Mesh Repair of Hernias of the Abdominal Wall

Wietske Vrijland

€ducost Publishers

Cover design: Sacha Hart-Schellart

Printpartners Ipskamp B.V., Enschede

ISBN 90-9016661-0

Mesh repair of hernias of the abdominal wall

Correctie van buikwandhernia's
met kunststof materiaal

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de
Rector Magnificus
Prof.dr.ir. J.H. van Bemmel
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
woensdag 19 maart 2003 om 15:45 uur
door

Wietske Willemijn Vrijland

geboren te Enschede

Promotiecommissie

Promotoren:

Prof.dr. J. Jeekel
Prof.dr. H.J. Bonjer

Overige leden:

Prof.dr. Th.J.M. Helmerhorst
Prof.dr. H.W. Tilanus
Prof.dr. J.B.M.Z. Trimbos

CONTENTS

CHAPTER 1

GENERAL INTRODUCTION

1.1 Overview of the thesis

Hernia of the ventral abdominal wall

A hernia of the abdominal wall is a permanent or intermittent protrusion of abdominal contents outside the abdominal cavity through a defect in the abdominal wall. Approximately 75% of all hernias occur in the inguinal region. Other types of hernias of the ventral abdominal wall are incisional, umbilical, epigastric and Spigelian hernia. In chapter 1 an overview of hernias of the abdominal wall is described. The incidence, clinical implications and treatment options and their complications are described, based on the available literature regarding this subject.

Since there are numerous methods for abdominal wall hernia repair, without consensus about the preferred method, we decided to perform a randomized clinical trial to compare mesh and non-mesh repair for inguinal hernias. This randomized clinical trial is described in chapter 2.

The preferential method of hernia repair is discussed in an editorial, not only for inguinal hernias, but also for other types of abdominal wall hernias such as incisional hernias and large umbilical hernias. Endoscopic hernia repair was included in this editorial, which is described in chapter 3.

Complications of mesh repair of abdominal wall hernias

Ideally, prosthetic mesh is placed preperitoneally. If the mesh can be placed between the abdominal wall and peritoneum or prefascially, opening of the abdominal cavity can be avoided and the peritoneum and the abdominal contents are not exposed to injury. For uncomplicated inguinal hernias prefascial or preperitoneal placement of mesh is easy to perform, but for incisional and recurrent umbilical hernias intraperitoneal placement of mesh is often unavoidable. Possible complications of intraperitoneal mesh placement are adhesions and entero-cutaneous fistulas.

Adhesions developing after abdominal surgery are abnormal attachments between tissues and organs. The formation of adhesions results from peritoneal laceration and is enhanced by the presence of foreign materials in the abdominal cavity such as sutures and prosthetic mesh. An introduction to postoperative adhesion formation is described in chapter 4.

An animal study on the formation of adhesions in the presence of a non-absorbable mesh which is often used in hernia repair is described in chapter 5. This mesh is applied with and without coverage by an absorbable mesh, which was suggested to prevent the formation of adhesions. A newly developed mesh with an inert surