage) or median (range)*

	Pain free *Number (perc)*	Not pain free *Number (perc)*	p-value
Patients	*79 (40%)*	*121 (60%)*	
Factors:			
• Gender. (%)			0.02*
male	28 (54%)	24 (46%)	
female	51 (34%)	97 (66%)	
• Age median (years)	44 (9-79)	47 (6-81)	0.02
• Duration of pain median (months)	12 (1-132)	12 (1-180)	0.24
• Number of previous operations (median)	2 (0-23)	2 (0-18)	0.77
• Type of previous operation (%)**			
- appendectomy	39 (49%)	56 (46%)	0.77
- gynaecological procedures***	21 (41%)	54 (56%)	0.12
- others	41 (52%)	74 (61%)	0.24
• Instrument (%) ****			0.12
- argon laser	19 (24%)	15 (13%)	
- scissors	25 (34%)	46 (40%)	
- electrocoag.	15 (20%)	33 (28%)	
- ultracision	15 (20%)	22 (19%)	
• Completeness (%)			0.19
- complete	69 (87%)	96 (79%)	
- almost complete	7 (9%)	12 (10%)	
- incomplete	3 (4%)	13 (11%)	
• Major complications			
- number (%)	3 (4%)	9 (7%)	0.37

* subgroup analysis: gender difference was only significant comparing males with females with previous gynaecological operations (P=0.005)
** total percentage more than 100% because of more previous operations in many patients.
*** percentages related to female patients only.
**** total number of patients is 190, treated with only one single technique.

analysis showed that the percentage of females who were pain free (34%) was significantly less than the corresponding percentage (54%) among males (p=0.02). Subgroup analysis however, showed that this difference was only significant in comparing males with females with previous gynecological operations (54% vs. 28%; p=0.005). It was also found that patients who were

pain free were generally younger as compared to those who were not pain free (median ages, respectively, 44 and 47; p=0.02). None of the other investigated factors were associated with the probability of being pain free. Multivariate analysis showed that age and being a female with prior gynecological operations were both independent factors which are related to the probability of becoming pain free.

Discussion

Adhesions are a substantial cause of hospitalization, mainly because of chronic abdominal pain, infertility and intestinal obstruction. In the USA, treatment of the complications accounted for 846.415 days of in-patient care and $1.3 billion for costs of hospitalization and surgical expenditures in 1994.[6] Less invasive surgical techniques for adhesiolysis by laparoscopic approach have contributed to a decreased hospital stay for the procedure itself as for the recovery time.[7] Adhesiolysis by laparotomy has never gained popularity because of high morbidity and the risk of recurrence of new adhesions. The recurrence rate of adhesive small bowel obstruction after previous adhesiolysis in open surgery is as high as 46%.[11] Laparoscopic surgical procedures are associated with less regrowth of adhesions compared to open surgery.[12] Adhesions do reoccur after laparoscopic surgery, but denovo adhesions are much less common.[13] Jung et al. described 36 patients with symptoms due to adhesions, who were treated by adhesiolysis in open surgery. More than half were satisfied. One death occurred because of a perforated gastric ulcer.[14] Open adhesiolysis appears not be safer than laparoscopic adhesiolysis. Open adhesiolysis in the treatment of mechanical adhesive small bowel obstruction may account for 3% (simple obstruction) up to 15 % mortality.[5,8,9] The complication rate in laparoscopic adhesiolysis for chronic abdominal pain is about 10%.[10] The risk of visceral injury during the blind introduction of the Veress needle and the first trocar is between 0.05% and 0.2%.[15] Preoperative sonography of adhesions, as recommended by Borzellino, is not sensitive enough to rely on, and was not used.[16] One surgeon (HJB) routinely used the Hasson technique, while the others used the blind introduction of the Veress needle, but always far away from the scar and operation field. The ninth intercostal was chosen as the preferred site for Veress needle introduction in those patients with previous surgery in the lower half of the abdomen. In the last 50 patients the blunt tip Optiview trocar has been used after establishing the pneumoperitoneum.

In our series of 200 patients 12 major complications (6%; 11 perforations and one bleeding) were seen during and after laparoscopic adhesiolysis. Serious morbidity (laparotomy, sepsis) was caused by a bowel perforation in 11 patients (5,5%). Two of these 11 patients died. The incidence of intestinal perforations, which occurs during laparoscopic procedures for symptomatic adhesions is reported to occur in about 10%.[10] About 40% of these perforations are not present or not recognized during the procedure and cause a life-threatening perforation-peritonitis afterwards.[17] These perforations might be caused by thermal lesions.

The ultrasonic technique is attended by much lower temperature, and causes probably less late perforations than with electrodissection. Mortality figures for laparoscopic adhesiolysis for chronic abdominal pain are not well known. The small numbers of patients in most series probably shade the incidence. Bowel perforations do also occur after laparotomy. Van Goor et al. described 21% bowel perforations in patients at secondary laparotomy through the same incision.[18]

The efficiency of diagnostic laparoscopy in patients with chronic abdominal pain has been shown by many authors.[1,2,19] The results of therapeutic laparoscopies for intra-abdominal adhesions reported about 80% satisfied patients after a short time follow-up.[1,10] In our series, a complete adhesiolysis could be performed in 83% of the patients with an early success rate of 74% (less pain or pain free) after three months. Results after a longer follow-up have also been reported by Schietroma who performed laparoscopic adhesiolysis on 41 patients with chronic abdominal pain and found 84% of patients who were symptom free or reported significant amelioration of their pain after a follow-up with a median time of 18 months (12-41 months).[20] Hallfeldt et al. (16 patients) showed the same results after a follow-up of 18 months.[21]

A relapse of pain was found by Saravelos in 26% of patients after laparoscopic adhesiolysis.[22] Kolmorgen described more relapses correlated with a longer follow-up.[23] The good results in the first trimester after surgery and worse results afterwards oblige one to refer to a placebo effect of laparoscopic adhesiolysis. Surgery can produce substantial placebo effects, which can be as high as 50%.[24] Moreover, the mean placebo score is correlated with the mean score for the active treatment.[24] This placebo effect is especially influenced by the expectations of the patient, and the quality of the doctor-patient relationship.[25] In our series, this psychogenic analgesia due to a powerful doctor-treatment placebo effect might play an important role in the ascertained pain relief.

The study was designed to find factors in patients with chronic abdominal pain (probably due to adhesions) to encourage or discourage a laparoscopic adhesiolysis. Comparing good versus bad results (first analysis), we could not detect a single factor that individually influenced the outcome except the negative effect of a perforation with conversion to laparotomy for closure of an iatrogenic bowel defect. A perforation causes significantly worse results with serious morbidity and mortality. This might be explained by the laparotomy itself and the short follow-up, but after at least 4 months of follow-up in these patients the outcome had not changed. Analyzing the probability of being fully free of pain after laparoscopic adhesiolysis (second analysis), a significant favorable effect was found in younger patients ($p<0.02$), while women operated before because of gynecological pathology were significantly less pain free than men ($p<0.02$).

In conclusion, other pathology was found in 6% of the patients and treatment of this pathology led, in 85% of cases, to good results. Therapeutic laparoscopic adhesiolysis for chronic abdominal pain was performed (almost) completely in 92% of 200 patients and has led to a majority of satisfied patients, who were pain free or had less pain. Patients with younger age

have a higher chance of being pain free after laparoscopic adhesiolysis, while women after previous gynecological operations were significantly less pain free than males.
Effort should be directed to reduce the 1% mortality rate (2/200) and the incidence of bowel perforations during laparoscopic adhesiolysis, which occurred in 5.5% (11/200) of our patients and contributed significantly to bad results.

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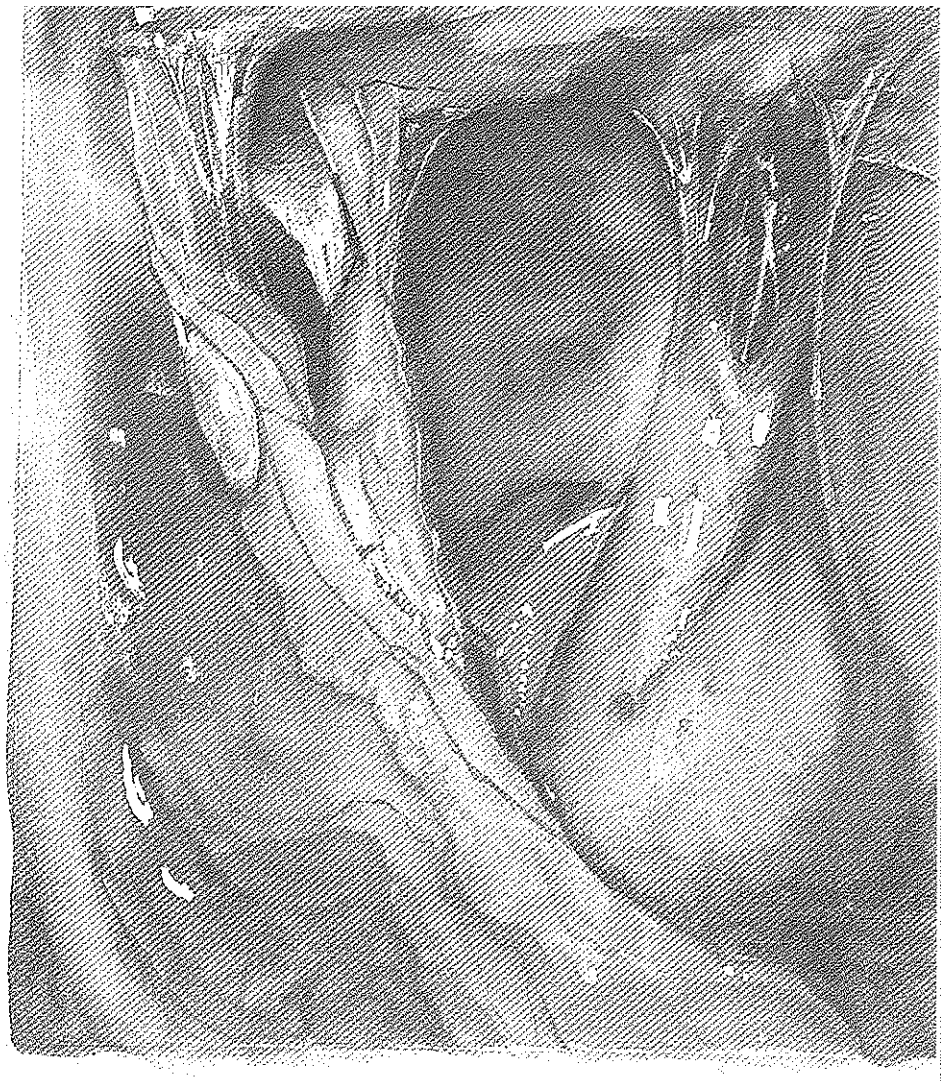

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Chapter 4

Safe laparoscopic adhesiolysis with optical access trocar and ultrasonic dissection
A prospective study

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Abstract

Background: The objective of this clinical study was to examine the feasibility, safety, and adequacy of hemostasis of combined use of an optical trocar and ultrasonic dissection in laparoscopic adhesiolysis in patients with chronic abdominal pain.
Methods: In 105 patients, identification of anatomic layers of the abdominal wall, establishment of pneumoperitoneum, completeness of adhesiolysis, hemostasis, complications and pain relief were studied.
Results: All abdominal wall layers could be determined during introduction as well as adherence of intra-abdominal organs at the introduction site. Ultrasonic dissection enabled an (almost) complete adhesiolysis in 103 (98%) patients and offered adequate hemostasis in 101 (96%) patients. Four perforations during laparoscopic adhesiolysis and no late (thermal) perforations were observed.
Conclusions: With an optical trocar a safe introduction site of the abdominal wall can be chosen. The ultrasonic technique offers a sound adhesiolysis with adequate hemostasis and fewer thermal perforations and adds to feasibility and safety of laparoscopic adhesiolysis.

Introduction

Laparoscopic adhesiolysis is a subject of ongoing debate. Doubt exists about the indication of laparoscopic adhesiolysis for chronic abdominal pain. Knowledge exists about the serious complications of laparoscopic adhesiolysis such as vessel and viscus perforation. The estimated frequency of these complications is between 5% and 25%.[22] Critical in the procedure is the needle insertion, trocar placement, and the adhesiolysis itself. Patients with previous abdominal operations pose a greater risk for perforations due to adhesive organs against the abdominal wall. Several safety measures for laparoscopic surgery have been proposed, such as subcostal insertion of the Veress needle,[17] use of an optical trocar,[10] radially dilating trocars,[2] and open introduction of the initial trocar.[3, 5, 18] The optical trocar (Optiview®, Ethicon, Endosurgery, Cincinatti, Ohio) is a blunt optical trocar, which is guided through the abdominal wall with the camera inside and controlled by the monitor. This device might combine the advantages of a safe and a fast penetration of the abdominal cavity.

Laparoscopic adhesiolysis with scissors is inconvenient because of bleeding. Electrodissection causes charring of tissue and delayed perforations because of its excessive heat production.[7,12,20,23] Bipolar electrosurgery has the advantage of reducing the electrosurgical complications but still has delayed thermal lesions.[23] The ultrasonic device for laparoscopic cholecystectomy was introduced by Amaral in 1994.[1] Several different laparoscopic procedures have been performed successfully with this device.[9, 23] The ultrasonically activated scalpel causes less heat production compared with electrocautery dissection, thereby theoretically lowering the risk of delayed perforations.

Thus far, no study has published the results of the use and safety of the optical trocar and the ultrasonic technique in laparoscopic adhesiolysis. In this prospective study the experience with the optical trocar and the ultrasonic device in laparoscopic adhesiolysis is described in patients with chronic abdominal pain and multiple previous laparotomies. The blunt introduction of the optical trocar, the identification of organs adhesive to the abdominal wall, and the lower heat production of ultrasonic dissection might reduce the complication rate of laparoscopic adhesiolysis.

Patients and methods

Patients

Patients with chronic abdominal pain were scheduled for a diagnostic laparoscopy if noninvasive investigation could not detect a cause for their pain. If adhesions were present at laparoscopy, adhesiolysis was performed. Chronic abdominal pain has been defined as continuous or intermittent abdominal pain with daily intake of analgesics and a duration of at least 3 months. All patients have been examined by a surgeon and all women also by a gynecologist. Patient characteristics are summarized in Table 1.

Table 1. *Patient characteristics at baseline*

Age (mean)	46 [range: 9–86]	
Gender	f: 88% m: 12%	
Duration of pain (months) (median)	20 [range: 3-240]	
Preoperative investigations	Blood tests	100%
	Urine analysis	100%
	Radiographic studies of small and large bowel	98%
	Colonoscopy	54%
	Ultrasound	90%
	CT scan	42%
	Ultrasound and CT scan	28%
Previous surgery (number) (median)	2 [range: 0-9] SD: 1.94	98 patients
Kind of previous surgery	Appendectomy	18 patients
	Gynaecological procedures: ovariectomy, hysterectomy; tube ligation excluded	15 patients
	General surgery: bowel resection, stomach resection, splenectomy, cholecystectomy	16 patients
	Combination of 2 of these kinds	41 patients
	Combination of 3 of these kinds	18 patients
Type of scar	McBurney incision	29 patients
	Pfannenstiel	20 patients
	Median laparotomy	77 patients
	Subcostal incision	29 patients
	Traverse incision upper abdomen	3 patients
Incidence of adhesions (number of organs involved with adhesions):		
Organs to organs (median)	2 (range:0-7)	
Organs to abdominal wall (median)	1 (range: 0-4)	

From September 1997 to February 2001, 105 patients underwent laparoscopic adhesiolysis. Ninety-eight patients had been operated before and 7 other patients were thought to have intra-abdominal adhesions due to previous abdominal trauma or inflammatory diseases. Concomitant pathology was diagnosed in 8 patients during laparoscopy (Table 2). All patients were operated by one surgeon (DJS) in a district hospital.

Table 2. *Concomitant pathology in 8 patients at diagnostic laparoscopy in 105 patients with chronic abdominal pain*

Diagnosis	No. of patients	Therapy
Incisional hernia	3	Mesh repair laparoscopically
Cholelithiasis	2	Laparoscopic cholecystectomy
Chronic appendicitis after appendicular mass	2	Laparoscopic appendectomy
Inguinal hernia dextra	1	Mesh repair laparoscopically

Surgical technique

The procedures were performed under general anesthesia. Neither nasogastric tubes nor urinary catheters were introduced routinely. For pneumoperitoneum a Veress needle was induced preferably caudally to the umbilicus. In case of a midline scar, the entry site was chosen left subcostally. In case of a traverse incision in the upper abdomen the Veress needle was introduced in the intercostal space just above the eighth rib in the midclavicular line on the left side. Proper placement was controlled with intra-abdominal pressure and with percussion of the abdominal wall. A pneumoperitoneum with carbondioxide was obtained at a maximum pressure of 12 mm Hg.

Optical trocar

The distal fold of the umbilicus was preferred as introduction site of the initial trocar (Optiview®, Ethicon, Endosurgery, Cincinatti, Ohio) in patients without a midline incision. Otherwise the introduction took place at least 5 cm lateral of the scar away from the expected location of adhesions. After a 12-mm skin incision the trocar was introduced bluntly by slowly rotating the device through all layers of the abdominal wall. The darkness of the abdominal cavity filled with carbondioxide was seen as a big black spot as background of the parietal peritoneum when pressure on the optical trocar was reduced from time to time during penetration. If not seen, an adherent organ at the puncture site was likely and the introduction was attempted elsewhere. After penetration of the parietal peritoneum the inner canula of the optical trocar was withdrawn, leaving the outer part for introduction of the optics.
Two instrumental ports (Ethicon, Cincinnati, Ohio) were guided through the abdominal wall under direct vision. These two trocars were placed beside the optic (0° optics; Storz, Tuttlingen, Germany) for easy handling. After checking for possible complications of the Veress needle, the abdominal cavity was examined with two atraumatic clamps (Aesculap) for adhesions and for concomitant pathology.

Ultrasonic device

The ultrasonic device (UD) (Ultracision®, Ethicon Endo-surgery Cincinnati OH) is an ultrasonically activated scalpel composed of a generator, a transducer and a functional tip vibrating with a frequency of 55.550 Hz, which can be extended with several devices. The

ultrasonic device has a 10-mm diameter and was introduced through a 10-mm trocar. The ultrasonic hook was used as dissection device and is reusable.
A complete adhesiolysis was intended. Sufficient tension on the organs is necessary to maximize the effect of ultrasonic adhesiolysis. If bowel loops were very adherent with the parietal peritoneum, the latter was released from the abdominal muscles and not lysed from the bowel. The lysis of different organs should be done slowly to allow sufficient time to seal small vessels. Small bleedings were dealt with by the UD; if not successful, monopolar electrocautery was used. Concomitant pathology was also treated with the UD during the same procedure.

Assays

The feasibility of the optical trocar was judged by the visualization of all anatomic layers of the abdominal wall and recognition of the black hole. Its safety was measured by the number of perforations caused by its introduction.
The efficiency of the ultrasonic dissection was evaluated by the necessity of other devices for hemostasis and for adhesiolysis. The feasibility of the technique was assessed by the completeness of the adhesiolysis. Complete adhesiolysis was defined as release of all adherent abdominal organs from the abdominal wall and between abdominal organs themselves (enterolysis). Almost complete adhesiolysis was defined as a complete adhesiolysis in the painful part of the abdomen as far as the instruments could reach; adhesions out of reach of the instruments were left untreated. To lyse these adhesions more trocars should have been introduced to reach them. Incomplete adhesiolysis was defined as inability to lyse the adhesions in the painful part of the abdomen. The safety of the technique was represented by the number of complications. Bleeding with necessity for blood transfusion and perforation of viscera were classified as complications.
Pain was assessed 2 and 6 months after laparoscopic adhesiolysis. Patients classified their pain according to four categories: worse, unchanged, less pain and disappearance of pain.

Results

Optical trocar

The main outcomes of both devices are summarized in Table 3. In 102 of the 105 patients (97%) a pneumoperitoneum was established by the Veress needle. Potential complications of the Veress needle in the abdominal cavity due to its placement were optically controlled after introduction of the optical trocar and the optics; no complications were noted. In three patients transperitoneal position of the Veress needle was doubtful and the optical trocar was introduced uneventfully without a previous pneumoperitoneum.
Using the optical trocar, during penetration, every single layer of the abdominal wall could be well recognized and differentiated from each other in every patient (100%). In case of a pneumoperitoneum, a black (dark) hole could be seen in all patients but one just before

Table 3. *Results of the use of optical trocar and ultrasonic dissection in 105 patients, who underwent laparoscopic adhesiolysis for chronic abdominal pain*

Procedure	No. of patients successfully applied	No. of patients not successfully applied	Number of complications	Remarks
Use of optical trocar: feasibility and safety	105 all abdominal layers were recognised	none	none	one recognised adherent organ
Use of ultrasonic device: efficiency	101	4 electrocautery used for hemostasis	none	no other devices necessary for dissection
Use of ultrasonic device: feasibility	103 (almost) complete adhesiolysis	2 incomplete adhesiolysis		1 incomplete accepted (conversion because of perforation)
Use of ultrasonic device: safety	101	4	no bleeding, 4 perforations	1 perforation not related to dissection

penetration of the parietal peritoneum, and after that the penetration of the abdominal cavity was completed. In this single patient the penetration of the abdominal wall was done successfully at another site. Subsequent laparoscopic evaluation revealed an adherent omentum at the first puncture site. No complications related to introduction of the optical trocar were noticed.

Ultrasonic dissection

No instruments other than UD were necessary for adhesiolysis. In four patients electrocautery had to be used for sufficient hemostasis of bleeding from larger omental vessels.

A complete adhesiolysis could be achieved in 97 patients (92%). In six patients the laparoscopic adhesiolysis was almost complete. In these six patients the adhesiolysis was not terminated because of shortcomings of the ultrasonic dissection technique. An incomplete laparoscopic adhesiolysis was done twice. One of these patients, a 47-year-old male, had a small bowel loop fixed at the aorta; the risk of vascular damage of the aorta was considered too high and the laparoscopic procedure was initially converted. The other patient was a 53-year-old female who had been operated three times; a perforation in the small bowel was made during dissection of the bowel from the pelvic floor. A laparotomy was done, the defect closed, and the adhesiolysis completed.

Four serious complications were noticed; three small bowel perforations and one bladder perforation. One of them is the described 53-year-old female. In another patient, a 45-year-old female after previous abdominal hysterectomy, a perforation was made in the ileum with spill of bowel contents. The defect was closed laparoscopically with endogia stapling technique. The next day septic shock (Clostridium perfringens) developed with skin necrosis of the lateral part of the abdominal wall and multiple organ failure. At laparotomy no perforation was present.

Table 4. *Pain relief in 105 patients 3 and 6 months after laparoscopic adhesiolysis (percentages)*

Pain relief	3 months (%)	6 months (%)
Disappearance	31	20
Less	39	39
Unchanged	22	31
Worse	8	10

The patient recovered and was discharged 3-weeks later. In the third patient (female, 58y) with a history of sigmoid diverticulitis and six previous operations in the lower part of the abdomen, a traction perforation occurred of a jejunal loop during dissection; the defect was closed laparoscopically with the endostapler technique. Three days after the adhesiolysis a fecal discharge from the vagina was noticed, due to a fistula between the sigmoid colon and the vagina. Conservative treatment was successful.
The fourth major complication was a bladder perforation, made during the dissection of a small bowel loop from the bladder. The defect was sutured laparoscopically and a bladder catheter was inserted for 1 week. Recovery was uneventful. No delayed perforations were seen in this series.

Pain relief

Two months after laparoscopic adhesiolysis 70 % of patients (74/105) had less pain or were pain free. Six months after lysis 59% of patients (62/105) were improved. All results are summarized in Table 4. The six patients with almost complete adhesiolysis had results not different from those of patients after complete adhesiolysis.

Discussion

Optical trocar

The traditional approach of the abdominal cavity for laparoscopic surgery is a closed trocar penetration after the establishment of a pneumoperitoneum with a Veress needle. Visceral lesions in closed introduction have been reported between 0.06 and 0.4%.[11] Half of these visceral lesions are caused by the trocar and consist of damage to the small bowel ranging from superficial serosal damage to perforation. However, all other intra-abdominal organs may also be involved and these have a high mortality rate of 5% up to 15 %.[16] The rate of major vascular injuries with the closed technique varies from 0.02% to 0.24%.[11] Vascular lesions are mostly caused by the Veress needle and in a minority of cases caused as a consequence of trocar introduction.[16]
The eighth intercostal space as the site for the Veress needle has been chosen three times to avoid adhesions after a previous traverse incision in the upper abdomen. We found an easy introduction due to the short passage and adherent parietal peritoneum. This site is at least 5 cm away from the diaphragm. Childers has chosen the left ninth intercostal space after median laparotomies and has recommended this as a safe site in patients with high-risk subumbilical adhesions.[6]

Very large randomized studies might show differences in safety of a specific trocar. Catarci et al., after evaluation of nearly 13,000 laparoscopic procedures, found the open approach to be the safest way with minimal risk of visceral and vascular injury (0.09%) versus 0.27% complications with an optical trocar. They did not mention either the indication for the use of an optical trocar, or its type of the tip (blunt or sharp introduction). They stressed its learning curve.[5] Hashizume emphasizes that with the open Hasson technique only the vascular and visceral risks of the Veress needle and of the initial trocar introduction are diminished and that some visceral lesions are made by the second and following trocars even if introduced under direct vision (0.02%).[11] Radially expanding trocars have peritoneal access by dilatation rather than by dissection. The smaller instrument for introduction has a potential advantage for fewer complications but this has not been proven.[2] The cost of an optic trocar is equal to that of the usual disposable trocar. For adhesiolysis we prefer disposable second and third trocars because the glide of a disposable trocar is more convenient for multiple very accurate movements.

During this study the optical trocar was used in patients with multiple previous abdominal operations and no complications related to the introduction were experienced. The penetration of the optical trocar through the abdominal wall is easy to perform and its use hardly has a learning curve, but this can also be due to the authors' experience with laparoscopic surgery. In almost all patients (102/105) a previous pneumoperitoneum could be established. Even when a pneumoperitoneum cannot be achieved, the optical trocar access is safe. String et al. used this trocar without a pneumoperitoneum in 650 different laparoscopic procedures with two small-bowel and gallbladder perforations (0.3%).[25] This technique avoids the complication risk of the Veress needle puncture, but misses the black hole as indication of distance between abdominal wall and abdominal organs and one has to rely on the movements of the bowel to differentiate the parietal from the visceral peritoneal layer. In our hospital the optical trocar has also been used without a previous pneumoperitoneum in 50 patients with morbid obesity and lap band placement without complications. Lifting the abdominal wall does not change the position of the peritoneum in relation to the intra-abdominal organs.[4]

Ultrasonic dissection

Ultrasonic dissection technology involves the application of ultrasound to the tissues producing three effects - cavitation, coagulation, and cutting - which act synergistically. The feasibility of these properties of the ultrasonic dissection for laparoscopic adhesiolysis has not been published. The great advantage of UD is the simultaneous dissection and hemostasis and therefore minimal need for exchange of instruments during the procedure with decreased operating time as a result.[8] In four patients electrocoagulation had to be used to control bleedings from larger (omental) vessels. Ohtsuka et al. experienced reliable hemostasis with minimal thermal damage harvesting the internal mammary artery with ultrasonic dissection.[21] Although coagulation with ultrasonic dissection seems slower than with electrosurgery, its result in hemostasis is equal.[14]

In 98% of our patients a complete or almost complete adhesiolysis could be achieved. In two patients the adhesiolysis was incomplete because of vascular risk of the aorta and because of a bowel perforation and the necessity of a conversion. These results do not differ from those of electrodissection. With this technique an (almost) complete adhesiolysis was obtained in 93% of patients (162/174). In 12 patients (7%) the dissection was incomplete and accepted because the perforation risk of further lysis of very adhesive small bowel loops with electrodissection or scissors was thought to be too high.[26]

In this series no bleeding complications were seen. Four perforations were made (one not related to dissection) and recognized during the dissection. This 3,8% (4/105) incidence of perforations is low compared to the literature in which visceral perforations during laparoscopic adhesiolysis have been reported in up to 25% of patients.[22] In these reports 40% of bowel perforations were not recognized during the operation. These late perforations might have been caused by thermal lesions due to high temperature (570°F) of the electrodissection device. In this series no late perforations were diagnosed, probably because of the lower temperature of the tip (180°F) and the minimal lateral energy spread of the UD. Meltzer et al. confirmed this in a porcine model.[19] Morphological changes of the cystic duct after sealing with ultrasonic technique happen within the first 1.5 mm of the cutting edge.[13] In this series no patient died, but there was one patient with multiple organ failure; Reich, however, has reported mortality figures in laparoscopic adhesiolysis up to 5%.[22]

Ultrasonic dissection has some concomitant advantages. In patients with a pacemaker the ultrasonic device can be used without additional security measures,[24] it produces no smoke and the lower temperature of the tip of ultrasonic dissection causes less charring and less tissue necrosis. A 5-mm UD will have an advantage in separating closely fixed organs and more precise dissection might be expected.

We found 70% cured or improved patients 3 months after laparoscopic adhesiolysis. These results seem worse after 6 months. Pain relief is difficult to compare with other series because of different studies and pain scores. Several investigators found about the same results, varying between 45% and 84% patients with less pain or without pain.[7, 20] Kolmorgen and Schulz showed 38% of patients with less pain after 2 years follow-up. This confirms worse results after a longer follow-up period.[15]

In conclusion, besides a carefully chosen entry site, the optical trocar identifies all layers of the abdominal wall and adherent organs and contributes to safe abdominal access in patients after multiple previous laparotomies. Ultrasonic dissection is a very feasible technique for laparoscopic adhesiolysis and might reduce the risk of bowel perforations by preventing the incidence of late (thermal) perforations.

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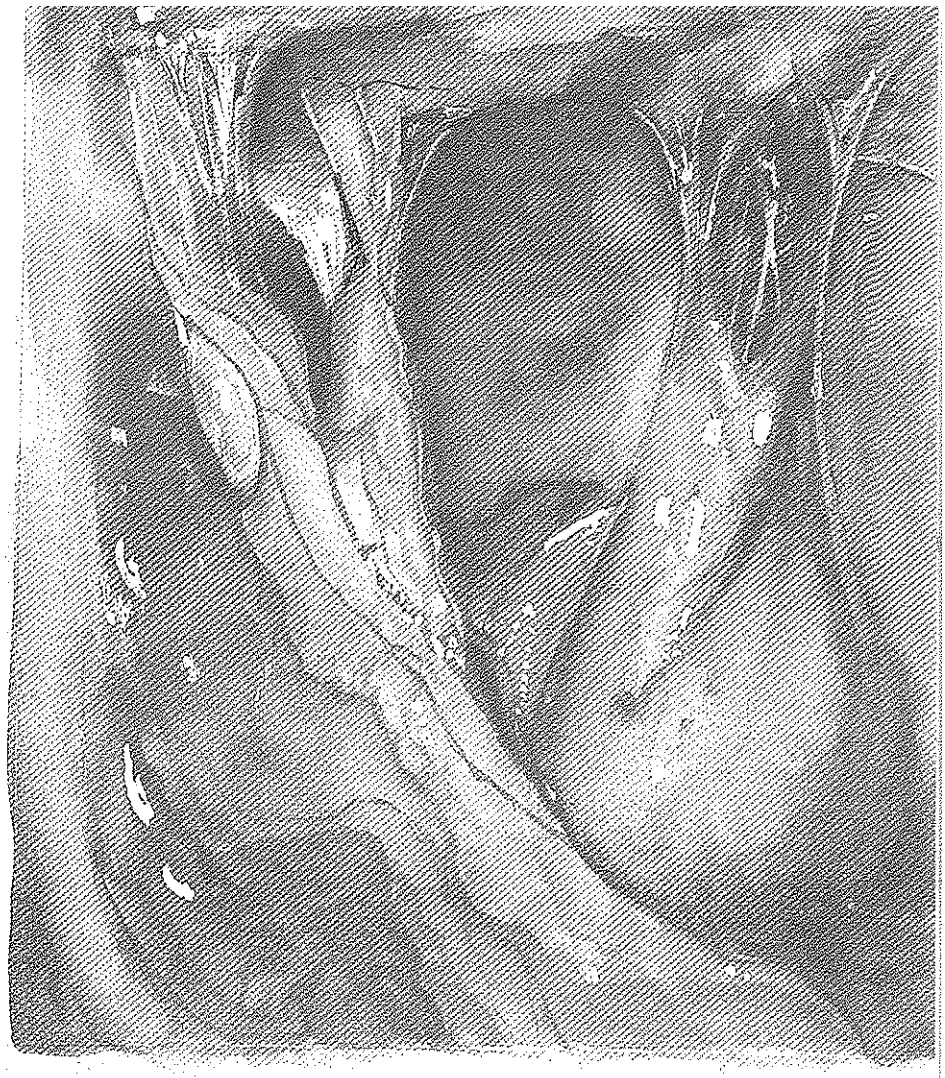

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Chapter 5

Reduction, regrowth and denovo formation of abdominal adhesions after laparoscopic adhesiolysis A prospective analysis

Original article
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Abstract

Objective: Evaluation of any persistent reduction of incidence, extent and type of abdominal adhesions after laparoscopic adhesiolysis in patients with chronic abdominal pain after previous surgery.
Design: Prospective study.
Subjects: Patients with relaparoscopy (24) after primary laparoscopic adhesiolysis (368 patients).
Interventions: 368 patients underwent laparoscopic adhesiolysis because of chronic abdominal pain. Regrowth and denovo abdominal adhesions were determined in a qualitative and quantitative way in 24 patients, who underwent after the first laparoscopic adhesiolysis a second look procedure because of recurrent pain after a mean follow-up of 16 months.
Main outcome measures: Reduction of incidence, extent, type and severity of abdominal adhesions between organs and the abdominal wall, and denovo adhesion formation after laparoscopic adhesiolysis.
Results: Incidence, extent, type and severity of abdominal adhesions between organs and the abdominal wall are significantly reduced after laparoscopic adhesiolysis. After adhesiolysis of adhesions between organs themselves, no significant reduction could be demonstrated. Denovo adhesions were present in 5 (5/24) patients.
Conclusions: Laparoscopic adhesiolysis results in a significant reduction of adhesions between organs and the abdominal wall. Denovo adhesions do occur in about 20% of patients.

Introduction

Adhesions of the visceral and parietal peritoneum are the consequences of surgical mechanical trauma and desiccation of these peritoneal surfaces.[5,9] Damaging of the peritoneal layers results in release of growth factors and cytokines and the synthesis of thrombin and fibrinogen, the start of a fibrin network. A key fibrinolytic enzyme, tissue type plasminogen activator (tPA), is also released from the peritoneum and stimulates the solution of this fibrin network.[8] Somehow, the fibrinolysis is not powerful enough and the fibrin network persists and will form permanent adhesions. Ellis et al. and Luijendijk et al. reported the formation of permanent adhesions from these fibrin bands in 68 –100% of patients after one or more laparotomies.[5, 14]
Surgery for adhesions seems contradictionary. Adhesions do develop after each laparotomy and the number of adhesions increases the more laparotomies have been done.[23] So open surgery will not diminish the number of adhesions, and is not the solution of this problem.
Laparoscopic surgery induces less surgical trauma, less introduction of foreign material in the abdominal cavity like glove powder, uses fewer instruments inside the abdomen, has lower risk of contamination, needs a minimum of surgical entrance wound and so might avoid most causes responsible for adhesion formation in laparotomic surgery. Indeed clinical and experimental studies show fewer adhesions after laparoscopic operations compared with the open technique.[1, 6, 10, 12, 13, 15, 16, 19, 22]
Theoretically, laparoscopic adhesiolysis might be the answer for symptomatic adhesions, because fewer adhesions are induced compared with the open technique. To determine whether or not laparoscopic adhesiolysis permanently reduces the number of adhesions we re-evaluated 24 patients after laparoscopic adhesiolysis and could assess the regrowth of adhesions and denovo adhesion formation at second look laparoscopy.

Patients and methods

Patients

From January 1992 till January 2000, a total of 368 patients underwent laparoscopic adhesiolysis. Diagnostic laparoscopy was performed in patients suffering from chronic abdominal pain (358) or bowel obstruction (10) likely to have been caused by adhesions due to previous abdominal surgery. Chronic abdominal pain was defined as continuous or intermittent pain for at least one month. If adhesions were present, laparoscopic adhesiolysis was performed. Patients younger than 18 years old, and patients with current treatment by psychologist or psychiatrist, and patients using laxatives, sedatives, morphines, antipsychotics, antidepressants or central nervous stimulating drugs were excluded. To exclude other abdominal pathology than adhesions multiple non-invasive investigations were performed prior to laparoscopy. Ultrasound was almost invariably done besides radiographic studies of the small bowel and colon. A minority of patients underwent CT scan, colonoscopy, gastroscopy and ercp.

All patients were operated by four laparoscopically experienced surgeons in three hospitals. Ninety-eight percent of patients had a follow-up period of at least one year after each operation. Eight percent of patients were complicated, predominantly because of iatrogenic bowel perforations. Two patients (0,5%) died as a consequence.
Gender, age, duration of pain, number and type of previous abdominal operations, location, extent, type of adhesions were recorded in each patient beside factors that could possibly determine pain relief, and factors that might influence the occurrence of complications. Endpoints of the study are pain relief, complications, safety of technique, and recurrence rate of adhesions after laparoscopic adhesiolysis. The first three endpoints were analysed separately. In this study the risk of recurrence and denovo formation of adhesions after laparoscopic adhesiolysis is analysed.

Twenty six of these 368 patients were reoperated and could be analysed for recurrent adhesions. Re-laparoscopy because of chronic abdominal pain was only performed at least six months after the previous laparoscopic adhesiolysis and only after a relapse of pain after a three months period with less pain or without pain. In case of new adhesions a second (laparoscopic) adhesiolysis was performed. Two patients were excluded from analysis. One patient because of postoperative bleeding and another one because of a fever period from unknown origin after the initial laparoscopic adhesiolysis. It was assumed that these postoperative events could induce adhesions themselves. The remaining twenty-four patients underwent a subsequent laparoscopy (23 patients) or laparotomy (1 patient) for recurrent abdominal pain (22), recurrent bowel obstruction (1) and gastrocolic fistula (laparotomy), and were subject of this study. All 24 patients (22 females and 2 males, mean age 51 years) had been operated previously by laparotomy (mean 3,1 laparotomies (range: 1-6)) for various reasons (Table 1) at least one year ago. No abdominal interventions were performed between the laparoscopic adhesiolysis and the subsequent laparoscopy or laparotomy. The mean time between laparoscopic adhesiolysis and the second laparoscopy or laparotomy was 16 months (range: 2-54). In three patients the initial laparoscopic adhesiolysis was not complete. One patient asked to lyse only the adhesions in the painful part of the abdomen, and in another patient with bowel obstruction only the obstructive bands were lysed. In the third patient extensive laparoscopic adhesiolysis was performed during a three hours session only in the lower half of the abdomen and the procedure for the upper half was planned two months later. In these three cases only the lysed part of the abdomen was evaluated.

Table 1. *Kind of surgery (74 laparotomies) in 24 patients previous to first laparoscopic adhesiolysis*

	Number	%
Appendectomy	15	20
Cholecystectomy and stomach surgery	15	20
Bowel surgery	12	16
Gynaecological surgery	22	30
Other surgery	10	14
	74	100

Surgical technique

All procedures were performed under general anaesthesia. No urinary catheters nor nasogastric tubes were introduced routinely. The Veress needle was used to establish a pneumoperitoneum (maximum pressure 12 mm Hg) and was inserted at a virgin part of the abdominal wall. The Optiview® trocar (Ethicon, Summerville, NJ, USA) was used as initial trocar for the optic system. In two cases with uncertain proper placement of the Veress needle the abdominal cavity was penetrated directly with the Optiview® trocar without a pneumoperitoneum. Proper placement of the next two or three portals were optically controlled. A high flow CO_2 insufflator (Storz, Tuttlingen, Germany) was employed. In the first 5 patients of this study (till 1997) electrotechnique was used for adhesion dissection, from then on an ultrasonic device (Ultracision®, Ethicon, Summerville, NJ, USA) was preferred.

Adhesion assessment

Adhesions were assessed between organs and the abdominal wall, and between the organs themselves by one surgeon for location (incidence), extent, type and severity. Incidence was defined as the number of organs involved. The extent of the adhesions between organs themselves was scored by counting the individual adhesional bands (Table 2). For the assessment of the extent of the adhesions between organs and the abdominal wall, the latter was divided in 4 quarters. The extent of these adhesions was scored as a percentage of that quarter covered by adhesions (Table 2). In case more quarters were involved, the extent scores of the different quarters were added. The type of adhesions was determined according to Zühlke [25] (Table 3). If different types were present, the highest type was scored. The severity of adhesion formation was calculated by multiplying the extent and type of the adhesions.[13,24] Regrowth is defined as new (recurrent) adhesion formation at sites where adhesions were present at first evaluation. Denovo adhesions are defined as new adhesions, which were not present (at that site) at first evaluation. Laparoscopic adhesiolysis related data included complications and completeness of the adhesiolysis. Complete adhesiolysis (and enterolysis) was defined as a division of all adhesions between abdominal organs and the abdominal wall and all adhesions between abdominal organs themselves (enterolysis). If not all adhesions were lysed, the dissection was incomplete.

Statistical analysis

All data were collected prospectively. Analysis was done with the Statistical Package for the Social Sciences (SPSS, Chicago, Illinois, USA) software. Percentages were compared using Fisher's exact test and continuous variables with the Mann-Whitney's test. The incidence, extent, type and severity of adhesions at subsequent laparoscopy were compared with the adhesions present at the first laparoscopic adhesiolysis using Wilcoxon's signed rank test. The p-values given are two sided; p=0.05 was considered as limit of significance.

Table 2. *Scoring model of extent of adhesions between organs and between organs and the abdominal wall*

Extent score	Adhesions between organs	Adhesions between organs and the abdominal wall (per quarter)
	Number of adhesions	Covered percentage
0	No adhesions	No adhesions
1	1	Covering less than 25%
2	2	Covering between 25 and 50%
3	3	Covering between 50 and 75%
4	4	Covering more than 75%
5	5	
6	More than 5 or multiple adhesions	

Table 3. *Type of abdominal adhesions. Classification of abdominal adhesions according to Zühlke* [25]

Zühlke type	Characteristics
1	filmy adhesion, easy to separate by blunt dissection
2	stronger adhesion, blunt dissection possible, partly sharp dissection necessary; beginning of vascularisation
3	strong adhesion, lysis possible by sharp dissection only; clear vascularisation
4	very strong adhesion, lysis possible by sharp dissection only, organs strongly attached with severe adhesions; damage of organs hardly preventable

Results

Patients

All 24 patients had adhesions between abdominal organs and the abdominal wall at first adhesiolysis and 5 were free of them at second adhesiolysis (Table 4). Nine patients had no adhesions between intra-abdominal organs at first adhesiolysis and at second look in 13 cases. These differences are not statistically significant. Three patients were completely free of adhesions at second look and 21 patients had regrowth of pre-existing adhesions or denovo adhesions. All procedures were uneventful.

Regrowth of adhesions

The number of organs involved with adhesions (incidence) is shown in table 4. The small and large bowel and the omentum were mostly involved with adhesion formation between organs as well as between organs and the abdominal wall.

Table 5 shows the differences between incidence, extent, type and severity of adhesions at first and at second laparoscopic adhesiolysis. Significant reduction of incidence, extent, type and severity was found after laparoscopic adhesiolysis of adhesions between organs and the abdominal wall, but not after lysis of adhesions between organs themselves.

Table 4. *The number of organs involved with adhesions (incidence) in 24 patients at first and second laparoscopic adhesiolysis*

	adhesions between organs* themselves		adhesions between organs and the abdominal wall	
	First adhesiolysis (15/24 pat.) [1]	second adhesiolysis (11/24 pat.) [1]	First adhesiolysis (24/24 pat.) [2]	second adhesiolysis (19/24 pat.) [2]
Liver	1	1	3	2
Stomach	-	-	3	1
Small bowel	17	13	8	5
Large bowel	8	6	12	5
Omentum	5	4	14	12
Female organs	3	2	0	1
Bladder	6	6	0	0
Incidence	40	32	40	26

* in case of adhesions between the same kind of organs, the organ is counted twice.
[1] 15 patients had adhesions between organs at first adhesiolysis, and 11 patients had adhesions between organs at second adhesiolysis.
[2] all 24 patients had adhesions between organs and the abdominal wall at first adhesiolysis, while nineteen patients had this kind of adhesions at second adhesiolysis.

Table 5. *Reduction of adhesions after laparoscopic adhesiolysis in 24 patients*

Adhesions between organs:	First adhesiolysis	Second adhesiolysis	P value
Incidence (number of organs)	40	32	0.293
Extent (mean)	2.42	1.54	0.054
Type (mean)	2.04	1.46	0.146
Severity (mean)	8.54	5.33	0.066
Adhesions between organs and abdominal wall:			
Incidence (number of organs)	40	26	0.005
Extent (mean)	2.67	1.58	0.001
Type (mean)	2.88	1.92	0.002
Severity (mean)	8.17	4.04	0.001

Denovo adhesions

In 5 patients new or more adhesions were present at second laparoscopic adhesiolysis at sites where they were not or less present at first laparoscopic adhesiolysis (denovo adhesions): In two out of nine patients, who had no adhesions between abdominal organs at first adhesiolysis, adhesions were present between organs at second look. In another patient the extent, type and severity of the inter-organ adhesions had a higher score at second laparoscopic adhesiolysis than before which points to extension of the pre-existing adhesions. More adhesions to the abdominal wall at second adhesiolysis appeared in one patient and one trocar site adhesion was found in another patient at second look.

Other 344 patients.

To show that these adhesion-related outcomes are not divergent from the adhesion data of the other 344 (368-24) patients, their results are described:

Adhesions between organs were present in 70% of these 344 patients. The mean extent of these adhesions is 2.32, with a mean type classification of 2.03 and a mean severity score of 8.47. Adhesions between organs and the abdominal wall were demonstrated in 97% of patients, with a mean extent of 2.62, with a mean type classification of 2.83 and a severity score of 8.12. All these outcomes do not significantly differ from those of the selected group of patients.

Discussion

Trauma to the parietal and visceral peritoneum during surgery is considered as a major cause of inevitable adhesion formation.[5] Although Risberg [18] concludes that surgeons can minimise trauma by using minimal invasive surgery, this may not be a panacea for adhesion prevention and laparoscopes may cause as much or more peritoneal trauma as the surgeon's fingers.[3] Our choice for blind introduction of the Veress needle in patients selected for adhesions seems contradictionary. Hashizume et al. reported a risk between 0.06 and 0.4% of visceral lesions due to closed introduction; but half of these lesions were caused by a trocar and not by the needle itself.[7] In all 368 patients the Veress needle was placed without complications. The entry site was far away from the area of expected adhesions, and in difficult cases the left ninth or even the eight intercostal space seemed to be a convenient site for safe introduction.[21]

Little evidence exists for less adhesion formation after laparoscopic surgery compared with laparotomy. However, animal studies have shown not only a reduction in adhesion formation but also anatomic differences in adhesions compared between open and laparoscopic surgery. Laparoscopic Nissen fundoplication in the rat leads to less postoperative adhesion formation (less extensive and less severe) than with the open procedure. The adhesions in the laparoscopic group were of the parietal type rather than visceral adhesions between organs.[13] Tittel et al. did similar observations comparing laparoscopic and laparotomic cholecystectomy in dogs.[22] In a pig model Reissman et al. demonstrated minimal adhesion formation after laparoscopic anterior resection compared with the open procedure.[17]

Also in humans a reduction in adhesion formation could be demonstrated. Semm et al. showed with diagnostic laparoscopy 50% reduction of adhesions in favour of laparoscopic surgery after previous abdominal open and laparoscopic operations for gynaecological procedures.[20] In the study of Polymenas et al. a diagnostic laparoscopy was performed after laparoscopic and open cholecystectomy and a significant lower rate of adhesions was noticed in favour of laparoscopic cholecystectomy.[16] These studies also show denovo adhesion formation after laparoscopic surgery although less than with open surgery.

No studies have been done to evaluate differences between adhesion (re)formation after open and laparoscopic adhesiolysis. With laparoscopic adhesiolysis a reduction in severity of

adhesions is induced by the adhesiolysis itself, but regrowth and denovo adhesions should also be expected, although possibly to a lesser degree than with open adhesiolysis.
Second look procedures have been performed in women, evaluating reformation of adhesions after laparoscopic gynaecological surgery in particular laparoscopic adhesiolysis for infertility.[2] This present study is the first prospective analysis of regrowth and denovo formation of adhesions after previous laparoscopic adhesiolysis.
Five patients demonstrated denovo adhesions. Two of these cases might be disputed because adhesions were subjectively classified as more extensive at sites where they have been previously. Despite denovo adhesions, mean values for incidence, extent, type and severity are decreased after laparoscopic adhesiolysis. These differences are only significant for adhesions between organs and the abdominal wall.
These 24 patients were reoperated because of recurrent chronic pain. We realise having induced an important study bias in the group of 24 patients, ultimately operated upon, although the quantity and quality of the adhesions in these selected 24 patients were not different from the group of 344 patients. This critique may however be interpreted in the opposite way: when a substantial reduction is obtained in adhesion extent and severity in patients with recurrent pain, then this reduction will probably be present or even more prominent in patients without complaints. This last conclusion, being a hypothesis should have to be substantiated by a control group before being accepted. For us it was too difficult to obtain the permission of patients to perform a second look laparoscopy if they do not exhibit complaints any more.
No data are available of adhesion reformation after laparotomic adhesiolysis. In general, adhesion formation is progressive the more laparotomies have been done.[4, 14]
We conclude that in this series despite regrowth and denovo formation of adhesions, laparoscopic adhesiolysis reduces permanently the quantity and quality of adhesions between abdominal organs and abdominal wall.

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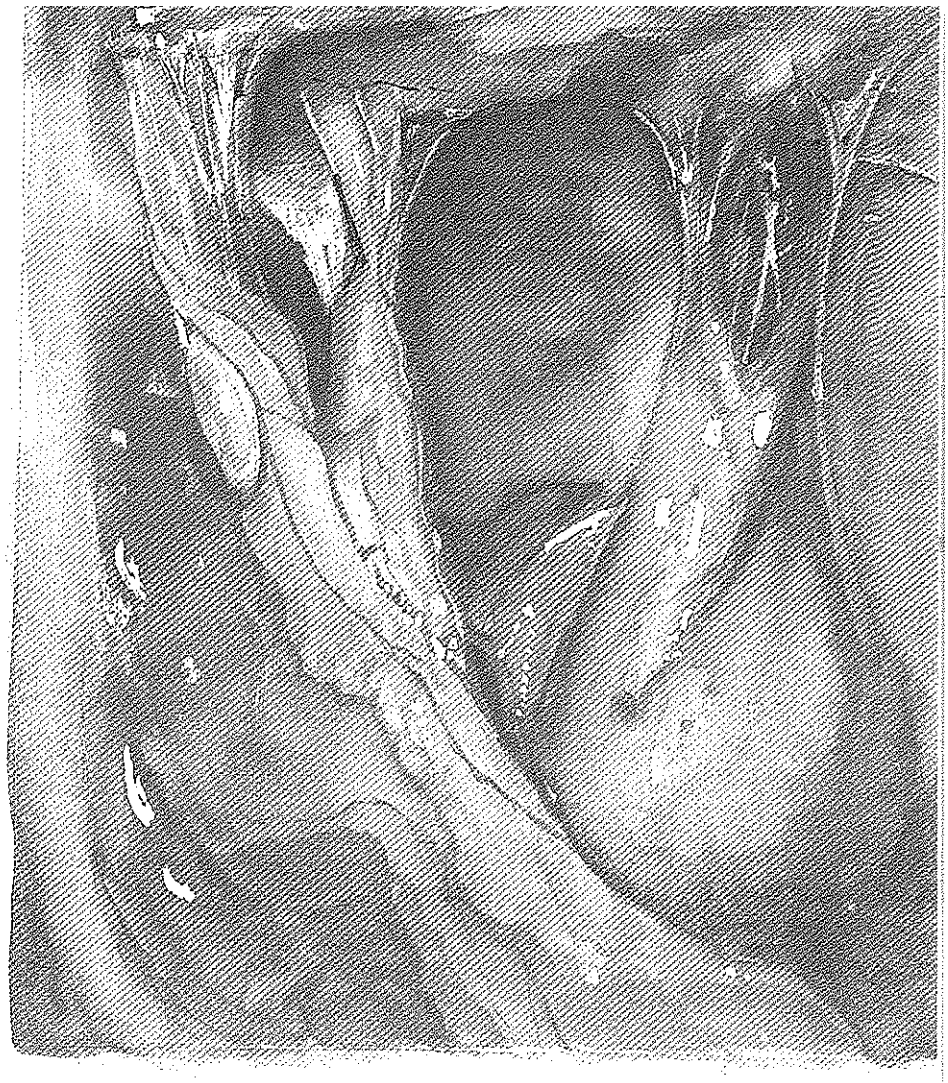

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W.W. Vrijland
et al.

Chapter 6

Fewer intraperitoneal adhesions with use of hyaluronic acid-carboxymethylcellulose membrane

Introduction

Prevention of the formation of adhesions during surgery entails reducing surgical trauma and avoiding contamination of the abdominal cavity with foreign materials. Other means have been sought to reduce postoperative adhesions. Theoretically, a mechanical barrier between adjacent tissues could provide a way of reducing adhesion formation by preventing tissues and organs from adhering to each other. Regeneration of damaged peritoneum is completed within 7 days after surgical trauma.[1] To avoid the persistent presence of foreign material within the abdominal cavity and still attain the intended effect, a temporary barrier not resolving within 7 days is preferable. HAL-F Bioresorbable Membrane (Seprafilm; Genzyme Corp., Cambridge, MA, USA) was developed to serve as a mechanical barrier between surgically damaged tissues. Resorption of this biodegradable membrane starts after 7 days. In animal studies and in one randomized clinical trial, it has been shown that Seprafilm reduces the incidence, extent and severity of postsurgical adhesions.[2]

The incidence of adhesions after (partial) colectomy is high, so this procedure provides a suitable model for studies of adhesion prevention.[3,4] A Hartmann procedure with second-stage restoration of the continuity of the colon was chosen as a model to examine the effectiveness of Seprafilm membrane.

The aim of this prospective clinical randomized multicenter trial was to assess the effectiveness of this antiadhesions membrane in reducing the number, incidence and severity of adhesions in patients with diverticulitis or obstruction of the rectosigmoid.

Randomized trial

Between April 1996 and September 1998, all patients requiring a Hartmann procedure for diverticulitis or obstruction of the rectosigmoid were randomized to receive Seprafilm™ or to serve as a control patient at eight participating general hospitals.
Patients were not included if they were pregnant, or had carcinosis peritonei, had received any other investigational product, or had their abdomen irrigated by povidone-iodine, corticosteroids, heparin, salicylates, non-steroidal antiinflammatory drugs, dextran or antibiotics. If patients were likely to require reoperation within 3 weeks after Hartmann's procedure or if concomitant disease would probably interfere with restorative surgery, they were not included. Patients were informed about the trial both orally and in writing and signed informed consent. Randomization was achieved by opening a sealed envelope at the time of surgery marked by study number and containing directions whether to use Seprafilm or not. Randomization was obtained according to a balanced computer-generated list, stratified by hospital.
Seprafilm is a membrane developed for the temporary separation of tissues mechanically damaged during surgery. It is composed of chemically modified sodium hyaluronate, a glycosaminoglycan, and carboxymethylcellulose. No adverse or toxic effects have been described with the use of these substances. Seprafilm is commercially available in a size of 12.7x15.2 cm. To evaluate the effectiveness of Seprafilm, a two-stage surgical abdominal procedure was chosen, allowing the application of the anti-adhesions material at the initial surgery and the evaluation of adhesions formation at follow-up surgery. We evaluated the effectiveness of Seprafilm after the Hartmann procedure.
Age, sex, weight, height, primary clinical diagnosis, medical history, medications and abdominal surgical history were noted at admission. Obesity was defined as a body mass index of 30 or more. Abnormalities found during physical examination were documented.
Surgery was performed according to Hartmann: the sigmoid colon was resected, a colostomy was created, and the rectal stump was closed. Documented factors related to the procedure included length of midline incision, description and length of colon segment resection, method of closure of the rectal stump, whether the omentum had been removed, and whether the peritoneum had been sutured. Duration of surgery, complications and additional surgical procedures were also noted. If the patient was randomized to receive Seprafilm, the number of membranes applied under the midline incision and in the pelvic area was noted. In the pelvic area, the rectal stump was covered with Seprafilm. The organs directly underlying the midline incision just before closing the wound were covered as well. The surgeon was asked to state whether adhesions were present at the time of initial surgery and to score their location, extent and type. In addition, the surgeon was asked whether the patient had peritonitis and, if so, whether the spread through the abdominal cavity was local, locoregional, or diffuse.
After surgery, wound healing was observed. A mild wound infection was defined as redness surrounding the laparotomy wound, a moderate wound infection was one that produced pus,

and a severe infection was defined as wound dehiscence and wound edge necrosis. Results of the histologic examination of the resected colon were documented.

Evaluation of adhesions was performed during surgery for closure of the colostomy and reanastomosis of the rectal stump. Adhesions were assessed by a surgeon unaware of the patient's random assignment. Evaluation of the incidence, extent and type of adhesions in the midline was performed through laparoscopy. After mobilisation and repositioning of the colostomy in the abdomen, a 10-mm trocar was inserted in the colostomy opening after partial closure. Subsequently, the abdominal cavity was insufflated.

Adhesions from the midline incision to intraperitoneal sites or organs were identified, and the extent and type were scored. Extent was assessed by estimating the overall length of the incision covered by adhesive tissue by palpating the skin surface along the midline incision, while laparoscopically viewing the peritoneal surface of the anterior abdominal wall. The margins of the adhesions along the midline incision were demarcated on the skin surface and the corresponding incisional length was measured. The type of adhesions was determined according to Zühlke et al [5] (Table 1). If subsequent laparotomy was performed, laparoscopical findings were confirmed. Within the pelvic cavity, the incidence of adhesions was evaluated under direct vision or laparoscopically. Organs and intraperitoneal sites involved in a pelvic adhesion were scored. The extent of adhesions in the pelvis was assessed by the percentage of adhesions covering the area, (Table 2) and the type was assessed according to Zühlke.

Evaluations were recorded on videotape allowing postoperative masked reevaluation by two independent observers. Severity of adhesion formation was calculated by multiplying extent and type of adhesions for both locations. The extent of adhesions to the total midline incision was multiplied by the estimated type of adhesions and evaluation of the pelvis was done according to the method described before.

Table 1. *Macroscopic classification of abdominal adhesions according to Zühlke*

Zühlke type	Characteristics
1	filmy adhesion, easy to separate by blunt dissection
2	stronger adhesion; blunt dissection possible, partly sharp dissection necessary; beginning of vascularization
3	strong adhesion; lysis possible by sharp dissection only; clear vascularization
4	very strong adhesion; lysis possible by sharp dissection only; organs strongly attached with severe adhesions; damage of organs hardly preventable

Table 2. *Score of extent of adhesions in the pelvic area*

	Extent
0	No adhesions present
1	Mild: covering up to 25% of the pelvis
2	Moderate: covering 26-50% of the pelvis
3	Severe: covering 51-75% of the pelvis
4	Extreme: covering more than 75% of the pelvis

Statistical analysis was done with SPSS (Chicago, Illinois, USA) software. Percentages and continuous variables were compared using the Fisher exact test and Mann-Whitney test. Increases in the incidence and severity of adhesions after surgery compared with the adhesions present at initial surgery were analyzed using the Wilcoxon signed rank test. The probability values given are two-sided; p=0.05 was considered as the limit of significance. The analysis was by intention-to-treat.
The protocol was approved by the Ethical Committee of the University Hospital Rotterdam and separate approvals were obtained from the Ethical Committee of the Catharina Ziekenhuis Eindhoven; the Diakonessehuis Utrecht; the Reinier de Graaf Gasthuis, Delft; the Groene Hart Ziekenhuis, Gouda; the St. Clara Ziekenhuis, Rotterdam; the Merwede Ziekenhuis, Dordrecht; and the Westfries Gasthuis Hoorn.

Results of trial

A total of 71 patients were randomized, of which 4 patients were found to be ineligible. One patient had dementia of which the surgeon was unaware, and three patients withdrew after randomization. Of the remaining 67 patients, 32 patients were randomized to receive Seprafilm and 35 to serve as controls. In the Seprafilm group, 11 patients were lost to follow-up: 6 underwent relaparotomy within three weeks after initial surgery, 2 died, and 3 had concomitant disease not allowing the second-stage procedure. In the control group, 14 patients were lost to follow-up: 5 underwent relaparotomy within 3 weeks, 5 died and 4 had concomitant disease not allowing the second-stage procedure.
A total of 42 patients could be evaluated, 21 in the Seprafilm group and 21 in the control group. An intention-to-treat analysis was performed. Groups were comparable regarding preoperative data (Table 3). No significant differences were found regarding medical history and preoperative physical examination. Use of medication showed no differences between groups. Fourteen patients in the Seprafilm group and 15 in the control group had no history of previous abdominal surgery. No significant differences were found between the groups for frequency and type of previous abdominal surgery.
Intraoperative data did not differ significantly (Table 4). The resected colon segment classified as 'other' in the Seprafilm™ group, was an ileocoecal resection. The procedures classified as 'other' in the control group were a subtotal colectomy, a left hemicolectomy, and a colostomy for a rectovaginal fistula that had developed after a low anterior resection for a villous adenoma of the rectum. Preexisting adhesions were identified in nine patients in the Seprafilm group; five of these patients showed adhesions to the sites involved in future evaluation. Preexisting adhesions were present in five patients in the control group; three of these patients showed adhesions to the sites involved in future evaluation. These differences were not significant.
One patient received three Seprafilm membranes at the midline incision, 16 patients received two membranes and 4 patients received one membrane. The latter four patients had an incision

Table 3. *Preoperative data*

		Seprafilm™ group	Control group
Age (years, median) (range)		59 (34-81)	60 (28-85)
Sex (n)	male	13	11
	female	8	10
Obesity	yes	2	2
	no	16	12
	not described	3	7
Diagnosis	diverticulitis	17	17
	other	4	4

Table 4. *Intraoparative data*

		Seprafilm™ group	Control group
Length of midline incision (cm) (mean±SD)		20 ± 4.2	20 ± 6.8
Resected colon segment (number)	sigmoid	20	18
	other	1	3
Length of resected segment (cm, median, range)		18 (10-60)	15 (10-45)
Closure rectal stump (number*)	sutured	6	8
	stapled	18	17
Drain placed (number)	yes	10	10
	no	11	11
Peritoneum sutured	yes	3	0
	no	18	21
Duration of surgery (min, median, range)		103 (75-180)	100 (60-260)
Adhesions present (number)	yes	9	5
	no	12	15**
Peritonitis	no	4	5**
	local	7	6
	locoregional	6	5
	diffuse	4	4

* three rectal stumps in the Seprafilm™group and four rectal stumps in the control group were sutured and stapled
** data of one patient missing

length at initial surgery of 15, 15, 25 and 30 cm, indicating that the area under the midline incision had only been partially covered by Seprafilm. In the pelvic area, two membranes were applied in nine patients, one membrane was applied in nine patients and no membrane was applied in three patients.

Complications consisted of three accidental bowel perforations, occurring in two patients in the Seprafilm group and in one patient in the control group. Accidental injury to the bladder occurred in one patient in the control group.

Additional surgical procedures during the Hartmann procedure occurred in 14 patients. In the Seprafilm group, three patients underwent appendectomy, two patients underwent surgical decompression of the small bowel, one patient had his peritoneal dialysis catheter removed, and one patient underwent resection of an ovarian cyst and partial small bowel resection for accidental bowel perforation. In the control group, three patients underwent additional appendectomy, two patients underwent splenectomy, one patient underwent suturing of a iatrogenic bladder injury, and one patient underwent partial small bowel resection for an abscess in the mesentery. Median blood loss was 350 ml (range 10-1.200) in the Seprafilm group and 400 ml (range 50-2.000) in the control group.

Postoperative wound healing was abnormal in eight patients in the Seprafilm group, and in three patients in the control group. In the Seprafilm group, four patients had a mild to moderate wound infection with redness of the wound and/or pus discharge, two patients had an abscess related to the midline incision that required drainage and two patients showed a dehiscence; they were treated conservatively. In the control group, three patients had an abscess, two were related to the midline incision and one was related to the colostomy. The abscesses were treated with drainage. One patient with a wound infection and one patient with a dehiscence received antibiotics. Pelvic healing was abnormal in one patient in the control group; this patient appeared to have a fistula from the small bowel to the vagina that required reoperation.

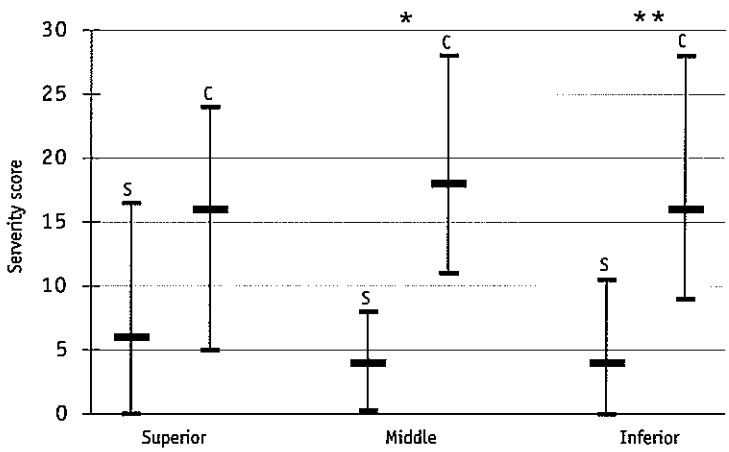
In the Seprafilm group, histologic examination of the resected tissue showed diverticulitis in 16 patients and colon carcinoma in two patients; in two patients no histologic examination was performed. In the control group, histology showed diverticulitis in 13 patients, colon carcinoma in one patient, ischemic colitis in one patient; in 6 patients no histologic examination was performed.

Time between initial surgery and follow-up surgery did not differ significantly between groups: In the Seprafilm group the median interval was 5 months (range 2-16) and in the control group the median interval was 4 months (range 1-30).

A significant increase was found for both groups in the severity of adhesions at second-stage surgery compared with initial surgery, in terms of both the total midline incision ($p=0.007$) and the pelvic area ($p=0.013$). The incidence of adhesions found during evaluation did not differ significantly between the groups (Table 5). The severity of adhesions in the superior, middle and inferior segment of the midline incision was evaluated in all patients, as well as in the pelvic area. Significant differences in severity between groups were found for the middle and inferior segment of the midline incision and the total midline incision (Figure 1). In addition, the pelvic

Table 5. *Incidence of postoperative adhesions assessed during evaluation at laparoscopy*

Adhesions to the midline incision		Seprafilm™ group (N)	Control group (N)	p-value
Superior segment	yes	14	17	0.48
	no	7	4	
Middle segment	yes	15	20	0.09
	no	6	1	
Inferior segment	yes	14	18	0.28
	no	7	3	
Total midline incision	yes	19	21	0.48
	no	2	0	
Adhesions to the pelvic area				
	yes	16	19	0.41
	no	5	2	



S = Seprafilm™group

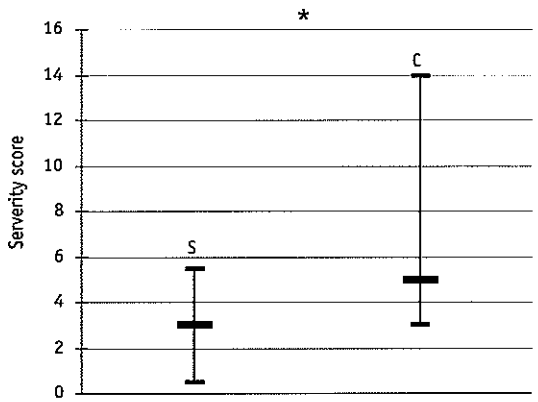
C = Control group

* p < 0.0001

** p = 0.002

Figure 1. *Severity of adhesions per site (extent x type), superior, middle and inferior part of midline incision (median, 25 percentile, 75 percentile)*

area showed a significant difference between groups regarding the severity of adhesions (Figure 2). Performing a per-protocol analysis by excluding the patients from the Seprafilm group that had not received any membranes during initial surgery showed comparable figures (p=0.043).



S = Seprafilm™group

C = Control group

* p < 0.0001

FIGURE 2. *Severity of adhesions in the pelvis (extent x type) (median, 25 percentile, 75 percentile)*

The median severity of adhesions for the total midline incision showed a significant difference: 18 (25th-75th percentile: 7-44) for the Seprafilm group and 50 (25th-75th percentile: 41-67) for the control group (p=0.002).

Videotapes of the second-stage surgery were made in 26 patients, 10 in the Seprafilm group and 16 in the control group. Evaluation of adhesions to the total midline incision was possible for 10 patients in the Seprafilm group and 12 in the control group. Evaluation of adhesions in the pelvis was possible for 6 patients in the Seprafilm group and 10 in the control group. Severity score for the midline incision was 14 (25th-75th percentile: 8-25) for the Seprafilm group and 53 (25th-75th percentile: 46-66) for the control group. Severity score in the pelvis was 0 (25th-75th percentile: 0-2) in the Seprafilm group and 5 (25th-75th percentile: 2-10) in the control group. These severity scores were not significantly different from the values scored by the surgeon at restorative surgery.

Discussion

Adhesions develop in the vast majority of patients after abdominal surgery,[9,10,11] and may lead to complications. Assessment of the postoperative incidence, severity and location of adhesions has not frequently been described, because no noninvasive method is available. The design of the current randomized clinical study allowed evaluation of the development of adhesions after

insertion of Seprafilm during a Hartmann procedure. Prevention of adhesions has only been evaluated in only one other randomized study.[2]

It is generally assumed that filmy adhesions lead to less complaints and complications than more dense adhesions. However, data on this subject are not available.

The severity of adhesions was significantly less in the patients who received Seprafilm compared with the group which served as controls. This finding corresponds to the results of Becker et al.[2] who performed a randomized clinical study to assess the value of Seprafilm in reducing the incidence and severity of adhesions in patients undergoing colectomy and ileal pouch-anal anastomosis with diverting-loop ileostomy, and consequent ileostomy closure with laparoscopic evaluation of formed adhesions. However, Becker et al. described a significant decrease in incidence of adhesions as well, and this could not be confirmed by our results. A possible explanation for this discrepancy is that in the current study, 34 (81%) had peritonitis demanding emergency surgery, whereas in the study mentioned above peritonitis was not present in any patient. Peritonitis has been described to disturb naturally present mechanisms involved in reducing the formation of adhesions, and therefore theoretically promotes the formation of adhesions.[6] As a consequence, measures aiming at the reduction of postoperative adhesions might be less effective if peritonitis were present.

Blood loss was described as having a diminishing effect on the efficacy of a cellulose barrier for reduction of postoperative adhesions.[7] Becker et al.[2] found no relation between blood loss and anti-adhesion effect of Seprafilm, and because blood loss was comparable between that study and the present one, blood loss is not a very likely explanation for a reduced effect of the membrane.

Theoretically, the relatively high incidence of pre-existent adhesions could explain the absence of reduction of adhesion formation in the Seprafilm group. Reformation of adhesions after adhesiolysis has been described to be high, the recurrence rate possibly depending on the technique of adhesiolysis, applied anti-adhesions methods, and time between initial surgery and evaluation of reformation.[8,12,13]

Seprafilm is not easy to handle, and some experience is needed to apply as intended. Application in areas that are more difficult to reach than the areas used in this study may bring about difficulties. Theoretically, dislocation is possible after application, and this may interfere with the membrane's anti-adhesions effect. To prevent dislocation of the membranes, the bowel was not held aside while closing the fascia; theoretically this could result in inadequate closure of the fascia and dehiscence, although no significant difference was found in the incidence of dehiscence between the groups. Devices that would be easier to handle would probably provide a more effective means to reduce postoperative adhesions.

This study describes only the incidence and severity of postoperative adhesions. No results are available yet about the effect of Seprafilm use on reducing the incidence of small bowel obstruction, chronic abdominal pain, and infertility. To assess these clinical parameters and determine the cost-effectiveness of Seprafilm, large studies with a long-term follow-up are needed.

In conclusion, we found a reduction in the severity of formation of adhesions after the application of Seprafilm in patients undergoing the Hartmann procedure compared with controls. Particularly in the case of planned relaparotomy, as with a Hartmann procedure, the application of Seprafilm will facilitate reexploration and may lower the risk of damaging the bowel during surgery. Therefore, it is considered advisable to use Seprafilm as an anti-adhesions barrier after colorectal surgery if relaparotomy is expected.

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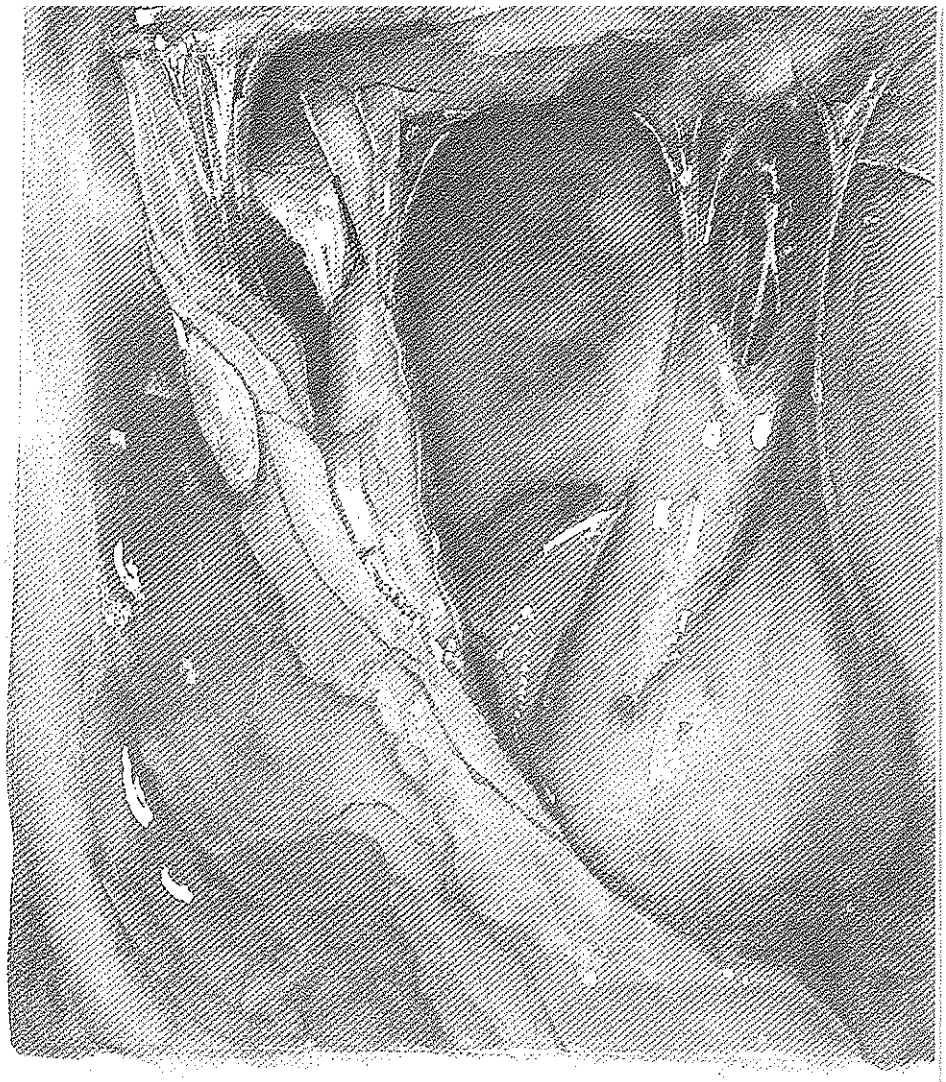

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Chapter 7

Abdominal adhesions: intestinal obstruction, pain and infertility A review

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Abstract

Adhesions cause bowel obstruction, chronic abdominal pain and infertility. In this review the incidence, clinical signs, diagnostic procedures and treatment of these sequels of abdominal surgery are discussed. Laparoscopic treatment of bowel obstruction, chronic pain and infertility is feasible in selected patients, and was described to cause less newly formed adhesions. Randomized controlled trials to compare adhesion formation after open and laparoscopic surgery should be executed with long-term follow-up to assess the success rates, and to compare the morbidity and mortality.

Introduction

Adhesions are abnormal fibrous structures in the abdominal cavity. Surgery is the most common cause of adhesions. Mechanical injury of the peritoneum and peritoneal ischemia due to manipulation and retraction of abdominal tissues during surgery predispose to formation of adhesions. [22, 53, 59] Exposing the peritoneum to foreign material such as powder, gloves or intra-abdominal prosthetic meshes is another source of adhesions. [22, 45, 59] Peritoneal adhesions can also develop in the absence of surgery. Inflammatory diseases of the peritoneum, gut or ovarian tubes are known to induce adhesions in the abdomen as well, but these rarely cause intestinal obstruction. [65]

Adhesions are responsible for the majority of bowel obstructions in the Western world. [2,4] Chronic abdominal pain and infertility are other manifestations of abdominal adhesions. [50, 73] One third of patients who has undergone open general surgery of the abdomen, is readmitted to the hospital for causes related to abdominal adhesions.[23] Gynaecologic procedures carry a similar faith; more than one third of women is hospitalised for adhesive disease after gynaecologic surgery.[57] The costs of surgery for abdominal adhesions exceed one billion dollars annually in the USA,[80,81] and therefore adhesive disease is a considerable societal burden. [41, 44, 105]

Adhesiolysis for intestinal obstruction

Adhesions after abdominal surgery account for up to 79% of acute intestinal obstructions, depending on the duration of follow-up and the type and number of previous surgeries. [2, 6, 15, 16, 22, 61, 71, 108] Bowel obstruction due to adhesions can occur as early as within one month after surgery, but intervals up to 20 years have been reported. [22] The highest number of reoperations for intestinal obstruction occurs after colorectal surgery.[4] Bowel perforation or enterotomy have been suggested to be associated with an increased risk of small bowel obstruction due to adhesions. [108]

Management of small bowel obstruction caused by adhesions is controversial because surgery induces new adhesions, whereas conservative treatment does not remove the cause of the obstruction.[4] Conservative treatment involves nasogastric intubation, intravenous fluid administration and clinical observation. Strangulation of bowel requires immediate surgery but the clinical diagnosis of intestinal ischemia can be difficult. Tachycardia, fever, focal tenderness, increased white blood cell counts and elevated lactate levels can indicate intestinal ischemia but are not very specific.[51] When intestinal ischemia is unlikely, a conservative approach can be continued for 24 to 48 hours.

Surgical lysis of adhesions which have caused ileus relieves the intestinal obstruction but the effect can be temporary. Recurrence of adhesive bowel obstruction has been reported at different rates. Barkan et al.[4] observed recurrences in 53% of patients after an initial episode

of bowel obstruction irrespective of conservative or operative treatment. Landercasper et al.[51] recorded recurrences of small bowel obstruction after surgical lysis in 29% versus 53% after conservative treatment. Operative treatment did cause more complications, 51% versus 14%, but mortality (4.7% versus 5.3%) was comparable. Therefore the authors recommend early operative treatment of severe small bowel obstruction, although the importance of other patient related factors is emphasised.

Adhesiolysis carries a mortality risk of 5% for a simple obstruction up to 30% for patient with strangulated or necrotic bowels.[22] Small bowel intubation is a therapy that can be performed additionally to adhesiolysis. It involves temporary insertion of a catheter in the small intestine to prevent renewed kinking of the bowel by the formation of adhesions. Recurrence of obstruction occurs in 4 - 25% after this procedure and a mortality rate of 25% was noted. Small bowel intubation is only recommended in case of severe adhesions.[47] One third of the English surgeons occasionally use this method.[89]

The extent of adhesiolysis is under debate. The approaches to adhesiolysis for bowel obstruction among general surgeons in the United Kingdom were established in 1993.[89] Half of all surgeons divided all adhesions to prevent recurrence of bowel obstruction while the other half limited adhesiolysis to those adhesions responsible for the obstruction.

The role of laparoscopy in the management of acute bowel obstruction is unclear yet. The potential advantages of laparoscopic surgery may include less postoperative adhesion formation as well as less wound infections and postoperative pain. However, particularly in patients with severely distended bowels and extensive, dense adhesions, limited working space is available rendering the procedure technically difficult. Until now, no comparative studies are available comparing adhesiolysis via either laparotomy or laparoscopy. Recently, Fischer and Doherty [24] published an overview of fourteen reports of laparoscopic adhesiolysis for small bowel obstruction. In a total of 918 patients with small bowel obstruction laparoscopy was performed, and in 71.5% of pations adhesions were the cause of bowel obstruction. Successful lysis of adhesions was described in 35% to 87% and the mean conversion rate was 32.2%. Reasons for conversion to a laparotomy included failure to identify the obstructing adhesion (41.3%), nonviable intestine requiring bowel resection (22.6%), iatrogenic perforation during laparoscopy (18%), and other causes such as patient intolerance of pneumoperitoneum (18.5%). Suter at al. described a series of laparoscopic adhesiolysis in 83 patients with a complication rate of 31% and a reoperation rate of 9%. Mortality in this series was 2.4%. Accidental bowel perforation and the need for conversion were associated with an increased complication rate. [97]

Laparoscopic adhesiolysis is associated with a considerable risk of bowel perforation. [27,29,43,55,56,82] Bowel perforation can occur during the establishment of pneumoperitoneum or during adhesiolysis itself. Diathermic lesions of the bowel are of particular concern because perforation might not occur immediately. One third of complications in laparoscopic surgery was reported to occur during establishment of pneumoperitoneum. [14, 32] Open laparoscopy to gain access to the abdomen has an undeniable advantage in reduction of visceral injuries and major vascular

injuries and is therefore advocated in laparoscopic surgery. [9, 33] This technique is of great value in laparoscopic adhesiolysis because bowels adherent to the anterior abdominal wall are prone to iatrogenic perforation during such procedures.
A bowel perforation during laparoscopic adhesiolysis is not always detected peroperatively. In only 35% of patients, gastrointestinal injury is recognised during the operation. After surgery, the mean delay for recognition of bowel injury in the majority of patients is four days.[14] It is assumed that delayed perforation of bowel are due to thermal lesions.

Adhesiolysis for chronic abdominal pain

Chronic abdominal pain is another sequel of adhesions. Continuous and colicky abdominal pain deserve discrimination. Continuous pain is considered to occur when adhesions retract viscera without obstructing them. Recently, sensory nerve fibers have been found in adhesions, suggesting the possibility of conducting pain after appropriate stimulation. [95] In patients with continuous pain, other causes of abdominal pain such as gastritis, galbladder stones, diverticulitis, pancreatitis, renal concrements, arteriosclerosis of visceral arteries, parasitic disease or lactase deficiency should be ruled out. In patients with colicky pain, obstruction is more likely. Auscultation of the abdomen or plain radiographs of the abdomen at the time of colicky pain can render intestinal obstruction more likely. When obstruction of the gut is considered, enteroclysis combined with either colonoscopy or barium enema are necessary to exclude inflammatory bowel disease, tumors of the bowel or volvulus.
Thorough investigations to exclude other pathology are of paramount importance to ensure proper selection of those patients with chronic abdominal pain who can benefit from adhesiolysis. Laparoscopy is most commonly used to assess and take down adhesions. Once adhesions have been found at surgery, it is difficult to determine which adhesions are liable for pain. Leidig et al. performed laparoscopy using local anaesthesia enabling the patient to indicate which adhesions were causing pain upon stretching. [54]
The success rate of adhesiolysis varies from 38 to 87%, while failure occurs in 13 to 54 % (Table 1). Interpretation of the outcomes of available studies is difficult since selection of patients, assessment of pain, extent and technique of adhesiolysis and length of follow-up varied greatly. To prevent adhesions, Ringer's lactate was occasionally left behind in the abdomen. [12, 68, 69, 86, 93] The extent of adhesiolysis was not described clearly in the reviewed studies. The extent of adhesions did not correlate to preoperative symptoms. [29, 79, 94] The site of chronic abdominal pain correlated well with the location of adhesions according to Stout et al. [94] whereas Rapkin et al. [79] failed to find this correlation. The pathophysiology of chronic abdominal pain is still poorly understood,[77] and psychosocial factors are supposed to play a role in chronic abdominal pain. [38] The success rate of adhesiolysis decreases with time. [49, 52, 84, 93, 98, 102, 106] The highest reported recurrence rate was 26%. [84] The longest pain-free interval was 2 years. [49] A longer duration of preoperative symptoms predisposes for a lower success rate. [64]

Table 1. *Outcome of adhesiolysis in patients with chronic abdominal pain with no other cause than adhesions*

	N	Cured/ improved	Unchanged/ worse	No response	Follow-up (months)	Method
Chan et al. 1985	43	28 (65.1%)	14 (32.5%)	1 (2.4%)	Minimum 6	Laparoscopy
Francois et al. 1994	35	28 (80%)	5 (14%)	2 (6%)	22 ± 4	Laparoscopy
Freys et al. 1994	58	46 (80%)	12 (20%)		Up to 30	Laparoscopy
Hallfeldt et al. 1995	16	14 (87%)	2 (13%)	-	4-18	Laparoscopy
Howard 1994	11	9 (82%)	-	2 (18%)	Mean 10.7 ± 3.8	Laparoscopy
Jung et al. 1986	27	16 (59%)	11 (41%)	-	?	Laparotomy
Klingensmith et al. 1996	19	14 (75%)	5 (25%)	-	3	Laparoscopy
Kolmorgen et al. 1991	153	58 (38%)	42 (27%)	54 (35%)	12-96	Laparoscopy
Lavonius et al. 1999	24	17 (71%)	5 (21%)	2 (8%)	4-43	Laparoscopy
Mecke et al. 1988	52	23 (44%)	16 (31%)	13 (25%)	6	Laparoscopy
Miller et al. 1996	19	16 (84%)	3 (16%)		Mean 18	Laparoscopy
Mueller et al. 1995	45	30 (67%)	6 (13%)	9 (20%)	6-36 Median 10	Laparoscopy
Nezhat et al. 1996	48	22 (46%)	24 (50%)	2 (4%)	Up to 60	Laparoscopy
Nezhat et al. 2000	48	67%	33%		2-5 years	Laparoscopy
Peters et al. 1992	24	11 (46%)	13 (54%)	-	9-12	Laparotomy
Saravelos et al. 1995	123	82 (67%)	41 (33%)	-	2-53 Mean 14	Laparotomy/ laparoscopy
Schietroma et al. 2001	45	34 (75%)	7 (16%)	4 (9%)	12-41 Mean 18	Laparoscopy
Schmidbauer et al. 2001	44	37 (84%)	7 (16%)	-	4-18 Mean 12	Laparoscopy
Steege et al. 1991	30	19 (63%)	11 (37%)	-	6-12 Mean 8.2	Laparotomy/ laparoscopy
Sutton et al. 1990	65	53 (82%)	10 (15%)	2 (3%)	1 -5 year	Laparoscopy
Tschudi et al. 1993	23	15 (65%)	4 (17%)	4 (17%)	5-36 Mean 18.3	Laparoscopy
Wipfli-Funke et al. 1995	105	63 (60%)	35 (33%)	7 (7%)	6	Laparoscopy

Unfortunately, no validated pain scores were used in most series and duration of follow-up was not described exactly by most authors. The (re)formation of adhesions are to be expected after adhesiolysis, [73] and the severity of adhesions increases with time. [103] This offers an explanation for the recurrence of pain. The temporary relief of pain might also be explained by the placebo effect. [8]

Adhesiolysis for infertility

Postoperative adhesion formation is an important factor in failure of reconstructive tubal surgery. The aim of reproductive surgery is to restore normal anatomy of the Fallopian tubes to allow passage of the ovum. Less traumatic, microsurgical techniques which were introduced in reproductive surgery during the past two decades, have reduced adhesions by 30%. [72]
If a second-look laparoscopy is performed after adhesiolysis, there is debate about the interval between these operations. Some gynaecologists advocate early second-look after one week to prevent transformation of fibrinous attachments into permanent adhesions. [3, 17, 62, 96, 99, 101] Others postpone second-look laparoscopy for three to twelve months to assess whether pregnancy occurs leaving secondary surgery unnecessary.[90] Second-look after one week showed recurrence of adhesions in 31 and 70 % of patients. Late second-look uncovered adhesions in 55 to 100 %. Pregnancy rates were only reported in three studies varying from 30 to 52 % (Table 2).

Surgical technique

Reduction of surgical trauma decreases formation of adhesions, as was shown in tubal surgery. Hence, laparoscopy is likely to induce less adhesions than conventional laparotomy. [27, 29, 35]
In experimental studies, laparoscopy caused less adhesions than laparotomy. [26, 30, 42, 58, 85, 100]
Lundorff et al. also observed less adhesions after laparoscopic tubal surgery than after open surgery.[60] DeWilde et al.[19] performed a second look laparoscopy three months after either open or laparoscopic surgery for acute appendicitis. Eighty percent of the patients after open appendectomy had abdominal adhesions while after laparoscopic appendectomy adhesions were found in only 20 % of patients.
Adhesiolysis can be performed employing various techniques. In two non-randomised studies in patients undergoing peri-adnexal adhesiolysis, success rates of CO2 laser surgery and electrosurgery did not differ at second look laparoscopy. Luciano et al. [58] showed no differences in effectiveness between Nd:YAG laser, CO_2 laser and electrosurgery in an animal study, although it was concluded that Nd:YAG laser worked slower and caused more tissue damage.
The role of adjuvants in preventing postoperative adhesion formation has been demonstrated in various clinical experiments. Hyaluronic acid based materials proved to reduce adhesions after intestinal and gynaecologic surgery. [7,104] Absorbable and non-absorbable mechanical barriers are considered to be effective in surgery for subfertility.[24] In a clinical study, adjuvants like dexamethasone, Ringer's lactate and dextran never proved to be effective. [24]

Table 2. *Outcome of patients with infertility who underwent second look laparoscopy (SLL) after adhesiolysis of adnexa*

	n	Adhesiolysis	Measures for adhesion prevention intra-abdominally	SLL: interval postop.	Recurrence of adhesions N(rate)	Method of initial surgery	Pregnancy n(rate)
Barbot et al. 1987	172	Electrosurgery/ Laser	Dextran	8 days	[53 (31%)]	Laparotomy	?
Daniell et al. 1983	10	Sharp	Ringer's solution, Dextran	28-42 days	100%	Laparotomy	total: 3 (30%)
DeCherney et al. 1984	11	?	Dexamethasone, Promethazine Dextran	1-19 months	[75-76%]	Laparotomy	?
Diamond et al. 1984	88	Laser	Dextran	within 12 weeks	100%	Laparotomy	?
O.L.S.G. 1991	68	Sharp/ Laser/ Electrosurgery	-	8-86 days(mean 39±2)	66 (97%)	Laparoscopy	?
Raj et al. 1982	22	?	Dexamethasone Promethazine Dextran, Ringer's solution	1 week - 2 years	[60% improvement, 35% comparable, 5% worse]	Laparotomy	?
Serour et al. 1989	22	Sharp/Electro-surgery	Ringer's solution, Hydrocortisone	9-12 months	12 (55%)	Laparoscopy	?
Surrey et al. 1982	31	Electrosurgery	Dextran, Heparine, Hydrocortisone	6 weeks	22 (71%)	Laparotomy	16 (52%)
Trimbos-Kemper et al. 1985	41	Electrosurgery via laparotomy	Steroids, Dextran	8 days	? (70%)	Laparotomy	20 (48%)

[..] data of whole study group, not only for adhesiolysis

Conclusion

The best treatment of adhesions is its prevention. Laparoscopic surgery appears to induce less adhesions than open surgery. To confirm this, patients who have enrolled randomized trials comparing open and laparoscopic surgery should be followed closely over a longer period of time to assess late morbidity of adhesions in either group. The value of anti-adhesive agents requires further studies before routine use can be advocated.

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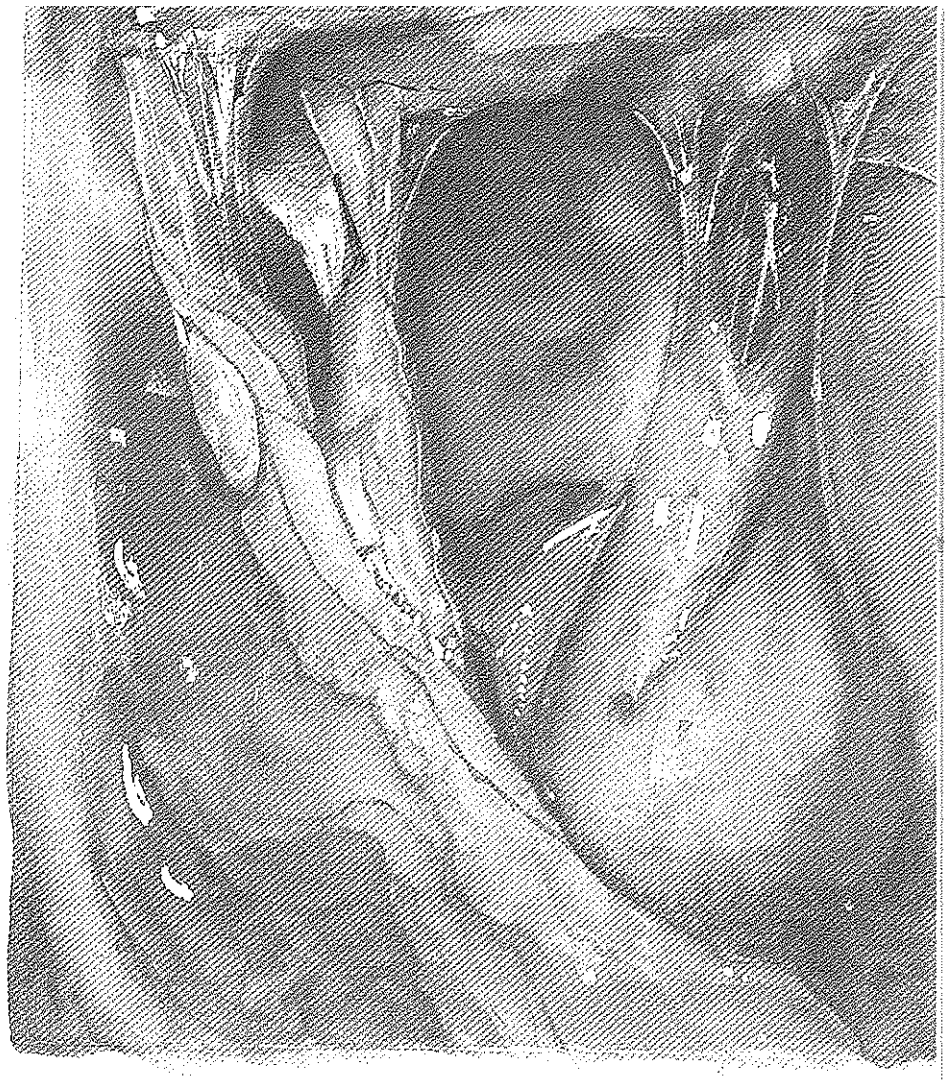

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Chapter 8

Benefit of laparoscopic adhesiolysis in patients with chronic abdominal pain A blind randomised multi-center study

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Abstract

Background: Laparoscopic adhesiolysis is controversial as a treatment for chronic abdominal pain. Its use has never been subjected to evidence-based treatment, but is based on common sense. We hypothesised that laparoscopic adhesiolysis leads to significant pain relief in patients with adhesions and chronic abdominal pain.

Methods: Patients were enrolled for diagnostic laparoscopy if they had chronic abdominal pain attributed to adhesions. Other causes for their pain had been excluded by standardised investigations. If adhesions were confirmed during diagnostic laparoscopy, then the patients were randomly assigned either to laparoscopic adhesiolysis or no treatment. Analysis was performed on an intention-to-treat basis. Only the operating staff was aware of the randomised assignment. Patients were blind for treatment and assessors for both treatment and outcome. Pain relief was assessed by VAS pain score (scale 0-100), pain change score, use of analgesics and quality of life score for one year. The primary aim was less pain and improved quality of life in the adhesiolysis group.

Findings: Of 116 patients enrolled for diagnostic laparoscopy, 100 were randomised for laparoscopic adhesiolysis (52) or no treatment (48). Both groups showed significant pain relief and significantly improved quality of life, but no differences could be demonstrated between the two groups (mean change from baseline of VAS score at 12 months: difference 3 points; p=0·53; 95% CI: -7 to +13). Complications, all non-lethal, occurred in 5 patients from the group of laparoscopic adhesiolysis.

Interpretation: Although laparoscopic adhesiolysis relieves chronic abdominal pain, it is not more beneficial than diagnostic laparoscopy alone, and we recommend, on the basis of our results, to abandon laparoscopic adhesiolysis as a treatment for adhesions in patients with chronic abdominal pain.

Introduction

Chronic abdominal pain remains a diagnostic and therapeutic challenge. Patients with chronic abdominal pain have often consulted many doctors, and have undergone extensive investigations, but in many cases no cause for their pain has been found.
Laparoscopy might be the next diagnostic intervention. This invasive technique can visualise types of pathology that cannot be diagnosed otherwise and can exclude some other causes of pain. In 35-56% of patients with chronic abdominal pain adhesions will be found as the only explanation. This suggests laparoscopy as the desired primary intervention in patients with chronic abdominal pain.[1,2]
Although adhesions are usually present in patients with chronic abdominal pain, some authors do not agree that adhesions are the cause of this pain.[3,4,5,6,7] Recently Sulaiman proved the presence of sensory nerve fibres in adhesions and postulated pain conduction to be a product of their own stimulation.[8]
Unlike adhesiolysis for strangulation or bowel obstruction, which has a mortality rate of 10%,[9] adhesiolysis by laparotomy for treatment of chronic abdominal pain has never gained acceptance.[10]
During the last 10 years laparoscopic techniques have been applied to adhesiolysis. The reported rates of chronic pain relief after laparoscopic adhesiolysis vary from 38% to 87%.[11,12] Others suggest that pain relief is due to patient reassurance by excluding serious morbidity at laparoscopy or due to a placebo effect based on a good doctor-patient relationship.[13,14] The question of whether laparoscopic adhesiolysis is a suitable treatment for chronic abdominal pain of uncertain cause remained unsolved.
We wanted to find evidence for pain relief after laparoscopic adhesiolysis by performing a blind randomised study. This trial compares pain relief and improved quality of life following laparoscopic adhesiolysis with diagnostic laparoscopy and answers scientifically the question of whether or not laparoscopic adhesiolysis benefits patients with adhesions and chronic abdominal pain.

Patients and methods

Protocol

Diagnostic laparoscopy was performed in all patients with chronic abdominal pain likely to have been caused by previous abdominal surgery. Chronic abdominal pain is defined as continuous or intermittent abdominal pain of at least six months' duration. Other pathology was excluded by standardised non-invasive specific diagnostics (see: exclusion criteria). If during laparoscopy adhesions were the only pathology present, patients were randomly assigned either to laparoscopic adhesiolysis or no treatment. They were unaware of their treatment assignment and the outcome assessment was blind. Pain relief was assessed by VAS (Visual Analogue

Score) pain score, VRCS (Verbal Rating pain Change Scale) pain change score, MQS (Medication Quantification Scale) score and MOS SF-36 (Medical Outcomes Study with 36 Item Short-Form Health Survey (pain part)) score preoperatively and at three, six and twelve months post-operatively. Quality of life was assessed with the other items of the MOS SF-36 questionnaire. After one year the randomisation result was revealed to the patient. Patients in the control group in whom pain persisted during that year underwent laparoscopic adhesiolysis on request. The ethics committee of each hospital approved the study and patients gave oral and written informed consent.

Exclusion criteria

1. Patient younger than 18 years old
2. Current treatment by psychologist or psychiatrist
3. Use of laxatives, sedatives, morphines, antipsychotics, antidepressants or drugs that stimulate the central nervous system
4. Abnormal outcome of standardised non-invasive specific diagnostics

- Biochemical investigation: sgot, sgpt, bilirubin, amylase, urea, creatinine
- Lactose tolerance test (LTT) or H_2 respiration test
- Faeces analysis of worms and worm eggs
- Ultrasound or CT scan of the abdomen
- Radiographic studies of small and large bowel (or colonoscopy)

Hospital selection

A mixture of university hospitals, teaching hospitals and non-teaching hospitals in the Netherlands was selected. The following hospitals participated:
1. Erasmus Medical Center, Rotterdam (university hospital). 2. Academic Medical Center, Amsterdam (university hospital). 3. Rijnstate Hospital, Arnhem. 4. Máxima Medical Center (Diaconessenhuis), Eindhoven. 5. Catharina Hospital, Eindhoven. 6. Medical Center Rotterdam-Zuid, Rotterdam. 7. Isala Hospitals, Zwolle. 8. Groene Hart Hospital, Gouda. Three other hospitals participated, but referred their patients for surgery to Gouda:
1. St. Antonius Hospital, Nieuwegein. 2. Reinier de Graaf Gasthuis, Delft.
3. Ikazia Hospital, Rotterdam.

Baseline Investigations

A standardised history and physical examination were performed. Patients completed a VAS (Visual Analogue Score) score,[15] and a MOS SF-36 (Medical Outcomes Study with 36 Item Short-Form Health Survey) score,[16] a registration survey (Dutch edition) measuring quality of life for chronic diseases. Analgesic intake was recorded during the week prior to surgery and was quantified by MQS (Medication Quantification Scale).[17]

Randomisation

If during diagnostic laparoscopy stricturing adhesions (adhesions stricturing a bowel loop with dilated lumen oral of the adhesion) were present, a therapeutic adhesiolysis was performed. After exclusion of other pathology and confirmation of adhesions, patients were randomly assigned to either laparoscopic adhesiolysis or no therapy (control group). This was determined by opening a sealed envelope in the operation room during the procedure. Envelopes had been prepared by the data-manager according to a computer-generated list with stratification per hospital.

Surgical technique

The procedures were performed under general anaesthesia. The routine use of nasogastric tubes or urinary catheters was not encouraged. No prophylactic antibiotics were given. The Veress needle was preferably punctured caudal of the umbilical fold. When a scar was present, the selected puncture site was left subcostal or intercostal between the eighth and ninth rib in the left midclavicular line. Pneumoperitoneum with carbondioxide was obtained at a maximum pressure of 12 mm Hg.

After pneumoperitoneum with the veress needle, abdominal access was obtained by a standard or an optical trocar (Optiview®, Ethicon, Summerville, NJ, USA). The open Hasson technique was applied in 12 patients, all in one hospital, based on their protocol as a teaching center. After the first trocar, a two or three port approach with 5 or 10 mm trocar sleeves was established under direct vision of a 10mm. zero degree laparoscope (Storz Tüttlingen, Germany). A 30° scope was utilized in case of inspection and adhesiolysis of adhesions fixed at the abdominal wall close to the laparoscope. A high flow CO_2 insufflator (Storz Tüttlingen, Germany) was used. Abdominal organs were exposed with atraumatic graspers (B. Braun, Aesculap). In a minority of cases dissection was performed with scissors but mainly with ultrasonic technique (Ultracision®, Ethicon Endo-surgery Cincinnati OH, USA). Electrocoagulation was sometimes used for further haemostasis. All surgeons had extensive experience in laparoscopic surgery in general and had performed laparoscopic adhesiolysis in at least 50 patients. They were allowed to apply their own techniques within limitations of the protocol. Procedures and adhesion assessments were video recorded; outcomes were reviewed by two surgeons.

Data collection and follow-up

Adhesions between organs and adhesions between organs and the abdominal wall were assessed by the surgeon for incidence, extent, type and severity. Incidence was defined as the number of organs involved. The extent of the adhesions between organs was scored by counting the individual adhesion bands. For the assessment of the extent of the adhesions between organs and the abdominal wall, the latter was divided into four quarters. The extent of these adhesions was scored as a percentage of that quarter covered by adhesions. When several quarters were involved, the extent score for that quarter was multiplied by the number of quarters involved. The type of adhesions was determined according to Zühlke.[18] In this classification types were

divided into four categories based on clinical and macroscopic criteria. If different types were present, the highest type was scored. The severity score for adhesion formation was calculated by multiplying the extent and type scores of the adhesions.

Data on laparoscopy and laparoscopic adhesiolysis included complications and completeness of the adhesiolysis. Bleeding was defined as the need for a blood transfusion; wound infection as the presence of a pus discharge, cellulitis or wound necrosis. Complete adhesiolysis was defined as a division of all adhesions between abdominal organs and the abdominal wall and of all adhesions between abdominal organs (enterolysis). If not achieved, the dissection was classified as incomplete.

Standardised physical examinations were carried out at an out-patient clinic every three months for a year by a doctor who was unaware of the randomisation and treatment. A VAS score (scale 0-100), a six-point VRCS score (pain-free, much improved, improved, unchanged, worse and much worse) and the use of analgesics was recorded after 3, 6 and 12 months. The intake of analgesics was recorded by the patients during one week, and categorised and quantified by MQS. Quality of life was measured at 6 and 12 months after the operation with the MOS SF-36 health survey questionnaire (higher scores reflect higher quality of life). Those control patients who underwent laparoscopic adhesiolysis after the one year follow-up were assessed in the same way over the following year. All forms were assembled separately by a member of the trial bureau. To ensure adequate follow-up, patients were contacted by telephone in the case of incomplete answers or unreturned forms.

Statistical analysis

A sample size of 120 patients was calculated, based on the existence of adhesion in 90% [19,20], a placebo beneficial pain relief of 25%,[13] and pain relief in 60% of patients after laparoscopic adhesiolysis after one year.[11,12] In order to detect 35% more pain relief after laparoscopic adhesiolysis beyond diagnostic laparoscopy with a power of 80% for a significance level of 5% (two-sided) using Fisher's exact test, 50 patients were required in each group.
All randomised patients were analysed on an intention-to-treat basis, irrespective of complications and of the completeness of the adhesiolysis.
Proportions were compared with the chi-square test. Outcomes of VAS scores, VRCS pain change values, MQS's and MOS SF-36 scores after the various intervals were compared with the Mann-Whitney U-test. Within-group comparisons with baseline were made with Wilcoxon's signed rank test. Pain analysis of the MOS SF-36 scores was performed with the outcomes of the pain items of this multidimensional questionnaire. For MQS analysis, the changes from baseline, and not the absolute values, were compared between the two groups.
Following laparoscopic adhesiolysis, two patients each had a single missing evaluation moment after 6 months. One patient refused further co-operation after three months. Two patients from the control group requested to be treated before the six months follow-up. One other patient

moved with loss of address at six months. The missing outcomes for painscores of these patients at six and twelve months were imputed, based on available preceding observations using least-squates regression. The effect of this imputation however was found to be negligible. P = 0·05 was considered as the level of significance.

Results

Five patients refused trial participation. One hundred and sixteen patients were included from August 1997 until January 2001. Three of 116 patients withdrew after enrolment and cried off their operation. Nine patients had no adhesions, one of these had a cicatricial hernia and

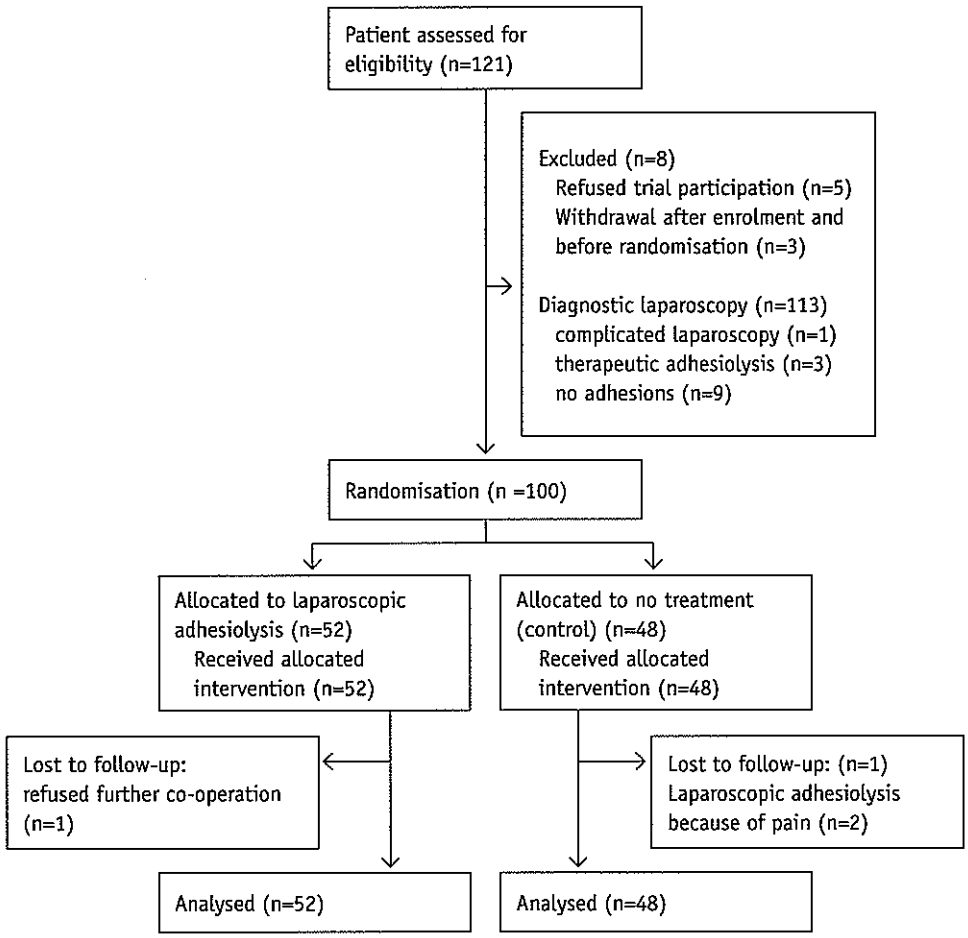

Figure 1. *Trial profile*

was successfully treated laparoscopically. Three patients underwent therapeutic adhesiolysis and in one instance a pneumoperitoneum could not be achieved. Therefore a total number of one hundred patients was randomised for laparoscopic adhesiolysis (52) or no treatment (48) (Figure 1). The patient characteristics at baseline are illustrated in Table 1. The two groups were similar except for the use of analgesics (MQS), which appeared higher in the control group, and for duration of pain, which was longer in the adhesiolysis group. Two patients were lost to follow-up. One of these patients refused further co-operation, and mentioned bad outcome. The other patient (control group) moved on after three months and her new address could not be traced. Three months after diagnostic laparoscopy, her VAS score declined from 60 to 3, and she classified her VRCS score as improved.

Complications of diagnostic laparoscopy

No complications during or after diagnostic laparoscopy.

Table 1. *Patients' baseline characteristics*

Characteristics	Randomisation assignment	
	adhesiolysis 52 patients	control 48 patients
General features:		
Age in years	45·4 *(14·5)*	47·8 *(12·3)*
Female/male	45 / 7	42 / 6
Body mass index	24·2 *(17-37)*	24·2 *(19-29)*
Pain factors:		
VAS score	57·2 *(17·9)*	56·0 *(18·0)*
MQS score	1·0 *(0-6)*	2·0 *(0-19)*
MOS SF-36 score	35·1 *(16·9)*	33·8 *(15·4)*
Duration of abdominal pain in months	30 *(6-240)*	18 *(6-180)*
Adhesion assessment:		
Number of previous abdominal operations	2·8 *(1·5)*	2·7 *(1·5)*
Adhesions between organs:		
- incidence	2 *(0-7)*	2 *(0-6)*
- severity	2 *(0-24)*	3 *(0-24)*
Adhesions between organs and the abdominal wall:		
- incidence	1 *(0-4)*	1 *(0-5)*
- severity	3 *(0-16)*	4 *(0-16)*
Type of previous operation: *(no. of patients)*		
Appendectomy	27	27
Gynaecological procedures	46	55
Bowel resections	7	17

Data are given as mean (SD) or median (range)

Complications and completeness of adhesiolysis

Six complications, all non-lethal, occurred in five patients; two small bowel perforations and one bleeding during the procedure; one abdominal abscess, one recto-vaginal fistula and prolonged post-operative paralytic ileus. All patients recovered.

In nine patients the adhesiolysis was incomplete. Four of these patients had a complete adhesiolysis in the painful part of their abdomen, but adhesions outside that painful part were left untreated. In five other patients a near-complete adhesiolysis was accepted in the painful area, because of increased risk of viscus perforation.

Pain relief and quality of life

Twenty-seven patients were pain-free or much improved 12 months after randomisation, 14 after laparoscopic adhesiolysis (14/52; 27%) and 13 in the no-treatment group (13/48; 27%). Forty-three percent of the patients in the adhesiolysis group experienced no change in their pain or had even more pain. The graded pain change scores did not significantly differ between both groups, and are illustrated in figure 2.

Outcomes of VAS scores demonstrate significant pain relief in both the adhesiolysis group and the control group at 6 months (Figure 3). The decrease in the MQS and the MOS SF-36 (pain part) scores follow the same pattern in both groups. Those reductions are significant between baseline and 6- and 12-months values ($p< 0{\cdot}001$).

Table 2. *Results of VAS, MQS and MOS SF-36 scores in patients in adhesiolysis and control group after 3, 6 and 12 months. (Data are given as means ± sem)*

	Adhesiolysis		Control		P-value
	No. of patients	Score (mean)	No. of patients	Score (mean)	
Vas					
3 months	52	38·6 ±3·2	48	32·7 ±3·9	0·21
6 months	52	38·6 ±3·5	48	40·2 ±4·2	0·77
12 months	52	38·9 ±3·4	48	40·5 ±3·7	0·63
MQS score‡					
3 months	52	0·7 (-0·6 ±0·2)	48	2·1 (-0·3)	0·26
6 months	51	0·7 (-0·6 ±0·2)	48	1·6 (-0·8)	0·92
12 months	49	0·8 (-0·5 ±0·2)	48	1·8 (-0·7)	0.53
MOS SF-36 score *(pain part)*					
6 months	51	51·2 ±3·0	47	50·1 ±3·5	0·73
12 months	51	51·0 ±3·3	47	49·7 ±3·2	0·84

‡ Numbers between parentheses represent the mean change from baseline, and the p-values correspond to these changes.

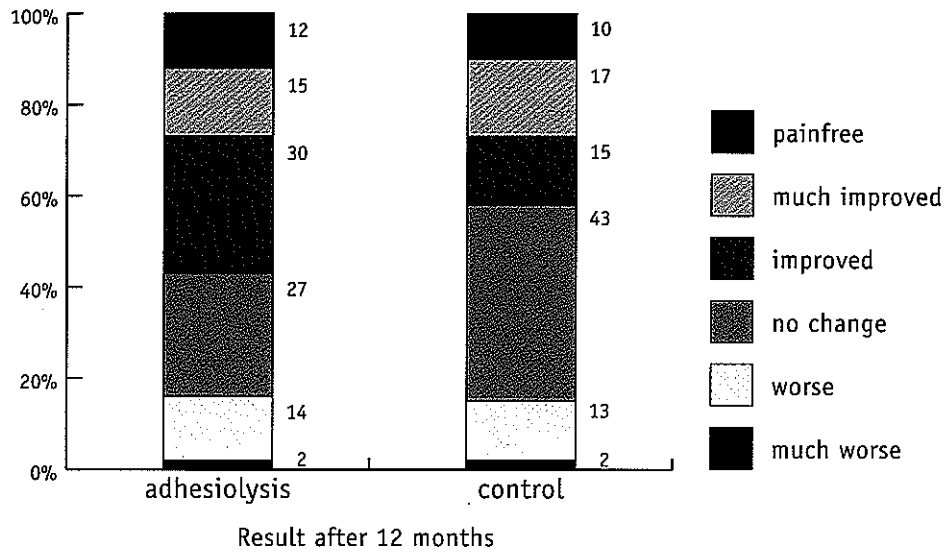

Figure 2. *Change of pain (VRCS score) in patients in adhesiolysis and control group at 12 months compared with baseline. (percentages of patients)*

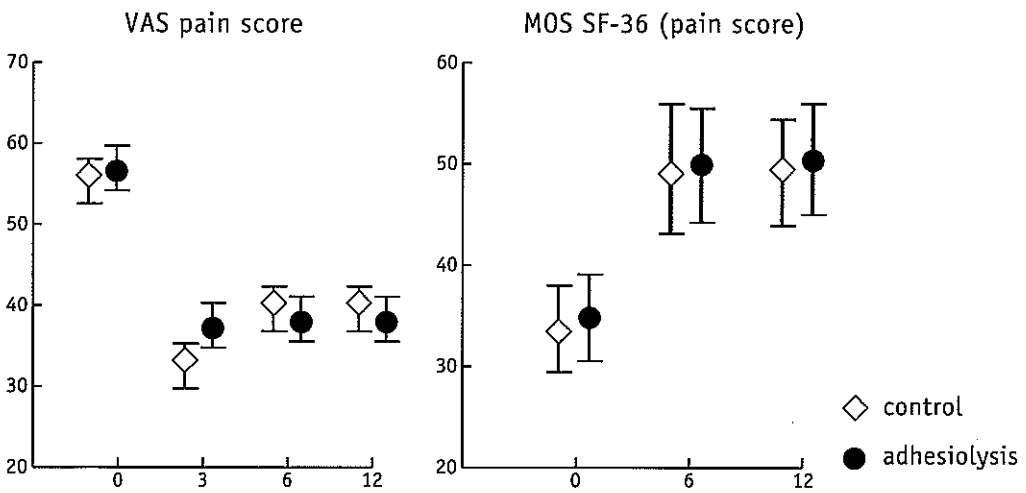

Figure 3. *Outcomes of VAS scores and MOS SF-36 scores (pain part) at baseline and at 3, 6 and 12 months after randomisation. (means ±sem)*

Moreover, comparing both randomised groups, no significant differences exist between the outcomes of all pain measurements at the appointed times (Table 2). The mean change from baseline of VAS score at 12 month is three points greater in the adhesiolysis group (p=0·53; 95% CI; -7 to+13). The mean change from baseline of the pain part of the MOS SF-36 score also did not significantly differ between both groups (difference 0; 95% CI; -7 to +8). Analysis of covariance of these changes, while taking account of duration of pain and MQS at baseline, produced similar results as those reported above.

The outcomes of the eight individual items of the MOS SF-36 measuring quality of life score at 12 months after laparoscopy were compared with those before laparoscopy (Table 3). Besides pain relief, four other items related to physical activities show significant improvement in each group. Patients' perception of their mental health, emotional functioning and their general health did not change significantly. Comparison of all eight items in both groups shows no differences at twelve months' analysis (Table 3).

Table 3. *Significance of within-group changes (12 months versus baseline) of quality of life scores (MOS SF-36 domains) in patients in adhesiolysis and control group, alongside differences between both groups at 12 months. (significant differences are expressed as +, corresponding to improvements)*

	Adhesiolysis group	Control group	Adhesiolysis group versus control group
Pain	+	+	-
Vitality	+	+	-
Physical functioning	+	+	-
Daily activities	+	+	-
Social functioning	+	+	-
Mental health	-	-	-
Emotional functioning	-	-	-
General health perception	-	-	-

Control patients with persistent pain

After a year's follow-up seventeen patients from the control group with persistent pain chose to undergo as yet laparoscopic adhesiolysis. After laparoscopic adhesiolysis the VAS score shows significant pain relief after 3 months but no longer does so after 12 months (p=0·17). MQS and MOS-SF-36 scores one year after adhesiolysis did not differ from preoperative values (p=0·21 and p=0·14 respectively). Pain change records in these 17 patients showed six patients with less pain and seven with worse results after one year.

Discussion

Some authors question the benefit of laparoscopic adhesiolysis and put the case that adhesions do not cause pain unless they are obstructing.[5,20] On the other hand, chronic pain relief after laparoscopic adhesiolysis has been demonstrated by several investigators, who found 45% to 84% of patients improved or cured.[21,22,23,24,25]
In this first prospective randomised study we have shown significant relief of chronic pain after laparoscopic adhesiolysis. However, patients with the same symptoms, the same pain scores and the same incidence and severity of adhesions who did not undergo adhesiolysis, but only diagnostic laparoscopy also experienced significant pain relief that was in no way different from that of the adhesiolysis group. This means that the value of laparoscopic adhesiolysis does not lie in the adhesiolysis.
Laparoscopic adhesiolysis causes 10% morbidity. Other series also show between 10% to more than 25% bowel injury in laparoscopic adhesiolysis during surgery for pain.[21,26] In difficult diagnostic laparoscopies with inconvenient adhesions, a surgeon must weigh the consequences of incomplete diagnostic laparoscopy against the risk of bleeding or viscus perforation; in most cases an incomplete diagnostic laparoscopy should be accepted.

The outcomes of those MOS SF-36 items related to physical activities differ from the outcomes of those items related to their emotional and mental attitudes and patients' own perception of their health and health expectations.
The improvement in items related to physical activity might be explained by pain relief. This relief may be experienced from the time of laparoscopy. Patients' emotions and perception of their mental and physical health might have changed since their last out-patient visit and trial enrolment and thus before they completed the preoperative questions of the MOS SF-36 score. If feelings of improvement were already present before the questionnaire, further improvement will be limited.

The significant pain relief in the control group is worthy of note. In this control group maximum pain relief was achieved after three months and diminished at six months. Kolmorgen also found worse results with prolonged follow-up. In twenty-five percent of 153 patients their pain recurred two years after laparoscopic adhesiolysis.[11] This short duration supports a placebo effect.[27] Elcombe found diagnostic laparoscopy to be therapeutic in women with chronic pelvic pain.[28] Bruxelle supposed a good doctor-patient relationship to have a powerful placebo effect.[14] The inefficacy of laparoscopic adhesiolysis and the possibility of a placebo effect is further supported by seventeen patients from the control group who subsequently underwent laparoscopic adhesiolysis after one year's follow-up because of persistent pain. These patients were informed of their randomisation and had already had additional attention, so an additional placebo effect in those patients was less likely to occur. Their pain scores after a second year follow-up did not differ from those at the end of the first year follow-up just before

laparoscopic adhesiolysis. Seven patients felt more pain after adhesiolysis and these results support our conclusion that laparoscopic adhesiolysis is of no value for chronic pain relief.

Diagnostic laparoscopy may benefit a patient by revealing other pathology. Constricting adhesions were found in three patients and a cicatricial hernia in another patient; these four patients were treated successfully. Nine (9/113) patients had no adhesions; this corresponds with other outcomes.[19,29] On the other hand diagnostic laparoscopy is responsible for 30% of complications in laparoscopic surgery,[26,30] and blind introduction of the Veress needle causes the 0·05 to 0·2% risk of visceral injury.[31]
It remains unclear to what extent diagnostic laparoscopy contributes to the relief of pain. A new study of patients with chronic abdominal pain comparing pain relief and quality of life after diagnostic laparoscopy versus a control group might answer this question.

Conclusion

Diagnostic laparoscopy is a safe procedure and if performed in patients with chronic abdominal pain, it may reveal curable disorders. Laparoscopic adhesiolysis carries additional morbidity and provides no additional pain relief for patients with chronic pain compared with diagnostic laparoscopy alone. Its value lies not in the adhesiolysis but in the diagnostic part of the laparoscopy.
Although performed world-wide, laparoscopic adhesiolysis has never been evidence-based. On the basis of our results we recommend that laparoscopic adhesiolysis should be abandoned as a treatment for adhesions in patients with chronic abdominal pain.

Contributors

D.J. Swank designed the study, wrote the protocol, introduced the study in the Netherlands, recruited and operated patients, and obtained and recorded data, and wrote the main frame of this article. S.C.G Swank-Bordewijk recruited the patients, designed the CRF forms, and obtained, recorded and analysed data. W.C.J. Hop contributed to the design and conditions of the study, organised the randomisation procedure, and analysed data. W.F.M. van Erp, I.M.C. Janssen and H.J. Bonjer recruited and operated patients, and obtained and recorded data. J Jeekel contributed to the idea, conditions and patients' selection, and accompaniment of the introduction of this trial in the Netherlands. All researchers wrote the report.

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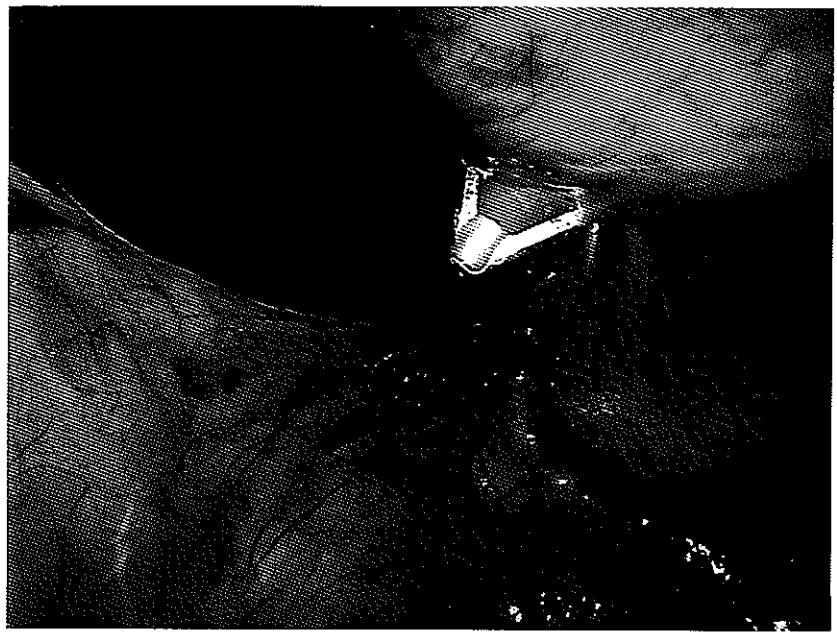
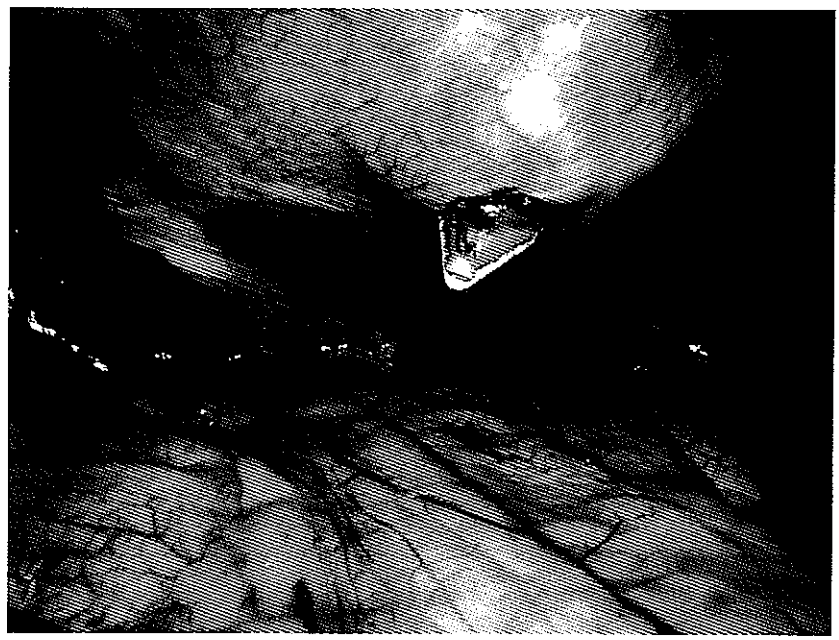
Diagnostic laparoscopy

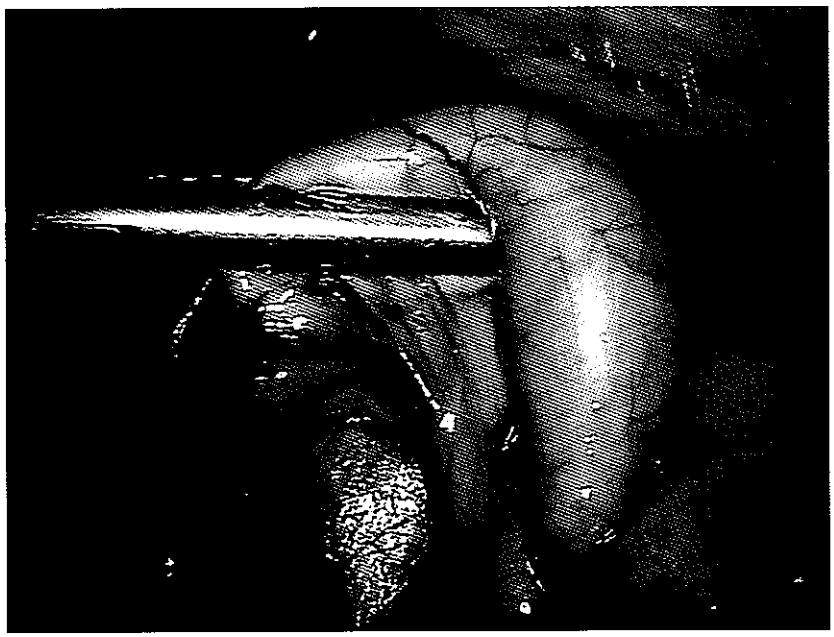


1. introduction of second trocar



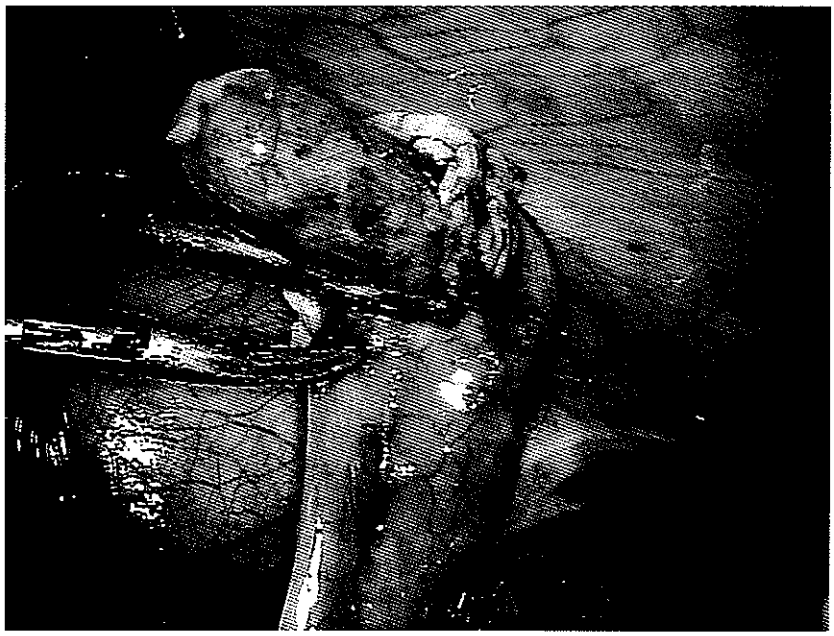
2. risk of organ damage

3. overview

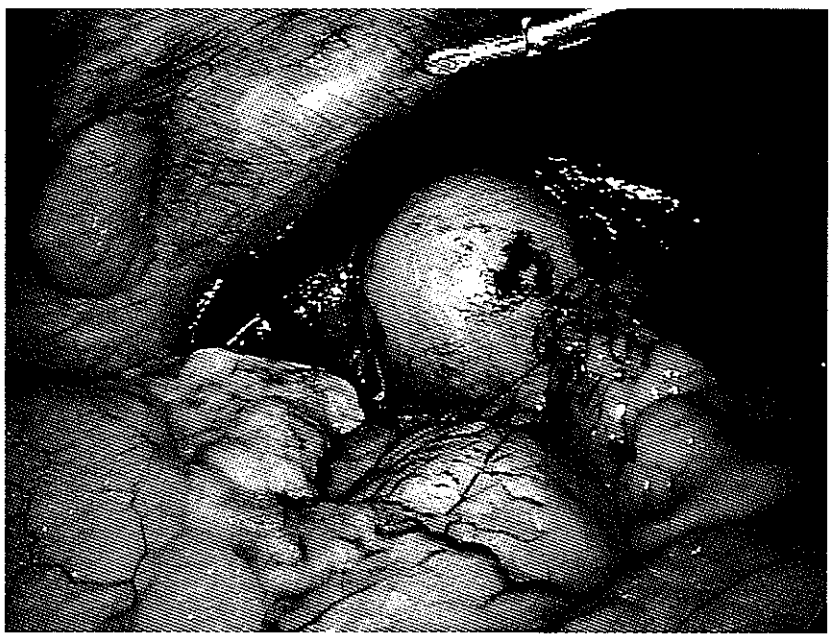


4. inspection of organs

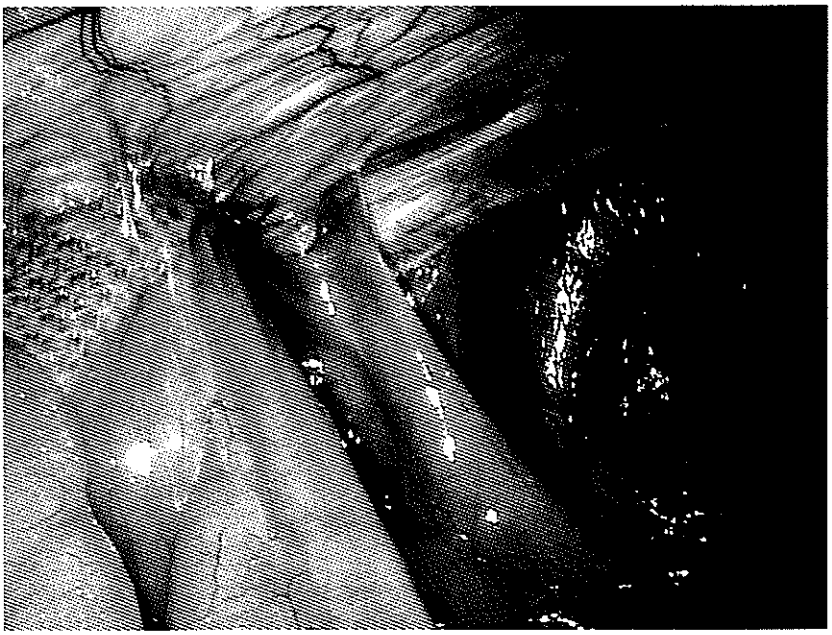
Pathology



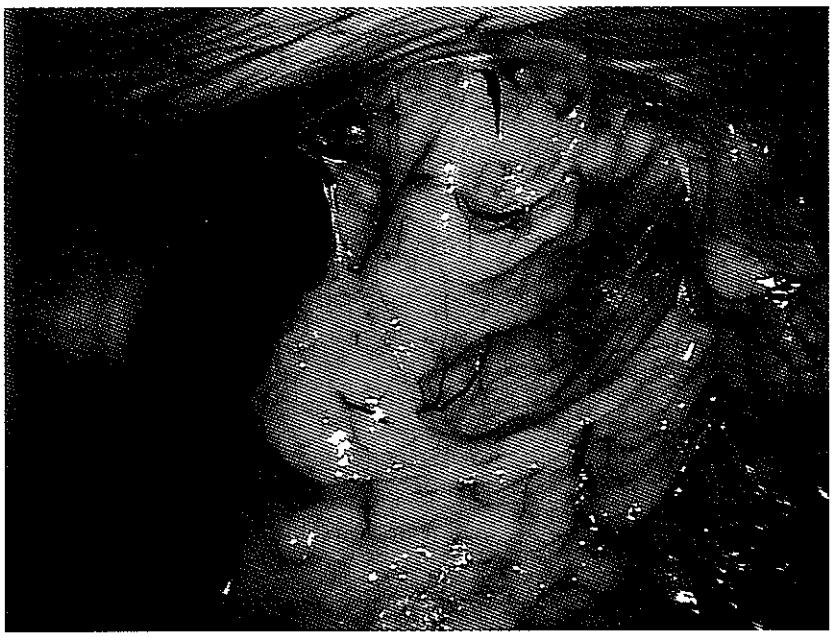
1. acute appendicitis



2. acute cholecystitis

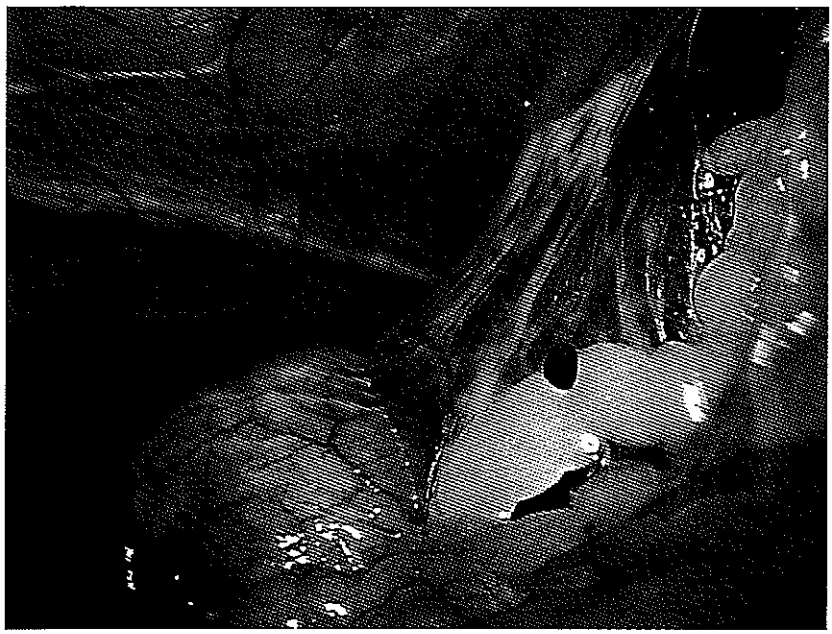


3. Spighelian hernia (Prolene mesh)



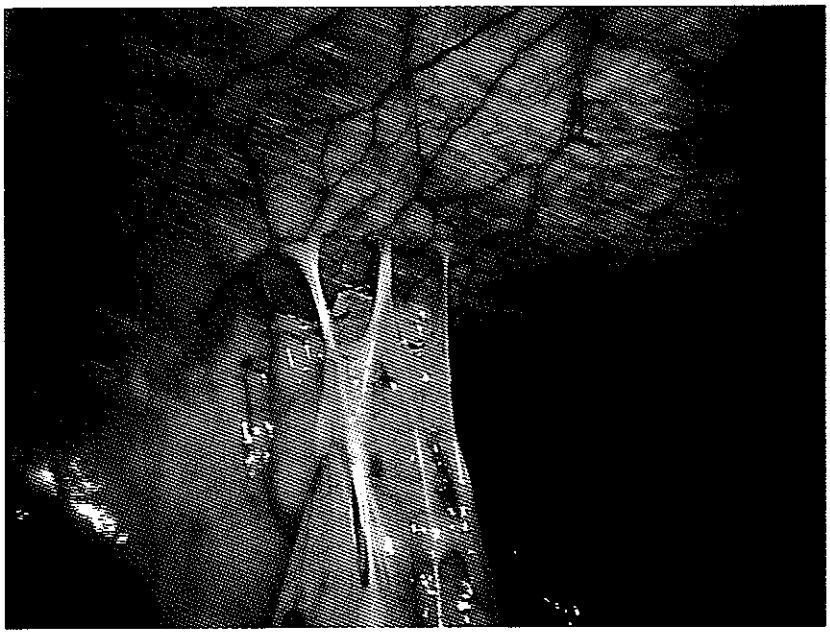
4. cicatricial hernia

Adhesion classification according to Zühlke

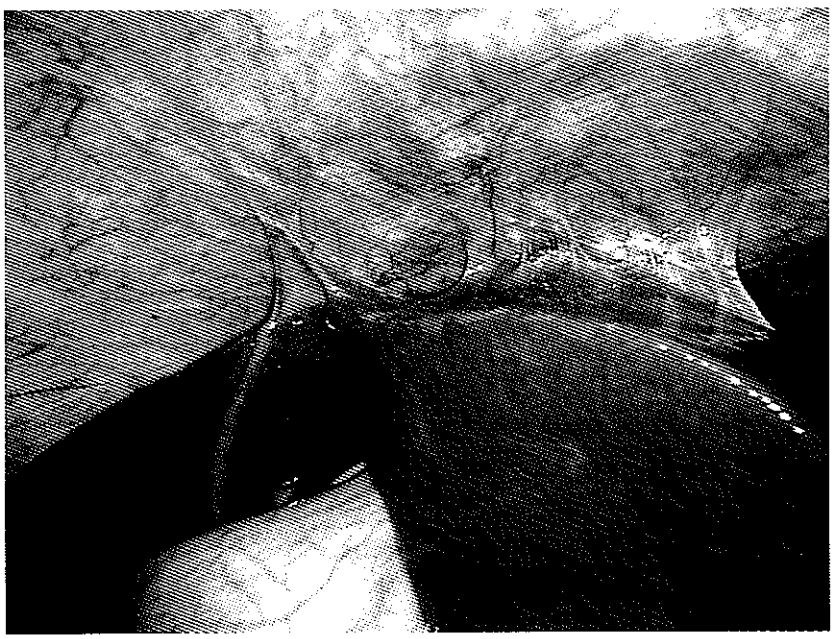


1. Zühlke 1

2. Zühlke 1 and 2

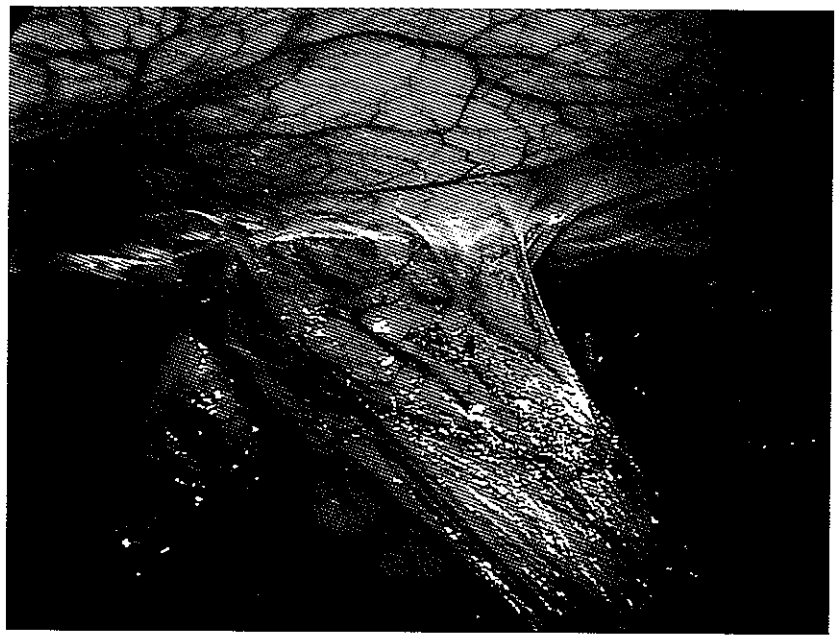


3. Zühlke 3

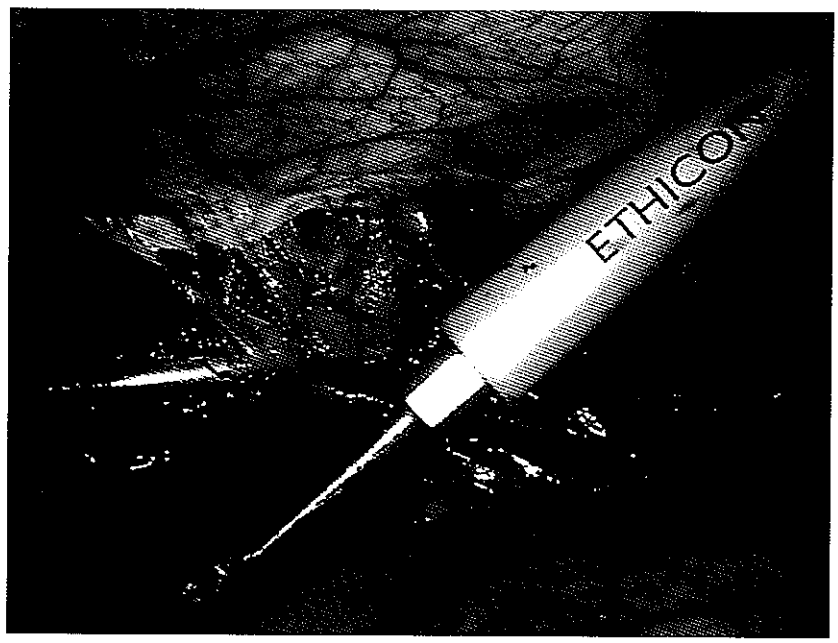


4. Zühlke 4

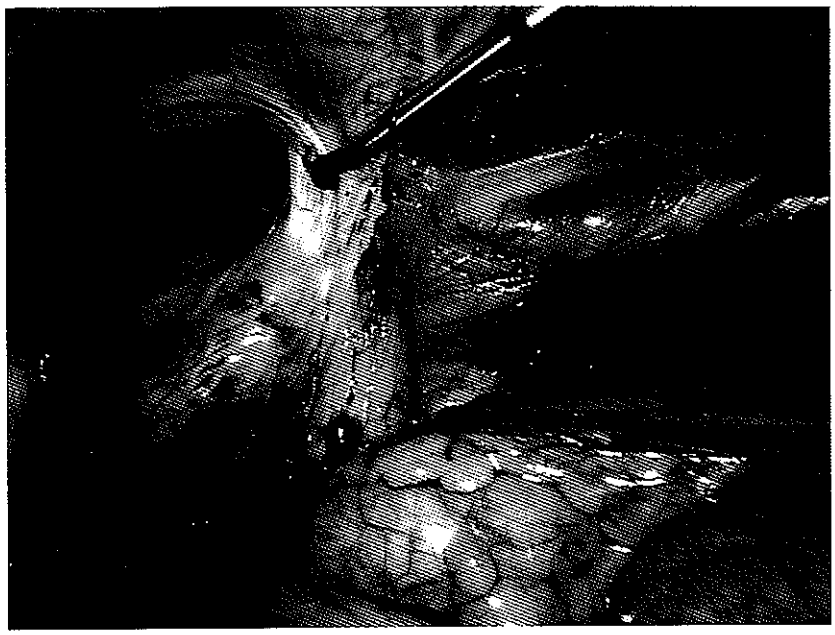
Adhesiolysis



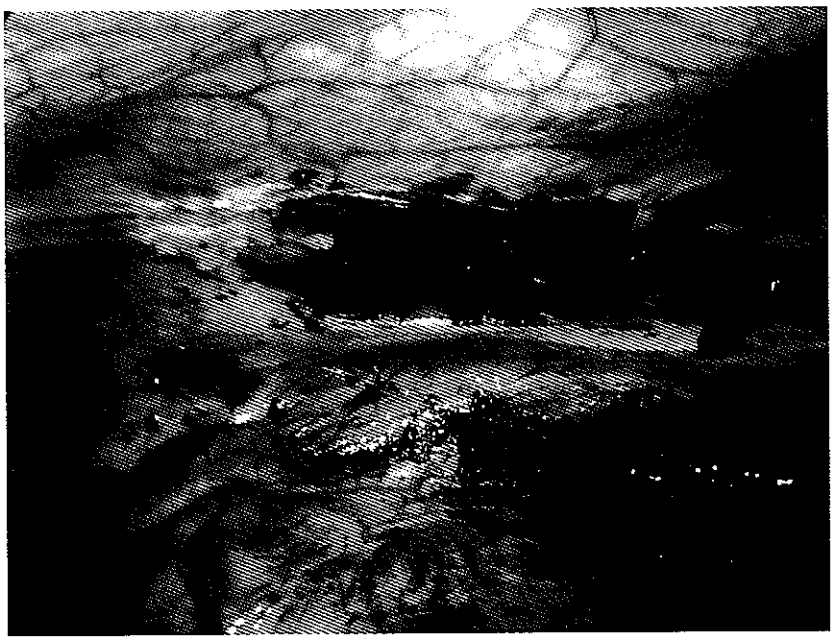
1. inspection



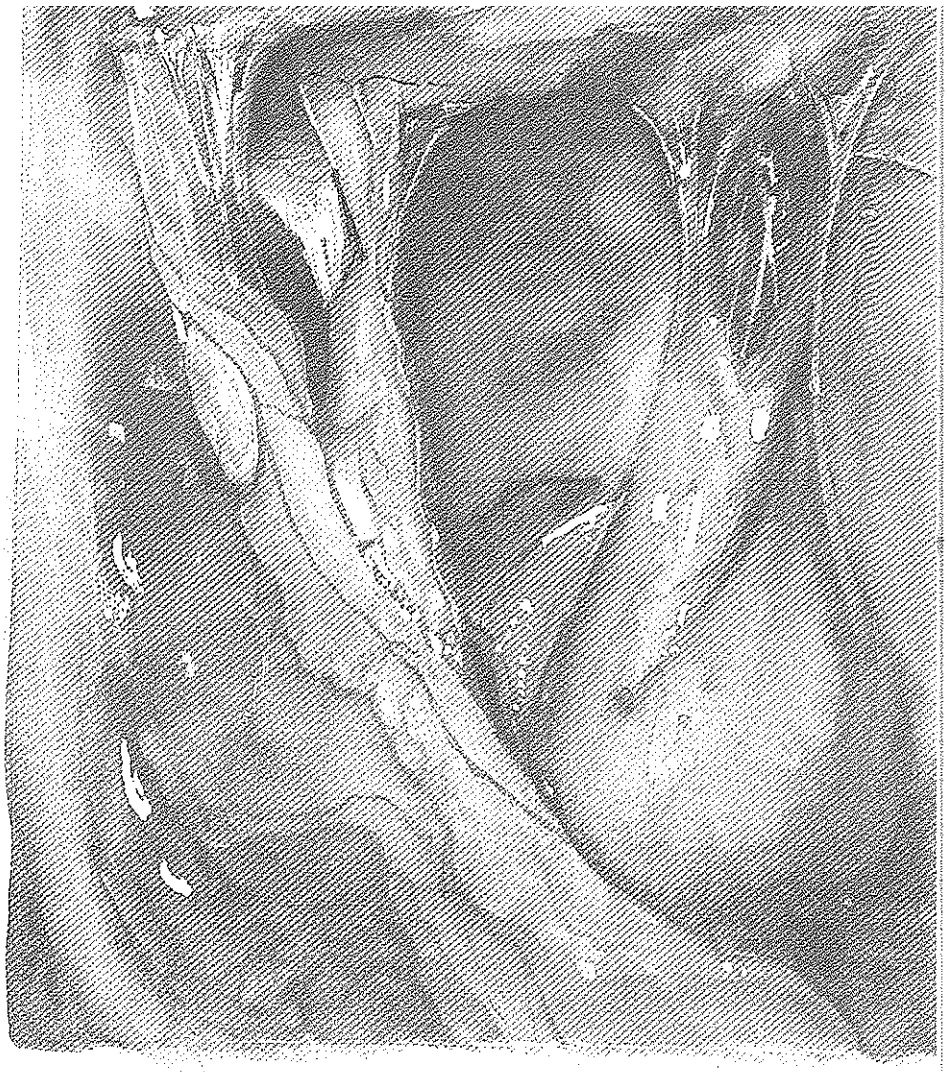
2. countertraction



3. ultrasonic lysis



4. result with peritoneal defect



Chapter 9

General discussion
Answers

This thesis is composed of different clinical studies.
These studies attempt to give answers to clinical questions, but
a patient can ask more questions than a surgeon can answer.

Question

A patient complains about longstanding chronic abdominal pain. She has undergone appendectomy and uterus extirpation several years ago and her pain has started a few months after the last operation. Many non-invasive investigations did not reveal any pathology. She asks your surgical advice about further investigations to find the cause of her pain. What do you propose?

Would you tell her to learn to live with her pain?
Would you send her to another doctor?
Would you suggest her a diagnostic laparoscopy?

Is diagnostic laparoscopy indicated in patients with chronic abdominal pain?

During eight years, 224 patients were prospectively selected and analysed for adhesions (chapter 3). These patients had undergone at least one previous abdominal operation and suffered from chronic abdominal pain. This was defined as continuous or intermittent abdominal pain with daily intake of analgesics and a pain duration of at least three months. They were scheduled for diagnostic laparoscopy if non-invasive investigations could not detect a cause for their pain. In 6 patients the laparoscopy was incomplete (chapter 3). In all other patients a complete diagnostic laparoscopy was performed. Five patients had neither adhesions nor other pathology. In 13 patients other pathology, with or without adhesions, was found and treated (Table 2; chapter 3). After (laparoscopic) treatment 11 patients were painfree, one had less pain and another patient experienced no relief. These disorders were thus present but not recognised with preoperative investigations. These laparoscopic procedures were performed without complications.

In another series, one hundred and sixteen patients included from August 1997 until January 2001, participating in the adhesiolysis trial underwent also a diagnostic laparoscopy. Before enrolment (and laparoscopy) all these patient underwent extensive non-invasive investigations (chapter 8). In one patient a pneumoperitoneum could not be achieved despite several attempts and she developed peritonitis one day later. She was laparotomized and showed two small bowel perforations. Eight patients had neither adhesions, nor other pathology. Four patients were treated laparoscopically. One patient had no adhesions, but a cicatricial hernia, and three other patients had stricturing adhesions on the small bowel and underwent therapeutic adhesiolysis. Three of these four patients became symptom free.

Diagnostic laparoscopy in these 340 patients with chronic abdominal pain showed in our series one complicated, and 6 incomplete procedures. Thirteen patients had no abnormalities at all in the abdominal cavity. However, 14 patients had other pathology than adhesions and were treated laparoscopically. Afterwards twelve of these patients were pain free, one had less pain

and the other one had no relief. Three patients had stricturing adhesions, and were treated laparoscopically, two of these were symptom free. All other patients had just adhesions.

Diagnostic laparoscopy is a safe procedure. The risk of visceral injury during the blind introduction of the Veress needle and the first trocar is between 0.05% and 0.2%. This might be diminished by using preoperative ultrasonography of the abdominal wall or the open introduction with the Hasson technique.[5, 6] Detection of underlying adhesions with ultrasound prior to laparoscopy was advocated by Borzelino. With ultrasound diagnostic accuracy of adhesions was 88,5% with a specificity of 32% and a sensitivity of 100%.[6] Uberoi found poor overall sensitivity (50-60%) with transabdominal ultrasonography, and judged this technique unreliable for routine use.[84] Localised abdominal pain and a reproducible punctum maximum pointed out by the patient is still the most valuable clinical hint of symptomatic adhesions.[25] Klingensmith performed diagnostic laparoscopy in 34 patients with chronic abdominal pain. In nine of these patients no abnormalities were found. Twenty patients (59%) with only adhesions and 9 patients with other disorders were treated. After treatment, a majority of these patients reported pain to be mostly or completely resolved.[48] In 265 patients with chronic abdominal pain as reported by Salky et al, the aetiology was established in 201 (76%) of cases. In 128 of these patients a definite therapeutic laparoscopic procedure was performed. Normal laparoscopic examination was found in 64 patients (24%).[69]
Salky and Klingensmith showed lower incidences of adhesions, but their patients were selected having chronic abdominal pain whether or not previous surgery was performed. Thirteen patients (4%) in our series had no adhesions, this is conform other results.[21,53] If adhesions have to be considered as pathology, than the diagnostic value of diagnostic laparoscopy is 96% in this patient group. If adhesions are normal physiology, pathology will be found in 5% until 50% of patients with chronic abdominal pain. Even in our last series with extensive preoperative investigations, 4 patients (3%) were found to have other pathology than normal physiological adhesions.

The incidence of complications in diagnostic laparoscopy is low. Thirteen patients undergoing diagnostic laparoscopy revealed no abnormalities. In 17 patients symptomatic disorders were diagnosed and treated during the same laparoscopic procedure and 14 of these 17 patients were symptom free afterwards. Even if no abnormalities are found, diagnostic laparoscopy may improve pain in as many as 32% of patients.[48] In general, 35% of patients affected by various conditions proved to react positively to placebo medication. Surgical "placebo therapy" seems to score even more placebo-effect.[15]

Answering the question:

Chronic pain in the abdomen should not be attributed to psychological or emotional causes unless the presence of organic pathology has been excluded by extensive non-invasive diagnostics and diagnostic laparoscopy.

Question

At diagnostic laparoscopy adhesions are found, impeding a complete examination of the abdominal cavity.

Is it feasible to lyse adhesions to complete the diagnostic laparoscopy?
And if one believes in therapeutic adhesiolysis, is it necessary to aim at a complete adhesiolysis?

Is laparoscopic adhesiolysis feasible? Is it wise trying to obtain a complete adhesiolysis?

Between October 1991 and September 1997, 157 patients underwent an attempted primary laparoscopic adhesiolysis by three experienced laparoscopic surgeons. Thirteen underwent a second adhesiolysis and four patients a third procedure accounting for a total of 174 operations. The feasibility of complete adhesiolysis was evaluated retrospectively (chapter 2). In 128 of these patients (74%) a complete adhesiolysis was performed; in 27 patients (16%) the adhesiolysis was almost complete; in these cases the procedure was not continued, because in our opinion further adhesiolysis would not benefit the patient, and all adhesions in the painful area were lysed.
The adhesiolysis was incomplete in 12 patients. In 2 patients due to impaired view by light absorption because of diffuse blood clots on the peritoneal surface, in 5 patients the procedure was suspended due to unrecognisable cleavage plane between the intestinal loops with too great perforation risk. In another 5 patients a visceral perforation was made during the laparoscopic procedure, the laparoscopic part discontinued and converted to a laparotomy to suture the defect.
The beginning of the adhesiolysis was made impossible due to technical difficulties, and limited us to an insufficient local diagnostic laparoscopy in 7 patients.
In another series of 200 patients (chapter 3), a *primary* laparoscopic adhesiolysis was done. Introduction of trocars was uneventful and a complete adhesiolysis was attempted. The laparoscopic adhesiolysis could be completed in 83%. An almost complete adhesiolysis was done in 9% and an incomplete lysis in 8% of these patients.
The individual factors influencing the completeness are shown in Table 2 (chapter 2). The number of previous operations and the application of electrocoagulation as dissection technique. were found to reduce significantly the chance to complete the laparoscopic adhesiolysis.[23, 24, 36, 58, 73]
In 105 patients the Ultrasonic technique has been applied for laparoscopic dissection of adhesions (chapter 4). A complete adhesiolysis could be achieved in 97 patients (92%). In six patients (6%) the laparoscopic adhesiolysis was almost complete. An incomplete laparoscopic adhesiolysis was accepted twice due to vascular risk of the aorta and due to a bowel perforation and the necessity of a conversion.

In our randomised trial (chapter 8) 55 patients underwent laparoscopic adhesiolysis. Complete adhesiolysis was possible in 46 (84%) patients, almost complete adhesiolysis was achieved in 4 (8%) patients, and in 5 other patients some adhesions were left untreated in the painful area because of increased risk of viscus perforation.
In case of an (almost) complete adhesiolysis all adhesions were lysed in the painful area. Only the adhesions out of the reach of instruments were left untreated. If adhesiolysis was incomplete, (some) adhesions in the painful area were not lysed because of technical difficulties or an unclear cleavage plane. In these cases a choice has to be made between completeness and the risk of bowel perforations with serious morbidity and mortality. Salky got round this difficulty and searched for the single symptomatic adhesion. Gentle pulling under local anaesthesia revealed the painful adhesion, which was lysed selectively. Such a procedure obviates extensive lysis of the other adhesions.[69]
The study of Mueller et al. indicates also that not all abdominal adhesions do cause pain. They believe that only those adhesions which involve limitation of movement of the organs are likely to cause pain.[58] This supports the concept that even incomplete adhesiolysis can benefit the patient if the symptomatic bands are lysed. In our patient group the same benefits were noticed; 80% relief or disappearance of pain in as well patients with incomplete adhesiolysis as in patients with (almost) complete adhesiolysis.
François reported 8.7% intestinal perforations due to trocar injuries and enterolysis. He stresses the importance of limiting enterolysis because of the perforation risk and the reasonable chance that the painful adhesion has already been lysed.[23, 24] It is good to remember that multiple previous operations are an important reason for incomplete adhesiolysis and an important factor causing complications during laparoscopic adhesiolysis. We also believe that in difficult cases with progressive risk of complications it is better to accept an incomplete adhesiolysis and to wait for the possible relief of pain. Regrowth of adhesions after complete adhesiolysis is almost certain. In 24 patients with a second-look procedure, we found no significant difference of the severity of inter-organ adhesions, which were present, were lysed, and re-evaluated after a mean period of 16 months after the adhesiolysis. These inter-organ adhesions are the ones responsible for bowel obstruction. A complete enterolysis will be only temporarily, and will not prevent bowel obstruction in all cases.

Answering the question:

Laparoscopic adhesiolysis is feasible, but it is more difficult and has more risk of perforations if performed after multiple previous laparotomies. Electrodissection is another factor reducing the chance of a complete adhesiolysis. Ultrasonic dissection in our patients allowed for (almost) complete adhesiolysis in 98% of patients.
If for diagnostic purposes a complete adhesiolysis is not necessary, the surgeon should not attempt a complete adhesiolysis. If the surgeon believes that all adhesions might cause pain, he should remember the perforation risk and the fact that the relief of pain after adhesiolysis was independent of the fact whether or not the adhesiolysis was complete, and might change his mind.

Question
How do you have to inform your patient?
Is laparoscopic adhesiolysis a safe procedure?
What are the risk factors?

The safety of laparoscopic adhesiolysis

Cook warned of the dangers of laparoscopy in patients with suspected bowel adhesions in 1977,[13] and was supported by Ikard, who considered bowel obstruction as the only indication for enterolysis and regarded a laparoscopic approach as inadequate and dangerous.[42] In 1987, Kjer suggested that the risk of laparoscopy being acceptable in patients after prior abdominal surgery if performed by competent laparoscopists.[47] Seven years later, laparoscopic adhesiolysis was recommended as an attractive surgical procedure for intestinal obstruction and chronic abdominal pain.[24]

In our first series (chapter 2), 174 patients underwent laparoscopic adhesiolysis. Besides two minor trocar related complications, 16 major complications occurred. Three patients suffered blood loss with a need for transfusion. Two of these bleedings could be managed during laparoscopy. The other patient had postoperative signs of shock and recovered well after transfusion. In 11 patients visceral perforations occurred, 3 times in the large bowel and 8 times in the small bowel. Four out of eleven bowel perforations (36%) were not recognised during the procedure and patients developed a generalised peritonitis two days (2) and four days (2) postoperative. Another patient got a bowel obstruction after one week, due to a small bowel volvulus and underwent a partial bowel resection. Another patient had signs of peritonitis on the second postoperative day, underwent a second laparoscopy, which revealed no pathology. Two of the complicated patients died. One patient had a small bowel perforation, seen and sutured during laparoscopic adhesiolysis. The other patient died of peritonitis due to a bowel perforation, not recognised during operation.

In this series laparoscopic adhesiolysis causes serious morbidity (9.2%) and mortality (1.1%). These morbidity figures were congruent with those from our randomised trial (chapter 8). Six complications of different character occurred in 55 patients (10.9%) without mortality. In these patients the ultrasonic technique has been applied, and no late perforations appeared.[1, 26, 27, 46, 59] In 105 other patients treated with ultrasonic dissection 4 patients were complicated. One bleeding and three small bowel perforations occurred. There were no late (thermal) perforations, probably due to the use of ultrasonic dissection.[30, 46, 73]

Analysis of predictive factors for complications revealed that the number of previous operations and the age of the patient significantly influenced the major complication rate. More previous operations and higher age of the patient lead to an increased risk. Literature reports in 5% to even 25% of patients intestinal perforations, occurring during laparoscopic procedures for symptomatic adhesions.[14, 25, 23, 25, 63, 83]

The risk of bowel perforation in open surgery for adhesions is even greater. A 10% mortality with laparotomy for treatment of mechanical adhesive bowel obstruction has been described by Jeekel.[44] In a review article written by Tera, 15,2% mortality was found in laparotomic surgery of the small bowel.[78] At secondary laparotomies through the same incision, 21% bowel perforations occurred. Also in open surgery, the number of previous laparotomies and the age of the patient appeared to be independent risk factors for bowel perforation.[85]
It must be remembered that in our series 36% of the bowel perforations were not recognised during the procedure. The symptoms of peritonitis after a direct perforation are usually clear within 1 or 2 days. Thermal damage to the bowel may be the cause for delayed bowel perforation. In these cases the clinical signs of perforation are usually seen after 4 days.[63]

Answering the question:

The number of serious complications after laparoscopic adhesiolysis is substantial. The morbidity and mortality of laparoscopic adhesiolysis is comparable with laparotomic dissection of adhesions. Higher age and a larger number of previous operations are predictive risk factors for complications and force the surgeon to a very careful patient selection. A significant number of complications remains unrecognised during laparoscopic adhesiolysis. This indicates the necessity for a careful postoperative control of the patients. High risk patients and patients with difficult dissections should not be treated in day surgery.

Question
Your patient is worried about this complication rate.
Can you offer her new techniques reducing the risk of bowel perforations?

New techniques in laparoscopic adhesiolysis

The serious complications of laparoscopic adhesiolysis such as vessel and viscus perforation occur in 5% up to 25% of patients.[11, 63] Critical in the procedure is the needle insertion, the trocar placement, and the adhesiolysis itself. We have entered these three critical moments, and have applied and assessed safety measures such as subcostal insertion of the Veress needle.[54] use of an optical trocar,[32] and application of ultrasonic dissection.[1, 26, 46, 59]
According to our protocol the distal umbilical fold is the preferred site for the Veress needle. A midline scar obliged to choose the entry site at least 5 cm away from the scar. After upper abdominal surgery and in case of a transverse incision in the upper abdomen the Veress needle was introduced in the intercostal space just above the eighth rib in the midclavicular line on the left side. This site is convenient for needle introduction because the parietal peritoneum is adherent to the abdominal wall and the abdominal wall in this region is usually thin. The spleen, diaphragm and thoracic organs are surprisingly much further away and the greater omentum protects the stomach.
In our patients the eighth intercostal space was used three times as entry site for the Veress needle. Childers has chosen the left ninth intercostal space after median laparotomies and has recommended this site as safe in patients with high risk subumbilical adhesions.[12] Midline incisions cause significantly more adhesions than Pfannenstiel incisions.[8]

In 105 patients, (chapter 4) who had underwent multiple previous laparotomies, and had been selected for laparoscopic adhesiolysis, an optical trocar (Optiview®) was used for introduction of the abdominal cavity. This trocar has a blunt tip and by slowly rotating the device it finds its way very easily through all layers of the abdominal wall. Using this optical trocar every single layer of the abdominal wall inclusive the parietal peritoneum could be well recognised and differentiated from each other in every patient. The darkness of the abdominal cavity filled with carbondioxide was seen as a big black spot as background of the parietal peritoneum when pressure on the optical trocar during penetration was reduced from time to time. If not seen, an adherent organ at the trocar site was likely present and the introduction was attempted elsewhere. This happened once and the penetration of the abdominal wall was done successfully at another site. Subsequent laparoscopic evaluation revealed an adherent omentum at the first site.
No complications related to the introduction of the optical trocar occurred. In three patients intraperitoneal position of the Veress needle was doubtful and the optical trocar was uneventfully introduced even without a previous pneumoperitoneum.

Very large randomised studies might show differences in safety of a specific trocar. Catarci et al. found after evaluation of nearly 13000 laparoscopic procedures the open approach the safest way with minimal risk of visceral and vascular injury (0.09%) versus 0.27% complications with an optical trocar. He did not mention the indication for the use of an optic trocar, and used a sharp optic trocar with a cutting knife at the tip.[11] The safety of an open introduction of the initial trocar was confirmed by others.[5, 11, 55] Hashizume emphasised that with the open Hasson technique only the vascular and visceral risks of the Veress needle and of the initial trocar introduction are diminished and that some visceral lesions are made by the second and following trocars even if introduced under direct vision (0.02%).[34]
In the same patient group the ultrasonic device (UD) [Ultracision®, Ethicon Endo-surgery Cincinnati OH, USA] was applied for adhesiolysis. The ultrasonic technique enables laparoscopically an (almost) complete adhesiolysis in 98% of patients with adequate hemostasis and fewer thermal perforations, and adds to the feasibility and safety of laparoscopic adhesiolysis.[46, 59, 78] No other instruments than UD were necessary for adhesiolysis. In four patients electrocautery had to be used for sufficient hemostasis of bleedings from larger omental vessels.
Ultrasonic dissection saves operation time. Simultaneous dissection and hemostasis minimise the need for exchange of instruments.[26] Four (3.8%) serious complications occurred; three small bowel perforations and one bladder perforation. In literature 40% of bowel perforations were not recognised during operation. These late perforations might have been caused by thermal lesions due to high temperature (570°F) of the electrodissection device.[34, 46] In this series no late perforations were diagnosed, probably because the tip of the Ultracision® is much cooler than the tip of electrodissection device (100°C versus 300°C) and because the minimal lateral energy spread of the UD.[56]
Ultrasonic dissection has some concomitant advantages. It produces less charring and less tissue necrosis and thus less adhesion reformation and in patients wearing a pacemaker, the UD can be used without additional security measurements.[74]

Answering the question:

In selected cases the eight intercostal space might provide a safer introduction site for the Veress needle. With an optical trocar a safe introduction site of the abdominal wall can be chosen. The ultrasonic technique offers adequate hemostasis and fewer thermal perforations and adds to the safety of laparoscopic adhesiolysis.

Question

Your patient wonders why the pain will not return. The adhesions were due to an operation, are lysed with another operation, and she expects recurrence of adhesions and therefore recurrence of her pain. Can you reassure her?

What is the recurrence rate of adhesions after laparoscopic adhesiolysis?

Surgery for adhesions seems contradictionary. One of the arguments against adhesiolysis is regrowth and denovo formation of adhesions. Adhesions do develop after each laparotomy and the number of adhesions increases the more laparotomies have been done.[81] So open surgery will not decrease the number of adhesions and is not the solution of this problem. Although Risberg concludes that surgeons can minimise abdominal trauma by using minimal invasive surgery, there is limited evidence for less adhesion formation after laparoscopic surgery if compared with laparotomies.[66] We wanted to know whether or not laparoscopic adhesiolysis permanently diminishes the extent of adhesions.

From January 1992 till January 2000, a total of 368 patients underwent laparoscopic adhesiolysis because of chronic abdominal pain (358) or bowel obstruction (10) (chapter 5). We got the opportunity for a second-look in 24 patients after a mean period of 16 months after their laparoscopic adhesiolysis. Location, extent and type of adhesions were assessed at first and at second "laparoscopy".

At second-look a significant reduction of incidence, extent, type and severity was found after laparoscopic adhesiolysis of adhesions between organs and the abdominal wall. Laparoscopic adhesiolysis of adhesions between organs (enterolysis) did not result in a permanent significant reduction of adhesions. Only three patients (3/24;12.5%) were completely free of adhesions and 21 patients had regrowth of pre-existing adhesions or denovo adhesions. In 5 patients new or more adhesions were present at sites where they were not or less present at first laparoscopy (denovo adhesions).

Clinical and experimental studies show fewer adhesions after laparoscopically performed operations compared with open surgery.[29, 43, 45, 50, 57, 61, 70, 79] Animal studies have shown a reduction in adhesion formation compared between open and laparoscopic surgery. [50, 65, 79] In human studies, Semm showed a 50% reduction of adhesions after laparoscopic gynaecological procedures,[71] while Polymenas found a significant lower rate of adhesions in favour of laparoscopic cholecystectomy.[61] These studies also show denovo adhesion formation after laparoscopic surgery although less than with open surgery.

Answering the question:

After laparoscopic adhesiolysis regrowth and denovo adhesions occur, but to a lesser degree than after open adhesiolysis. Despite regrowth and denovo formation of adhesions, laparoscopic adhesiolysis reduces permanently the quantity and quality of adhesions.

Question

Your patient will ask you to take preventive measures during or after laparoscopic adhesiolysis in order to limit regrowth of adhesions.
What would you tell here?

Which clinical measures can be taken to prevent postoperative adhesions, and what is the value of these preventive measures?

The two major strategies for reduction of postsurgical adhesions are adjusting surgical technique and applying adjuvants. Minimising surgical trauma c.q. laparoscopic surgery, minimising the risk of ischaemia, avoiding contamination of the abdominal cavity with foreign materials and bacteriae will attribute to fewer postoperative adhesions. Beside, specific preventive measures can be taken such as medication interacting the formation of fibrin or the stimulation of fibrinolysis. Local measures have been applied with intra-abdominal fluids and mechanical barriers between adjacent tissues.
We analysed 24 patients with a second look procedure after laparoscopic adhesiolysis [chapter 5]. These patients were operated with minimal invasive surgery, with Ultrasonic dissection of the adhesions, a technique without carbonisation, with incidental use of electrocoagulation for hemostasis, and without application of sutures or gauzes in the abdominal cavity.
At second-look a significant reduction of the adhesions could be determined of those adhesions fixating the organs to the abdominal wall, but not for the adhesions between the organs. At some sites, even more adhesions had reformed after enterolysis, and some denovo adhesions had occurred.
The more laparotomies have been done, the more adhesions will exist. With minimal invasive surgery the site of the trocars will be chosen away from the involved organ for easy handling of the instruments and better overview of the camera. Laparoscopic surgery has less wound and less direct contact of the trocar wound of the abdominal wall with the operation field inside. These 24 patients show limited reformation of pre-existing adhesions after laparoscopic adhesiolysis. Fewer adhesions after minimal invasive surgery has been confirmed with other operations in animals [50, 65, 79] and in human studies.[61, 71] The statement that a laparoscope causes as much damage as a surgeon's finger may be right, but a laparoscopist will use only one laparoscope and in open surgery at least 10 fingers will touch the vulnerable peritoneum.

We participated in a multicenter study evaluating the reduction of adhesions using a mechanical barrier (Seprafilm™) between the organs and pelvis and the abdominal wall (chapter 6). In this randomised study a significant increase in the severity of adhesions compared with their presence at initial surgery was found at second stage surgery whether or not Seprafilm had been applied. However, the severity of adhesions in the Seprafilm™ group was significantly reduced compared with the control group, both the adhesions adhesive with the midline incision as with

the pelvic area. Seprafilm appeared effective in reducing the severity of postoperative adhesions after major abdominal surgery.[3, 86]
A wide variety of therapeutic modalities such as dexamethason, NSAID´s and recombinant tPA affecting the cascade of fibrin synthesis and fibrinolysis has been examined with inconsistent results and serious side effects like haemorrhage and impaired wound healing.[18, 37, 67, 82]
From 1990, absorbable barriers such as polytetrafluoraethylene, oxidised regenerated cellulose (Interceed®) and hyaluronic acid/carboxymethylcellulose (Seprafilm™) have been placed between injured peritoneal surfaces to reduce postoperative adhesion formation in open surgery.[3, 7, 35, 86, 87] Fluid barriers, also suitable for laparoscopic surgery, such as ionically cross-linked 0.5% hyaluronic acid (Intergel™), 32% dextran 70 (Hyskon®) or 0.04% hyaluronic acid (Sepracoat™) have been applied resulting in fewer adhesions.[10,16] Hyaluron based agents do reduce adhesions after abdominal surgery, but do not affect the peritoneal fibrinolytic response to surgery.[64] Recently Icodextrin® showed significantly reduced postoperative adhesion formation after peritoneal trauma in rats. This liquid, in his original form used in peritoneal dialysis, has no serious side effects, and creates a constant fluid layer between injured surfaces during 5 days, the most active period of adhesion formation. [33, 80] Recent results of Icodextrin (ADEPT®, Shire Pharmaceuticals Ltd, Basingstoke, UK) are promising.

Answering the question:

Laparoscopic minimal invasive surgery is the technique of choice for adhesiolysis. Mechanical and fluid hyaluron based barriers will decrease the regrowth of adhesion, but the costs of these preventive measures oblige a careful consideration. The fluid Icodextrin® is much cheaper and deserves a randomised trial in humans.
Mechanical barriers can prevent adhesion formation with the abdominal wall, but can not be applied between organs and the retroperitoneum, the preferred site of adhesions causing bowel obstruction. It is yet unclear to what extent this reduction of adhesion formation has clinical importance, and whether these barriers will indeed lead to any prevention of bowel obstruction, infertility or chronic abdominal pain.

Question

After reconsideration of your information and search on the internet, your patient doubts about the indication of laparoscopic adhesiolysis.
Can you provide her scientific proof about the benefit of laparoscopic adhesiolysis?

The real benefit of laparoscopic adhesiolysis in patients with chronic abdominal pain

American Practise of Surgery (year 1910) page 726: "Extensive adhesions may be present without giving rise to symptoms unless the faecal stream should be interfered with by strangulation, stenosis or some form of mechanical obstruction".[60]
In 1992 Ikard stated that critical analysis fails to extract the association of adhesions and intrinsic pain from the realm of myth. Surgeons who disagree with this conclusion must prove their clinical success.[42] Before the laparoscopic era most surgeons and gynaecologists were non-believers adhesions being the cause of chronic abdominal pain and a laparotomy was not performed. The pain was considered as non-organic and results of surgery were based on placebo effects.[39, 62]
Since 1990 several prospective studies have been performed assessing the usefulness of laparoscopic adhesiolysis for chronic abdominal pain.[19, 25, 48, 49, 51, 58] Laparoscopic lysis of adhesions has been proposed as the therapeutic modality of choice, although their reports of success are controversial. Permanent good results, expressed as no pain or reduced pain, was reported in 38% [49] up to 84% of patients. [58] Recently, supporting objective evidence was obtained for the presence of sensory nerve fibres in adhesions, suggesting the possibility of conducting pain of its own stimulus. [76]

To evaluate the benefit of laparoscopic adhesiolysis, we first wanted to know the feasibility and the risks (chapter 2). In 174 procedures the adhesiolysis was completed in 74% of cases. Complications occurred in 9% of patients and two of these patients died. A higher number of prior laparotomies and a higher age of the patient cause significantly more complications. We were concerned about these figures.
With this knowledge we assessed of 224 patients (chapter 3) the results of laparoscopic adhesiolysis. We found an (almost) complete adhesiolysis in 92% of patients, and their pain disappeared or diminished in 74% of patients. Female gender, higher age and perforations leading to a conversion were factors, which caused significantly less results. Remarkably, incompleteness of the adhesiolysis did not influence pain relief. Five percent of patients were complicated. We were not satisfied with these results.
To improve the feasibility and to decrease the complication rate, we tried Ultrasonic dissection (chapter 4). This technique enables an (almost) complete adhesiolysis in 103 (98%) patients.

Four perforations (4%) during laparoscopic adhesiolysis occurred. These figures encouraged us for further research.
Despite good results in several prospective investigations, the value of laparoscopic adhesiolysis is not evidence-based. Our next step was a prospective, blind trial, which, after diagnostic laparoscopy, randomised between laparoscopic adhesiolysis and a control group (chapter 8). Randomisation put up 52 patients in the adhesiolysis group. In this group 57% of patients were pain free of had less pain after treatment. Their VAS score and their use of medicines were significantly lower than preoperative values. Their quality of life scores were significantly improved. These significant differences were measured after 6 months and had not changed at 12 months. However, no differences existed in the outcomes of all pain measurements and quality of life at all assessments in the control group if compared with the treatment group. Six complications occurred, in patients undergoing laparoscopic adhesiolysis, without mortality. This randomised trial was designed to confirm and to prove a significant pain relief in patients with chronic abdominal pain after laparoscopic adhesiolysis. After this trial we have to conclude that diagnostic laparoscopy should be encouraged, but that laparoscopic adhesiolysis should be abandoned.

Answering the question:

Outcomes from the randomised trial make clear that laparoscopic adhesiolysis carries additional morbidity and no additional pain relief for patients with chronic pain compared with diagnostic laparoscopy alone. It seems that laparoscopic adhesiolysis does not owe its value to the adhesiolysis but to factors around the diagnostic part of the laparoscopy. Elcombe found diagnostic laparoscopy to be therapeutic in women with chronic pelvic pain.[20] *Bruxelle supposed a good doctor-patient relationship as a powerful placebo effect.*[9]

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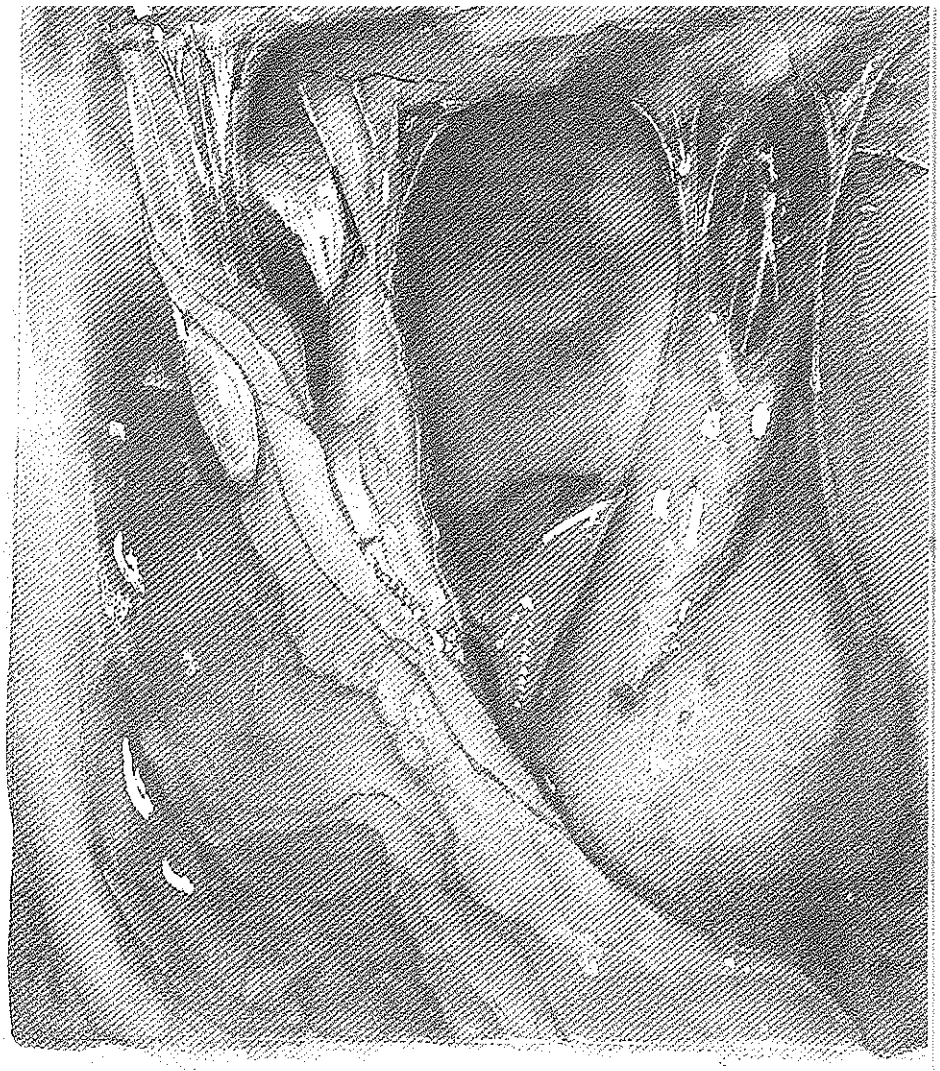

Chapter 10

Summary and conclusions

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Postoperative adhesions can be classified as normal physiology and harmless, but also as major pathology leading to life threatening disorders and even death. When adhesions are present, relaparotomies are more difficult and should not be underestimated by the junior surgeon. If the abdomen is opened through the same incision the risk of an iatrogeneous bowel perforation can be as high as 20%. The risk to die after surgery for adhesive small bowel obstruction is about 10%. Many people have undergone laparotomies and 90% of these patients will have adhesions in their abdominal cavity afterwards. Chronic abdominal pain occurs often after laparotomies for which a cause can not be found with non-invasive investigations. These patients develop their pain after abdominal surgery and ask for treatment for their pain due to abdominal adhesions. Adhesiolysis by laparotomy is not an option because more adhesions will develop afterwards.

Since 1990 adhesiolysis can be performed laparoscopically, and many surgeons with these skills performed laparoscopic adhesiolysis for chronic abdominal pain. At least 10 prospective studies were published describing good results with relief of pain in a vast majority of patients. We were impressed by the short time good results, but on the other hand were also impressed by the serious complications and even death. A few other studies showed less good results and emphasised the risks of this technique and disputed chronic abdominal pain to be an indication for laparoscopic adhesiolysis. This debate would never end, unless a randomised study could give the answer.

Professor Ellis, who classifies adhesions as normal physiology unless they are obstructing the bowel, confided to me that I should never be able to proof the benefit of laparoscopic adhesiolysis for chronic abdominal pain. I was convinced of the opposite, accepted the challenge, and prepared a response. A multicenter randomised clinical trial was designed to proof the benefit of laparoscopic adhesiolysis for chronic abdominal pain.

Chapter 1 comprises the general introduction. The history of laparoscopic surgery started 100 years ago. In those years the cystoscope was used for diagnostic purposes, and not before the seventies the advanced technique was used for organ surgery and even for resections. It was a gynaecologist, who removed laparoscopically the first appendix in 1983.

Ninety-three percent of the acquired adhesions are due to surgical trauma. Most adhesions are between the omentum and the abdominal wall and in 33% of the adhesions the small bowel is involved. Adhesions are a serious problem for the surgeon with considerable workload and impressive morbidity and mortality for the patient.

No consensus exists about a classification of adhesions. The clinical and histological classification of Zühlke satisfies best for a surgeon and this classification was applied in our studies.

An overview is given of the pathophysiology of peritoneal damage as trigger moment for a coagulation process leading to a tournament of leukocytes, mesothelial cells and fibrin from

the inner layer of the peritoneum. After five days macrophages produce growth factors and cytokines and recruit new mesothelial cells to complete the reepithelisation of the peritoneal surface. Contact between two injured surfaces will lead to coating of a sticky fibrin gel matrix resulting in bridging between organs. This primary adhesion will become permanent if this fibrin formation is more powerful than fibrinolysis.
Several measures can be taken to lessen or to prevent the adhesion formation. The surgical technique can be improved with minimal invasive surgery in order to decrease the injury of the peritoneal surface. Diminish the use of swabs, coagulation and sutures, and save the serosal fluid as it contains tPA, an enzyme that activates plasminogen to form plasmin, necessary for fibrinolysis.
The clinical presentation of adhesions varies between bowel obstruction, infertility and chronic abdominal pain. For all these disorders open or laparoscopic adhesiolysis has been performed. Several techniques have been used to decrease the incidence of complications. Preventive measures were extensively tried with diverse successes. There is no consensus yet about the indication of laparoscopic adhesiolysis for chronic abdominal pain possibly due to adhesions.

Chapter 2 presents the results of a retrospective study of 174 patients with chronic abdominal pain. These patients underwent laparoscopic adhesiolysis and were analysed for factors which might influence the complication rate and the feasibility of this technique. In 4% of these patients concomitant pathology was found. Major complications such as bleeding and bowel perforations were noticed in 16 patients (16/174: 9%). Two patients died (2/174: 1%) In almost 100% of patiens with a bowel perforation, either not recognised during laparoscopy or due to late thermal necrosis, revealed a generalised peritonitis in the days after the operation. Higher age and more previous laparotomies were independent factors associated with increased risk of these complications.
A complete adhesiolysis could be performed in the vast majority of patients (128/167: 76%) Only in 5 patients the risk of perforation was too high to fulfil the adhesiolysis. The number of previous operations and the use of electrocoagulation were independent factors impairing the completeness.

Chapter 3 reveals the study and the outcomes of a prospective analysis of pain relief after laparoscopic adhesiolysis. Two hundred patients underwent primary laparoscopic adhesiolysis. In 13 patients (13/224) concomitant disorders were found besides adhesions. An (almost) complete adhesiolysis could be performed in 92% of patients. Three months later 74% of the patients were pain free or had less pain. The remaining patients felt no change or had even more pain. Patients with complicated procedures (10%) had significantly worse results. Female gender, higher age and bowel perforations with laparoconversion appeared to be independent factors responsible for less chance being pain free after laparoscopic adhesiolysis. On the contrary, incompleteness of the adhesiolysis did not take effect on pain relief.

Chapter 4 shows the extra safety of the application of an optical trocar (Optiview®) and ultrasonic dissection in laparoscopic adhesiolysis. The use of a blunt tip optical trocar enabled us to penetrate the abdominal wall under direct vision and to identify all layers separately. If an intra-abdominal organ is adherent with the parietal peritoneum, the dark background of the abdominal cavity filled with carbondioxide is no longer present behind this layer and adhesions or adhesive organs should be suspected.
With ultrasonic dissection (Ultracision®), an (almost) complete adhesiolysis was achieved in 98% of patients (103/105) and this technique provides also simultaneous hemostasis. The temperature of the tip of the dissection device is much lower than the one of the tip of the electrodissection device with consequently less lateral tissue necrosis. This fact is probably the reason of the higher feasibility of ultrasonic adhesiolysis if compared with electrodissection. This lower temperature might also prevent late thermal perforations. These late perforations were not observed in this series and made the complication risk drop to as low as 4%. Both devices seem to improve the safety of laparoscopic adhesiolysis.

Chapter 5 portrays the enduring morphological results of laparoscopic adhesiolysis. In a prospective study of 368 patients in whom adhesions were assessed for incidence, extent and type, and who underwent laparoscopic adhesiolysis, 24 patients got a second-look laparoscopy after a mean period of 16 months. Incidence, extent, type and severity of adhesions between organs and the abdominal wall were significantly reduced. No reduction could be demonstrated after the previous adhesiolysis of bands between organs. Denovo adhesions occurred in 20% of patients. Despite regrowth and denovo formation of adhesions laparoscopic adhesiolysis did permanently reduce the quality and quantity of adhesions.

Chapter 6 demonstrates our experiences with the prevention of adhesion formation. Patients scheduled for a Hartmann procedure were enrolled in a prospective study with a second-look procedure offering the possibility of assessing adhesions. These patients were randomised for application of a preventive adhesion barrier (Seprafilm™) or no prevention after primary surgery. Seprafilm™ anti-adhesive membrane appears effective in reducing the severity of postoperative adhesions after major abdominal surgery, although the incidence of adhesions had not diminished. Therefore we recommend the use of Seprafilm™ when a relaparotomy or a second-look intervention is planned. Long-term studies are needed to assess the cost-effectiveness and the value of Seprafilm™ in the prevention of bowel obstruction, chronic abdominal pain and infertility.

Chapter 7 reviews the role of adhesiolysis in patients with bowel obstruction, chronic abdominal pain and in patients with infertility. Surgical lysis is the only available therapy for intra-abdominal adhesions. A Medline search was performed for the period from January 1970 to December 2001.

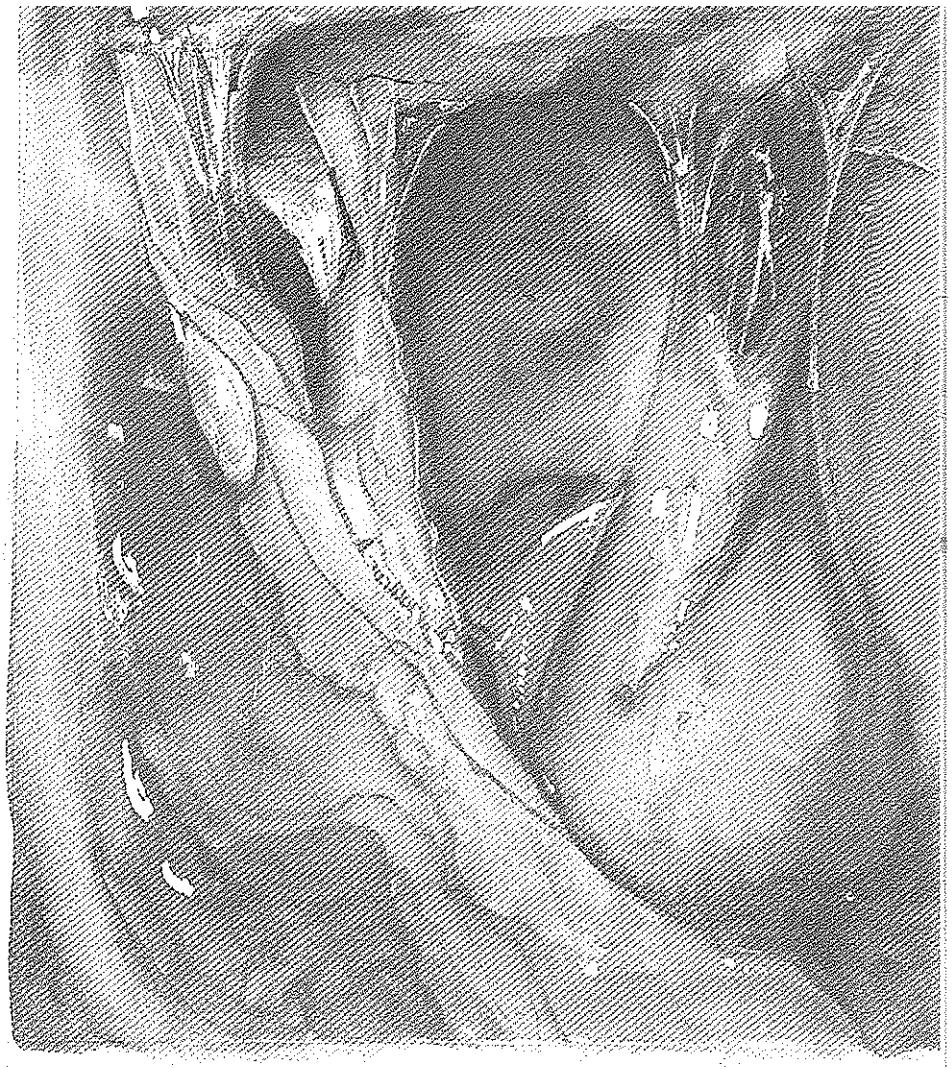
Complete small bowel obstruction and parameters like tachycardia, fever, focal tenderness, focal peritonitis and leucocytosis are forcing indications for laparotomy. The role of laparoscopy in the management of acute bowel obstruction remains unclear yet, especially because little working space is available in the acute phase for detection and treatment of adhesions, and the complication risk is great.
Meta-analysis of the data of the results of the different studies concerning the benefit of laparoscopic adhesiolysis in patients with chronic abdominal pain is not possible because of the big differences between the designs of these studies.
Second-look laparoscopy after adhesiolysis for infertility has never became popular and it is questionable whether it is ethically justified to perform this diagnostic procedure after surgery for infertility. No prospective randomised studies have been executed and selection of patients for surgery occurred in every study, making it impossible to draw conclusions.
Dissection of adhesions can be executed in various ways. There is no consensus about a preferred method. No randomised studies have been undertaken to compare sharp dissection, electrosurgery or laser dissection in humans. No difference was shown between electrosurgery and CO_2 laser in periadnexal adhesiolysis in two non-randomised studies, evaluated by second-look laparoscopy. Dissection is associated with a considerable risk of bowel perforation. It can occur during the installation phase of laparoscopy or during the adhesiolysis itself. Diagnosis of gastrointestinal injury is made intraoperatively in only 35% of patients undergoing laparoscopic adhesiolysis, and are clear postoperatively in the majority of patients with a mean delay of 4 days.

Chapter 8 investigates the real benefit of laparoscopic adhesiolysis for chronic abdominal pain. In this multicenter clinical trial, patients were enrolled for diagnostic laparoscopy if they had chronic abdominal pain attributed to adhesions caused by previous surgery. Other causes for their pain had been excluded by standard preoperative investigations. If adhesions were confirmed at diagnostic laparoscopy, then the patient was randomly assigned either to laparoscopic adhesiolysis or to diagnostic laparoscopy alone (control group). Pain relief was assessed by four pain scores and the quality of life was assessed with the MOS - SF 36 score. Outcomes of the pain scores demonstrate significant pain relief as well in the adhesiolysis group as in the control group at six months. The quality of life was improved for those items concerning physical activities, but not for patients' perception about their mental and general health and their emotional functioning. Results did not change after six months. However, no differences exist between the outcomes of all pain measurements and quality of life scores at all assessments if compared between both randomised groups. Six patients were complicated in the adhesiolysis group.
We have to conclude that laparoscopic adhesiolysis carries additional morbidity and no additional pain relief and no improvement of quality of life for patients with chronic pain compared with diagnostic laparoscopy alone. Although world-wide performed, never been

evidence-based, laparoscopic adhesiolysis should not be performed as a treatment for adhesions in patients with chronic abdominal pain.

Chapter 9 includes the general discussion of this thesis. Answers are given about most questions patients ask during a patient visit. With diagnostic laparoscopy, besides adhesions, 5-10% of concomitant disorders will be detected dependant of the extensiveness of the prior non-invasive investigations. Based on new knowledge, we can advise patients whether or not they should be operated for adhesions and whether they belong to a high risk group. We can value the expectations of pain relief and can inform that adhesions do reoccur after adhesiolysis and denovo adhesions will grow, but that the severity of adhesions between organs and abdominal wall are significantly diminished after laparoscopic adhesiolysis. The best advise for patients with chronic abdominal pain after prior laparotomy or laparoscopic procedure should be a diagnostic laparoscopy and should not be a laparoscopic adhesiolysis.

At last the truth is out.
Professor Ellis was wrong, I was able to proof the benefit of laparoscopic adhesiolysis, but the outcomes have proved him right: there is no benefit.



Chapter 11

Samenvatting en conclusies

Samenvatting en conclusies

Postoperatieve adhesies kunnen worden beschouwd als een eindresultaat van herstel van weefsels en dus als normale fysiologie, maar kunnen ook gezien worden als ernstige pathologie, die kan leiden tot levensbedreigende aandoeningen en zelfs tot de dood. Relaparotomieën zijn ten gevolge van adhesies technisch moeilijker en dienen niet onderschat te worden door onervaren chirurgen. Als de buik door dezelfde incisie wordt geopend, loopt de patiënt 20% risico op een iatrogene darmperforatie. Er is 10% risico op overlijden bij een operatie voor een dunne darm afsluiting, die veroorzaakt wordt door verklevingen (adhesies). Veel mensen hebben buikoperaties ondergaan en 90% van deze patiënten heeft dientengevolge verklevingen in hun buikholte. Ook hebben veel mensen chronische buikpijn waarvoor de oorzaak niet kan worden gevonden met niet-invasief onderzoek. Een groot deel van deze patiënten kreeg deze buikpijn na een chirurgische ingreep en wijten deze pijn aan adhesies en vragen om die reden een behandeling. Het losmaken van verklevingen (adhesiolyse) d.m.v. een laparotomie is geen optie omdat deze operatie weer nieuwe en meer adhesies tot gevolg heeft.
Sinds 1990 is het technisch mogelijk adhesiolyse laparoscopisch uit te voeren en vele chirurgen met laparoscopische vaardigheden verkiezen deze laparoscopische techniek bij patiënten met chronische buikpijn. Tenminste 10 prospectieve studies zijn gepubliceerd, waarin de goede resultaten - verlichting van de pijn bij een zeer grote meerderheid van de patiënten - worden beschreven.
Wij waren onder de indruk van deze - korte termijn - goede resultaten, maar daar tegenover stonden de complicaties en de mortaliteit, die deze laparoscopische ingreep soms met zich meebracht. Bovendien toonde een aantal andere studies minder goede resultaten aan en benadrukte ze de risico's van deze techniek en betwistte ze chronische buikpijn als een indicatie voor laparoscopische adhesiolyse.
Een gerandomiseerde studie zou een antwoord moeten geven op dit vraagstuk.

Professor Ellis, die de vorming van adhesies beschouwt als normale fysiologie, tenzij de darmen door de adhesies worden geobstrueerd, vertrouwde mij toe dat ik nooit in staat zou zijn het nut van laparoscopische adhesiolyse bij chronische buikklachten te kunnen aantonen. Ik was overtuigd van het tegendeel en accepteerde deze uitdaging. Het antwoord was een gerandomiseerd klinisch onderzoek, dat in meerdere ziekenhuizen is uitgevoerd, teneinde het succes van laparoscopische adhesiolyse te bewijzen bij patiënten met chronische buikpijn.

Hoofdstuk 1 beschrijft de algemene introductie. De geschiedenis van laparoscopische chirurgie begon honderd jaar geleden. Toentertijd werd de cystoscoop gebruikt voor diagnostische doeleinden en pas vanaf de zeventiger jaren werd deze verder ontwikkelde techniek gebruikt bij orgaan chirurgie en zelfs bij orgaan resecties. Anno 1983 was het een gynaecoloog, die als eerste een blinde darm laparoscopisch verwijderde.
Adhesies zijn een groot probleem voor de chirurg, veroorzaken een aanzienlijke werklast en de behandeling ervan leidt tot indrukwekkende ziekte- en sterftecijfers. Bij 93% van de patiënten

met adhesies zijn deze ontstaan t.g.v. chirurgische ingrepen. De meeste adhesies bevinden zich tussen het omentum en de buikwand en in 1/3 van de gevallen is de dunne darm hierbij betrokken.
Er is geen consensus over de ideale classificatie van adhesies. Voor een chirurg voldoet de klinisch / histologische classificatie van Zühlke het meest en deze classificatie is in onze studies toegepast.
Een overzicht wordt gegeven van de pathogenese van adhesies. Beschadiging van het peritoneum is een uitlokkend moment voor een stollingsproces, dat leidt tot mobilisatie van leukocyten, mesotheel cellen en fibrine, afkomstig uit de onderste laag van het peritoneum. Na vijf dagen produceren macrofagen groeifactoren en cytokines en nieuwe mesotheelcellen voltooien de reëpithelisatie van het buikvliesoppervlak.
Bij contact tussen twee beschadigde oppervlakken plakt een kleverige fibrine gel matrix de weefsels aan elkaar en vormt zo een brug tussen deze organen. Deze primaire adhesie is blijvend als de aanmaak van fibrine krachtiger is dan de afbraak ervan.
Verscheidene maatregelen kunnen genomen worden om de vorming van adhesies te verminderen of zelfs te voorkomen. Daar waar mogelijk kan minimaal invasieve chirurgie worden toegepast teneinde de beschadiging van de peritoneale oppervlakken te reduceren. Beperkt gebruik van gazen, coagulatie en hechtmateriaal in de buikholte leidt tot minder adhesievorming. Het buikvocht moet in situ blijven, daar dit tPA bevat - een enzym dat plasminogeen omzet naar plasmine – dat noodzakelijk is voor de afbraak van fibrine.
Klinisch presenteren adhesies zich op verschillende manieren, variërend van darm afsluiting, onvruchtbaarheid tot chronische buikpijn. Voor al deze aandoeningen is adhesiolyse toegepast, hetzij via laparotomie of op laparoscopische wijze. Verscheidene technieken zijn bedacht, zoals het gebruik van ultracision, teneinde de incidentie van complicaties te verminderen. Preventieve maatregelen, zoals applicatie van Seprafilm en Sepracoat, zijn uitvoerig getest met wisselende successen.
Tot op heden blijft het onduidelijk of laparoscopische adhesiolyse waardevol is voor patiënten met adhesies en chronische buikklachten.

Hoofdstuk 2 vermeldt de resultaten van een retrospectief onderzoek bij 174 patiënten met chronische buikpijn. Deze patiënten ondergingen laparoscopische adhesiolyse en werden gescreend op factoren, die van invloed konden zijn op het krijgen van complicaties en op de toepasbaarheid van de techniek. Bij 4% van deze patiënten werden in de buik ook andere afwijkingen gevonden dan adhesies. Ernstige complicaties, zoals bloedingen en darmperforaties kwamen voor bij zestien patiënten (9%). Twee patiënten overleden (1%).
In 40% van de patiënten met een darmperforatie werd deze pas na de operatie onderkend. Deze late darmperforaties, hetzij ontstaan doch niet herkend tijdens de laparoscopie of ontstaan na de operatie door hitte necrose, openbaarden zich in de dagen na de operatie als een gegeneraliseerde peritonitis. Hogere leeftijd en meer voorafgaande buikoperaties blijken onafhankelijke factoren te zijn met een grotere kans op bovenstaande complicaties.

Bij een grote meerderheid van de patiënten (128/167) was de adhesiolyse compleet. Slechts bij vijf patiënten was de kans op een perforatie bij doorgaan van de adhesiolyse zo groot dat de adhesiolyse niet werd voltooid. Een groter aantal voorafgaande operaties en toepassing van electrocoagulatie zijn onafhankelijke factoren, die een complete adhesiolyse in de weg kunnen staan.

Hoofdstuk 3 onthult het onderzoek en de uitkomsten van een prospectieve analyse van verlichting van pijn na laparoscopische adhesiolyse. Tweehonderd patiënten ondergingen voor de eerste keer een laparoscopische adhesiolyse. Bij dertien patiënten (13/224) werden andere afwijkingen naast adhesies in de buik aangetroffen. Een (nagenoeg) complete adhesiolyse kon worden verricht bij 92 procent van de patiënten. Drie maanden later had 74 procent van de patiënten minder pijn of geen pijn meer. De andere patiënten merkten geen verschil of hadden zelfs meer pijn gekregen na de operatie. Patiënten, waarbij tijdens de operatie complicaties optraden (10%), hadden significant slechtere resultaten. Het vrouwelijk geslacht, hogere leeftijd en darmperforaties (met als gevolg laparotomie) bleken onafhankelijke factoren te zijn, met minder kans om pijnvrij te worden na een laparoscopische adhesiolyse. Daarentegen had een onvolledige adhesiolyse geen significant ander effect op de pijn verandering. Patiënten met een incomplete adhesiolyse hadden dezelfde resultaten als die na een complete adhesiolyse.

Hoofdstuk 4 toont de extra veiligheid bij laparoscopische adhesiolyse van een optische trocar (Optiview®) en een snijtechniek op basis van ultrageluid (Ultracision®). Het gebruik van een optische trocar met een stompe punt stelde ons in staat de buikwand te penetreren onder direct zicht van de camera om zodoende alle lagen afzonderlijk te kunnen identificeren. Als een orgaan in de buik verkleefd is met de buikwand, dan verdwijnt de donkere achtergrond - van de met CO_2 gevulde buikholte - en kunnen adhesies verwacht worden.
Ultrasonore dissectie (Ultracision®) bewerkstelligt naast een (nagenoeg) volledige adhesiolyse bij 98% van de patiënten (103/105) tevens een afdoende hemostase. De temperatuur van de tip van dit apparaat is veel lager dan de temperatuur, die wordt bereikt bij toepassing van electrodissectie en dientengevolge is er ook minder weefselsterfte in de directe omgeving. Dit is waarschijnlijk de reden dat ultrasone adhesiolyse beter toepasbaar is dan elektrodissectie. De lagere temperatuur zou ook de late thermische perforaties kunnen voorkomen. Deze late perforaties zijn in dit onderzoek niet voorgekomen waardoor het aantal complicaties tot vier procent werd beperkt.
Beide apparaten lijken de veiligheid van laparoscopische adhesiolyse te verhogen.

Hoofdstuk 5 brengt in kaart de blijvende morfologische resultaten van laparoscopische adhesiolyse. Bij 368 patiënten werden voorafgaande aan een laparoscopische adhesiolyse de adhesies geclassificeerd op basis van het aantal, de uitgebreidheid en het type. Na gemiddeld 16 maanden werd bij 24 van deze patiënten nogmaals laparoscopie uitgevoerd. Het aantal, de uitgebreidheid en het type van de adhesies tussen organen en de buikwand waren significant

afgenomen. Er was geen reductie aantoonbaar van de adhesies tussen de organen. Bij 20% van de patiënten verschenen nieuwe adhesies op plaatsen waar ze voordien niet aanwezig waren. Laparoscopische adhesiolyse reduceert het aantal adhesies ondanks recidivering van bestaande adhesies en vorming van nieuwe adhesies.

Hoofdstuk 6 demonstreert onze ervaringen met preventieve maatregelen tegen adhesievorming. Patiënten, uit verschillende ziekenhuizen, gepland voor een Hartmann procedure, werden geïncludeerd in een prospectieve studie waarbij het opheffen van het stoma een mogelijkheid bood voor second-look en beoordeling van adhesievorming. Aan het einde van de primaire operatie werden patiënten gerandomiseerd tussen geen preventie of toepassing van een preventieve adhesie barrière (Seprafilm™).
De Seprafilm™-membraan bleek effectief te zijn bij het reduceren van de uitgebreidheid van postoperatieve adhesies na grote buikchirurgie, maar het aantal adhesies was niet afgenomen. Om die reden adviseren wij de toepassing van Seprafilm™ indien een relaparotomie of een second-look interventie op voorhand wordt gepland. Er zijn lange termijn studies nodig om de waarde en de kosten-effectiviteit van Seprafilm™ te kunnen aantonen bij de preventie van darmafsluiting, chronische buikpijn en onvruchtbaarheid.

Hoofdstuk 7 geeft een overzicht van de literatuur van de waarde van adhesiolyse bij patiënten met darmafsluiting, chronische buikpijn en onvruchtbaarheid. Alle artikelen uit de Medline tussen januari 1970 en december 2001 zijn hierbij betrokken.
Een volledige darmafsluiting en een afsluiting met parameters als tachycardie, koorts, locale drukpijn, locale peritonitis en leucocytose zijn harde indicaties voor een laparotomie en open adhesiolyse. De rol van laparoscopie bij de aanpak van een acute darmafsluiting is tot nu toe onduidelijk. Vooral in de acute fase is er weinig werkruimte in de buik voor de beoordeling en de behandeling van adhesies, waardoor het risico op complicaties groot is.
Een meta-analyse van de verscheidene studies over pijn vermindering na laparoscopische adhesiolyse bij patiënten met chronische buikpijn is niet mogelijk vanwege de grote verschillen tussen de bestaande onderzoeken.
Second-look laparoscopie na adhesiolyse vanwege onvruchtbaarheid is nooit populair geworden en het is de vraag of het ethisch verantwoord is om deze diagnostische ingreep uit te voeren na de voorafgaande behandeling van de onvruchtbaarheid. Er zijn geen prospectief gerandomiseerde onderzoeken geweest en in elke studie was er een patiënten selectie, waardoor het onmogelijk werd om het nut van adhesiolyse voor deze indicatie aan te kunnen tonen.
Voor de uitvoering van de adhesiolyse bestaan diverse technieken. Het is onduidelijk welke methode de voorkeur verdient, omdat er nog geen gerandomiseerde onderzoeken zijn gedaan waarbij scherpe dissectie, elektrochirurgie en laserdissectie bij mensen zijn vergeleken. Bij twee niet gerandomiseerde studies over adhesiolyse van de parametria, geëvalueerd door second-look laparoscopie, werd geen verschil aangetoond tussen elektrochirurgie en CO_2 laserbehandeling.

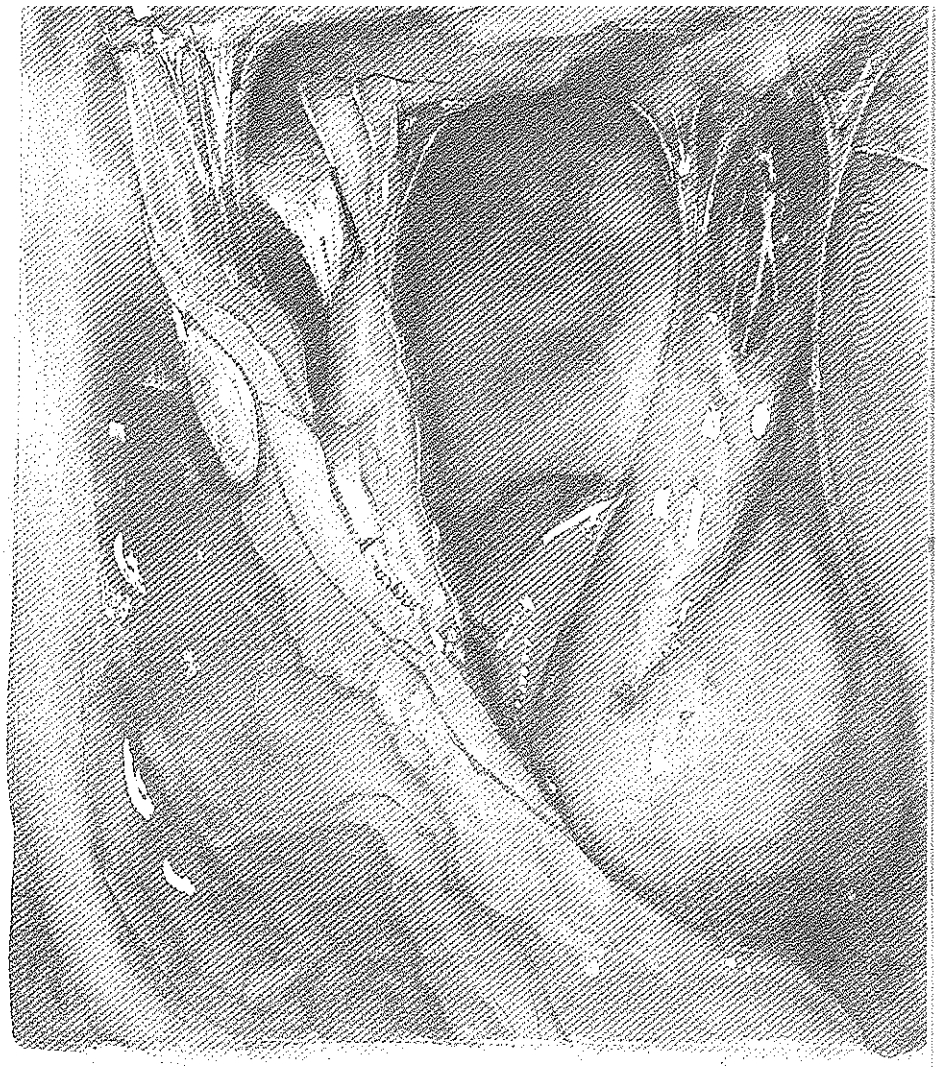
Laparoscopische adhesiolyse heeft een intrinsiek risico van darmperforatie. Dat kan ontstaan tijdens het inbrengen van de trocars of door de adhesiolyse als zodanig. Een darmperforatie wordt slechts in 35 procent van de gevallen onderkend tijdens de laparoscopische ingreep en bij een meerderheid van de patiënten wordt de laesie pas na gemiddeld vier dagen postoperatief gediagnosticeerd.

Hoofdstuk 8 onderzoekt het werkelijke nut van laparoscopische adhesiolyse bij chronische buikpijn. In deze klinische trial, die in meerdere ziekenhuizen werd uitgevoerd, werden patiënten geïncludeerd voor diagnostische laparoscopie als zij chronische buikpijn hadden, die werd toegeschreven aan adhesies. Andere oorzaken voor hun pijn werden uitgesloten door standaard preoperatief onderzoek. Als diagnostische laparoscopie de adhesies bevestigde, werd de patiënt gerandomiseerd tussen laparoscopische adhesiolyse of geen behandeling (controlegroep). De pijn verandering werd vastgesteld door middel van vier pijnscores en een score voor de kwaliteit van leven (MOS SF-36 score).
Na zes maanden toonden de pijnscores een significante vermindering van de pijn aan bij die patiënten, die adhesiolyse hadden ondergaan. De fysieke parameters van de kwaliteit van leven bij deze patiënten waren eveneens verbeterd, maar hun eigen gevoel van geestelijke en algemene gezondheid en hun emotioneel functioneren was er niet op vooruitgegaan. Deze resultaten veranderden niet meer na 6 maanden. Echter, er waren geen verschillen tussen de uitkomsten van alle metingen van pijn en van de kwaliteit van leven tussen de beide gerandomiseerde groepen.
Bij zes patiënten, die adhesiolyse ondergingen was het beloop gecompliceerd. Wij moeten concluderen dat laparoscopische adhesiolyse bij mensen met chronische buikpijn morbiditeit met zich meebrengt en geen toegevoegde waarde heeft voor verlichting van pijn of verbetering van de kwaliteit van leven boven alleen diagnostische laparoscopie.
Hoewel laparoscopische adhesiolyse wereldwijd wordt uitgevoerd, ondanks het feit dat het nut nooit wetenschappelijk is aangetoond, moet de indicatie voor de behandeling van adhesies bij patiënten met chronische buikpijn zeer kritisch worden beoordeeld.

Hoofdstuk 9 geeft de algemene discussie over deze dissertatie weer. Op de meeste vragen, gesteld door patiënten tijdens hun polikliniek bezoek, kan een antwoord worden gegeven. Met diagnostische laparoscopie worden, afhankelijk van de uitgebreidheid van de voorafgaande niet-invasieve onderzoeken, behalve adhesies, in vijf tot tien procent van de patiënten andere afwijkingen gezien. We kunnen patiënten op basis van nieuwe wetenschap adviseren of ze tot een hoog risico groep behoren. We kunnen inschatten in welke mate de pijn zal worden verlicht en we kunnen de patiënten informeren dat na een adhesiolyse er weer adhesies zullen ontstaan op dezelfde plaats of zelfs op een andere plaats, maar dat de ernst van de adhesievorming tussen organen en de buikwand significant zal zijn afgenomen. Het

beste advies, dat een medicus kan geven aan patiënten met chronische buikpijn na een voorafgaande buikoperatie is een diagnostische laparoscopie, maar geen laparoscopische adhesiolyse.

Eindelijk is er duidelijkheid.
Professor Ellis had ongelijk, ik was wel in staat het nut van laparoscopische adhesiolyse aan te tonen, maar de resultaten gaven hem gelijk: er is geen nut.



Dankwoord

Curriculum vitae

Dankwoord

Promoveren betekende voor mij terug naar Erasmus, terug naar mijn universiteit en terug naar Dijkzigt waar ik in 1975 ben afgewezen voor de opleiding chirurgie omdat ik niet de goede stropdas had gestrikt en geen gaatjesschoenen droeg. In 1997, 22 jaar later - met mijn plannen voor promotie - werd ik warm onthaald.

Prof.dr. J. Jeekel, mijn zeer gewaardeerde promotor. In de zomer van 1997 mocht ik mijn promotieplannen ontvouwen. "Haal 90% van je plannen af en werk de resterende 10% verder uit en kom over 2 weken terug." Na drie maal overleg mocht ik beginnen. Je begreep dat ik geen 5 artikelen kon schrijven in een wetenschappelijk half jaar en dat ik het werk naast een drukke chirurgische praktijk moest doen en je liet mij het tempo bepalen.
Je voorzag mijn concept artikelen van - overigens buitengewoon vriendelijk verpakt - messcherp commentaar en stuurde de concepten binnen 1 week weer terug, waardoor ik nooit het gevoel kreeg er even van af te zijn. "Sommige zinnen zijn niet goed genoeg, te wollig; kan korter, het Engels is wel goed, maar niet mooi; het kan nog beter...."
Het wachten op de goedkeuringen van de uitgevers duurde lang. "Houd vol, het kan snel gaan, stuur maar naar het allerhoogste..." "Mag ik al naar de pedel?" "Nee, nog even wachten, nog één artikel geaccepteerd en dan nog één." "Het komt goed...."
Volgens Antoinette, jouw onvolprezen secretaresse, kon ik beter de e-mails naar haar sturen, jij veegde ze nog wel eens uit...
Beste Hans, je was voor mij een ideale promotor; een promotor op maat. Je analyses waren oppervlakkig bezien onbegrijpelijk, maar na bestudering zo scherpzinnig en zo zorgvuldig. Je collegialiteit was buitengewoon en je onverzettelijkheid een voorbeeld.
Op mijn 51e ben ik je 52e (53e ?) promovendus.

Prof.dr. H.J. Bonjer. Assistent Jaap heb ik in mijn rol als oudste assistent nog een vasectomie onderwezen, en daarna mocht ik met veel genoegen je glanzende (laparoscopische) carrière meemaken. In het vliegtuig vanuit New Orleans werd het promotievuurtje aangewakkerd en leerde je mij de pitfalls van promoveren. Later volgden de concept artikelen en kreeg ik gratis een cursus frustratietolerantie. Je correcties waren niet fijnzinnig: "ik heb nog wel een paar aanpassingen" zei je en overhandigde mij een rood gekleurd epistel dat beslist zwart op wit was aangeleverd.
Je gevoel voor afronding en logistiek zijn minder ontwikkeld dan je wetenschappelijke en chirurgische kwaliteiten, maar dit heb je gecompenseerd met drie secretaressen. Deze ondertekenen gelukkig de nodige brieven met één van de twee fraaie Bonjer handtekeningen.
Beste Jaap, dank voor al je hulp en voor je rol als secretaris in de kleine commissie in het bijzonder.

Prof.dr. H.W. Tilanus, beste Huug, je participatie in de kleine commissie was voor jou vanzelfsprekend ondanks al je bezigheden. Je felicitaties kwamen al toen ik je de stapel artikelen overhandigde en ik je vroeg deze de komende vier weken door te lezen. Dank voor dit werk en voor je vertrouwen.

Dr. H. Van Goor, beste Harry, ik had je nodig om de kleine commissie te voltooien. Ondanks je overvolle agenda door de voorbereiding van het 6e internationale PAX symposium over peritoneum en je bijdrage aan de promotie van Wietske Vrijland bood je je hulp aan meteen nadat je, terug uit Londen, was geland. Zondagavond laat om 23 uur gaat dan je telefoon:"Met Harry,...,dat doe ik graag voor je." Klasse.

Prof.dr. M.A. Cuesta, beste Miguel, dank voor je participatie in de grote commissie. Wachtlijsten stonden je in de weg om zelf patienten van de studie te kunnen behandelen. Immer toonde je je interesse en je Spaanse warmbloedigheid als we elkaar ontmoetten.

Prof.dr. Th.J.M. Helmerhorst, dank voor uw participatie in de grote commissie. We hadden elkaar nog niet ontmoet en toch heeft u direct uw hulp aangeboden. Waar in de niet-medische wereld vind je dit nog?

Dr. H.J. van Geldorp, een inhoudelijke kennismaking; " je hebt toch wel een lange follow-up, ik heb toch het idee dat gynaecologische patiënten, als je ze lang vervolgt na adhesiolysis, minder pijn hebben...." Daarna directe bereidwilligheid voor deelname aan de kleine commissie. De vrijgevendheid van de ovariae en de gastvrijheid van de uterus hebben blijkbaar hun weerslag op hun behandelend arts.

W.A.P. Breeman, beste Wout, het was jouw promotie, die diepe indruk op mij maakte. Ook het feit dat je toen op tijd aanwezig was maakte indruk. Dat gold niet voor al die keren dat ik je ophaalde om naar de middelbare school te gaan en je immer bij het luiden van de schoolbel thuis nog aan tafel zat met je boterham met hagelslag. Zo´n promotie deed blijkbaar iets met je. Jouw verdediging was zo gloedvol en de scene zo echt, dat ik dat ook wilde meemaken; het startpunt van mijn promotie. Je logistieke adviezen heb ik alle opgevolgd; alleen je laatste advies om iemand anders te vragen voor de rol van paranymph omdat je het teveel eer vond, heb ik niet gehonoreerd. Vanzelfsprekend moest jij dat zijn en de eer is aan mij dat je het wilde zijn.

Mevr. Soewu, beste Lidy, dank en waardering voor jouw persoonlijke sympathie voor dit onderzoek en voor de morele en zakelijke ondersteuning van Johnson & Johnson bij de introductie van de trial in de andere klinieken. De instructie video hielp me bij de "verkoop" van het onderzoek in den lande en werd mede hierdoor een succes. Het feest kon beginnen.

Arto Pauw, beste Arto, jouw digitale kennis heb ik uitgebuit en je telkenmale gevraagd om voor elk artikel weer een programma te schrijven om alle data te kunnen invoeren. "Geef mij de items, het aantal spaties per antwoord en ik doe de rest." "Volgende week vroeg genoeg?" Als mens zo bescheiden, als hulpverlener zo groots. Ik hoop dat ik met mijn kennis en met mijn digiti ooit iets voor jou terug kan doen.

Dr. W.F.M. van Erp, beste Willem, in Kyoto gaf jij me het idee voor het onderwerp van dit onderzoek. Vervolgens een lading enthousiasme en daarna de gegevens van veel patiënten, die leidden tot het eerste artikel. Mijn eerste kick. Jij was weer de eerste, die wilde meewerken aan het multicenter onderzoek, hoewel je moeite had met de randomisatie, omdat je ervaring had met de goede resultaten van laparoscopische adhesiolyse. Je inzet is even groot als je glimlach en je vriendelijkheid. Jij deed de eerste lap chol in Nederland, ik de laatste lap adhesiolysis (voor chronische buikklachten). Als ik ooit buikpijn krijg, ben jij de eerste.... Ik ben je veel verschuldigd.

Veel collegae chirurgen hebben meegewerkt. Het multicenter onderzoek is uitgevoerd in 11 ziekenhuizen door meerdere chirurgen. Alle CRF's kwamen terug. Hulde aan Willem Bemelman, Willem van Erp, Ocker Repelaer van Driel, Ron van Doorn, Jack Jakimowicz, Willem Meijer, Johan Lange, Robert Pierik, Bert van Ramshorst, Laurents Stassen, Rob Ouwendijk (internist), Jaap Bonjer en Ignace Janssen.
Ignace, jij was al begonnen met de inclusie voordat je alle papieren in bezit had, je was een zeer trouwe partner en een actief adhesiolist en was bijna zelf begonnen met een onderzoek. Warm en goed. Als ik jou ooit kan helpen (met een promotie?).

Wietske Vrijland, beste Wietske, jij was mijn voorbeeld hoe alles moest gaan. Jouw onderzoek en het mijne liepen parallel; gelukkig liep jij voor en kon ik afkijken. Vele vragen over logistiek en praktische ondersteuning werden immer en per kerende mail beantwoord. Het was mij een waar genoegen om mee te mogen werken aan twee van je hoofdstukken en het was voor jou vanzelfsprekend om ze mij te lenen voor mijn boek. Mijn patiënten-inclusie in Dijkzigt ging van start tijdens jouw wetenschappelijk jaar en de voortgang werd gewaarborgd door Martijne van 't Riet. Zo deden jullie dat. Ik heb jouw (jullie) hulp zeer gewaardeerd.

Dr.ir. W.C.J. Hop. "Wim, als ik 500 patiënten opereer en ik vervolg ze 1 jaar en 80% heeft geen pijn meer, dan bewijs ik toch dat het een goede operatie is?" (shaggie) "Nee", was je antwoord, "daar heb je niks aan." "Je moet een sham groep hebben, die je niet opereert en als je die hebt kom je maar terug."
"Natuurlijk moet je significante verschillen krijgen bij de vergelijking met je controle groep, anders ben je niet geloofwaardig; met 10 variabelen is dat logisch." Tientallen uren (en shaggies) op je kamer, dagenlang *p* values ten opzichte van baseline uitgerekend, om je twee weken later met een nonchalant gebaar te horen zeggen dat The Lancet die niet wil zien.

Twee van de 120 patienten misten follow-up, dat vond je logisch. De andere honderden resultaten uitgerekend en in de goede kolommen gezet. "Werk ze uit, mail ze even door, dan kijk ik er even naar..."
"Tja, ik heb nog eens met Jeekel gesproken op een bijeenkomst over intention-to-treat en de missing data moeten er toch in." "Ja, maar Wim, hoe krijg je nou in hemelsnaam uitkomsten als je ze niet hebt?" "Dat is eenvoudig (shaggie): je rekent uit hoeveel pijn iemand na een half jaar zou hebben met een 2e graads functie van 12 cijfers uitgaande van twee pijnwaarden gerelateerd aan de uitkomsten van de gehele groep." En jahoor, na 10 uur rekenwerk was alles compleet. Dit werk ondanks dat je wist dat het de totaal uitkomst in de verste verte niet zou beïnvloeden (*p* oneindig klein). "Tja het moet wel zoals het hoort." Het kwam mij over als een virtual reality oefening van een patiënt met buikpijn waarbij evenwel na afloop de appendix toch echt in het bakje lag. Wim, ik kon je niet volgen en het viel mij zwaar als clinicus, die niet verder kan relativeren dan 1x standaarddeviatie om naar je toe te gaan en liefst nam ik Sonja mee, omdat die alle getallen van de patiënten waar je om vroeg wel kon terug vinden.
Na een interne verhuizing was je werktafel leeg en hoefden we niet langer te schrijven op een stapel artikelen van 1 meter in het vierkant en 30cm hoog.
Na 4 jaar werken hadden we eclatante uitslagen van alle patiënten, die geopereerd waren en na je analyses belde je me in een euforische stemming op dat ik gauw langs moest komen om te horen dat de ingreep niets meer deed dan niets doen... Hoe leg je een patiënte uit dat haar *p* 0,051 is en dat de behandeling dus niet helpt...?
"Je moet Hop vragen", zei Jeekel, "die is heel precies maar onvermurwbaar, maar bij collega's boven alle twijfel verheven." Jeekel had gelijk, je was onnavolgbaar, shaggie rokend, koffie zettend, schermpje kijkend en luisterend. Analyses tot en met getallen, die er niet zijn en alles staat erin. Mijn respect voor je is bijzonder groot. Als ik zo precies zou kunnen opereren als jij analyseren, had ik significant minder complicaties (*p*: 0,000001). Wim, mijn dank is 1/0.

B. McClements, beste Brian, een collega van Britse afkomst, die dagelijks met je samenwerkt, van grammatica zijn hobby heeft gemaakt en al mijn Engels wilde corrigeren en dat uitputtelijk heeft gedaan. "Your English is not wrong, but the English write it different...." Ik heb dankbaar gebruik van je gemaakt, het was nooit teveel. Brian, it was great (greatly?).

Dr. R.F. Schmitz, beste Roderick, collega chirurg, maat en wetenschappelijke sparring-partner. Weer zo iemand, die altijd bezig is en leeft voor zijn vak en desondanks uren tijd vindt om je te frustreren. "Hier snap ik niks van....,Outdated...,Wat bedoel je hier nou mee...., Dit is geen endpoint...., Suction is always allowed (for surgeons)...., Dat vind ik wel heel raar...., Dat is geen wetenschap." Uren en avonden en zaterdagen sparren tot het artikel weer was opgewaardeerd. "Het moet nog wel korter" (Roderick is gepromoveerd op een device voor circumcisie). Na jouw commentaar kon ik weer verder en leverde ik de volgende versie bij je in om deze de volgende dag weer terug te krijgen: "Dingeman, misschien moeten we even bij elkaar zitten" Ik kreeg dan het gevoel van een rechtbank met de dwingende taal van de

rechter "approach the bench please." Roderick, het was een haat-liefde verhouding. Je hebt een bijzonder stimulerende rol gespeeld, die ik vaak nodig had om verder te kunnen. "Steengoed man..."
Een grap in één van de artikelen heb je over het hoofd gezien:
Acknowledgement: the author thanks Dr. R.F. Schmitz for his outstanding corrections of every sentence, every word and even every punctuation mark. This has led to this wonderful article, in the right sequence, free of rubbish and full of science.

Dr. R.T. Ottow, beste Reyer, jouw anekdotes over promoties en procedures en je relativerende opmerkingen over artikelen en uitgevers hadden een betere uitwerking op mij dan temesta en valium. Je hebt een grotere rol gespeeld bij de totstandkoming van dit proefschrift dan je zult vermoeden. Juist in een periode, waarin ik het door allerlei omstandigheden moeilijk had en mijn gedachten wilde ordenen, was jij immer aanwezig en stond mij met raad en daad terzijde. Er zijn teveel mensen, die te weinig weten en teveel zeggen; doch jij bent één van de mensen, die alleen wat zeggen als dat nodig en nuttig is. Een vriend.

Dank aan mijn maten, die mij vrije weken gaven om te schrijven; mijn waarnemer Mike Liem; leden van de directie voor hun betrokkenheid en goedkeuring; secretaresses, die dubbele operatieverslagen moesten typen en honderden dossiers moesten aanvragen en een jaar na de ingreep het trial buro moesten bellen voor de randomisatieuitslag; arts-assistenten, die de laparoscoop uren moesten vasthouden; Groene Hart collega's, met name internisten en gynaecologen, die veel patiënten naar mij verwezen voor inclusie; Henny Peltenburg, die als internist een chirurgisch artikel corrigeerde; anesthesisten, die niet wisten of het bleef bij een korte diagnostische scopie of dat de ingreep werd verlengd voor een langdurige adhesiolyse; dames van het medisch archief, die boxen vol dossiers moesten opzoeken; bibliothecaresse Trees Moons, die alle externe artikelen opvroeg; Marjan van Oostveen en Marcel van de Belt die mijn lijf en leed revalideerden na twee operaties; en de operatie-assistenten, die geestelijk moesten lijden als een patiënt -met adhesies- volgens de randomisatie enveloppe toch niet mocht worden behandeld.

Mijn patiënten. De grootste dank dient uit te gaan naar mijn patiënten. Zij waren bereid om hun vertrouwen te geven aan een chirurg, die ze een half uur kenden en die een behandeling voorstelde, waarvan hij niet wist of het hun pijn kon verminderen en wel zei dat de ingreep kon leiden tot complicaties. Zij waren mijn uitkomsten en mijn conclusie. Ik ben hen zeer erkentelijk.

[OPTIMA], beste Ger, Olof en Jorn, dank voor jullie eindeloze geduld en incasseringsvermogen. Jullie begrip voor de klant en het streven naar een goed boek is vergelijkbaar met de relatie van een chirurg met zijn patient en het verrichten van een goede operatie. Als ik ooit iets terug kan doen...

Michaela Rothauer, lieve Michaela, je schilderij van een laparoscopische kijk in de buik spreekt meer boekdelen dan mijn artikelen. Je was zo enthousiast over mijn onderzoek dat je kunstzinnigheid hoogtij vierde en je een prachtig schilderij maakte. Adhesies werden separaat in aquarelvorm vereeuwigd en dienen als voorplaat van het proefschrift en zijn zo echt dat het een foto uit een buik zou kunnen zijn. Ik ben er heel blij mee. Je schilderij komt boven de bank en je aquarel wordt verduizendvoudigd. Grossartig, Vielen Dank.

Mijn familie. Zonder een warm nest en zonder harmonie was ik er waarschijnlijk nooit aan begonnen, en zonder jullie warme belangstelling en waardering was het nog moeilijker geweest. Lieve Moeder en zusjes, Janneke, Ria, Jorien en Irene; het spijt me dat het tijdpad langer liep dan ik gedacht en gehoopt had. Jullie kledingkast zal intussen wel uitpuilen van alle nieuwe kleding, die jullie voor elke nieuwe datum in een nieuw seizoen wilden aanschaffen. Een herenkostuum voor Henk, Aad en Frank is gelukkig tijdloos.

Michiel Swank, Michiel, het econometrisch rekenwonder van de familie. Wie kon je beter vragen dan Michiel een formule te ontwikkelen om het medicijngebruik van 120 patiënten gedurende 1 jaar om te rekenen naar vergelijkbare eenheden? De MQS uitkomsten zijn jouw verdienste en spelen een grote rol bij de resultaten. Veel dank voor dit bijzondere produkt.

Elmar Swank, Elmar, je Amerikaanse ervaring gedurende één jaar L.A. (Los Angeles, en deze keer geen Laparoscopische Adhesiolysis) kwamen van pas om het Nederlandse protocol voor de gerandomiseerde multicenter trial in het Engels te vertalen. The Lancet vroeg erom en dan moet je wel. Jij bood uitkomst en je hebt de 40 pagina's voor de Londenaren vertaald. Blijkbaar was het good enough. Thanks a lot.

Hilko Swank, Hilko, ondanks je streven om gemiddeld een acht te scoren op het gymnasium teneinde niet te hoeven inloten voor de medische studie en ondanks je vele bijkomende activiteiten en ondanks je urenlange inspanningen om kampioen roeien van Nederland te worden heb je ook nog tijd voor mij gemaakt om je steen(tje) bij te dragen. De vertaling van het medisch technisch Engels van de summary naar foutloos Nederlands kwam van jouw hand. Je vingers over het toetsenbord waren onnavolgbaar en ik wist niet dat er zoveel snufjes in de de computer zitten. Evenveel dank als bewondering.

Lieve kinderen Swank; jullie zullen pas later begrijpen hoe bijzonder het is als je als vader wordt geholpen door je nakomelingen. Gevoelens van geluk en trots wisselen elkaar af. Ik ben een rijk mens.

Lieve Sonja. Ik kan maar vier woorden bedenken, die op enigerlei wijze de rol kunnen beschrijven, die jij hebt gespeeld bij de totstandkoming van dit proefschrift: You are the best.

Ik probeer het toch:
Sonja, ik schreef alleen de artikelen, jij deed de rest. Je zorgde voor de goede ambiance, je schreef alle honderden (lieve) brieven aan de patiënten, je ontving honderden antwoordbrieven terug en voerde 10.000 items in in het juiste vakje van de database. Dagenlang zat je achter de computer, ondanks dat je onverwachts gevraagd was te komen werken in Den-Haag, Arnhem en Enschede. Je zei met je beminnelijkste glimlach dat er wel eens rare uitkomsten konden komen, zonder dat je de juiste aard ervan wenste te verklappen. Jij was de linking pin met Hop. Zijn vragen over de patiëntennummers en uitkomsten wist je uit je hoofd te beantwoorden en ik wist me geen raad als ik er een keertje alleen heen moest (het verschil tussen bezoek en bezoeking). Je organiseerde het feest en maakte het tot een feest. Immer was je aanspreekpunt voor mijn overwegingen en immer was je mijn vertrouwenspersoon in tijden van vertwijfeling. Ik zou er zonder jouw enthousiasme niet aan zijn begonnen en zonder jouw support was het nooit klaar geweest. Je bent vanaf het begin mijn ware partner geweest en als een dubbel promotie had gekund, was jij ook gepromoveerd.

Promotie: Ik zal het nooit meer doen, maar wel een ieder aanbevelen.

Curriculum Vitae

Dingeman Johannes Swank werd geboren op 16 februari 1952 te Oud-Beijerland. In 1969 werd het HBS-B diploma gehaald op de Rijks-HBS aldaar. Aansluitend volgde de studie Geneeskunde aan de Medische Faculteit te Rotterdam, die in 1975 werd afgesloten. In deze periode trouwde hij met zijn studiegenote Sonja Bordewijk.
Vanaf november 1975 diende hij gedurende ruim een jaar het land als luitenant bij de luchtmachtstaf te 's Gravenhage.
Van januari 1977 tot januari 1978 een tijdelijk intermezzo als assistent Interne Geneeskunde in het Ikazia ziekenhuis te Rotterdam (hoofd: Dr. C.K.V. van Dommelen), waarna de opleiding tot algemeen chirurg kon aanvangen in het St. Clara ziekenhuis te Rotterdam (opleiders: Dr. P. van Leeuwen tot 1979 en A.A. van Puyvelde van 1979 tot 1984). In januari 1984 werd hij ingeschreven in het Specialisten Registratie Register. In 1980, 1982 en 1986, werden 3 zonen ingeschreven bij de Burgerlijke Stand.
In 1986 vestigde hij zich als algemeen chirurg in het St. Jozefziekenhuis te Gouda, werd lid van het Bestuur Medische Staf en nam in 1989 de voorzittershamer over. In deze periode initieerde hij de fusie met het Bleulandziekenhuis en begeleidde het fusieproces. Deze managementservaringen kwamen goed van pas tijdens de volgende drie jaren als stafvoorzitter van het nieuwe Groene Hart ziekenhuis. Na de fusie, met een grote maatschap Heelkunde bestaande uit 7 algemeen chirurgen en 1 plastisch chirurg werd het mogelijk zich meer toe te leggen op deelspecialismen. Dit werden Traumatologie, Oncologie en de zich snel ontwikkelende Laparoscopische chirurgie.
Het jonge vakgebied Laparoscopische chirurgie riep een aantal vraagstukken op, dat aanleiding gaf tot wetenschappelijk onderzoek, resulterend tot dit proefschrift. Het schrijven van de diverse artikelen voor dit proefschrift is een jaar vertraagd, door een tijdelijke functie van waarnemend directeur, wegens ziekte van een van de leden van de ziekenhuis directie.
Sinds maart 2001 is hij weer als gewoon full-time chirurg werkzaam.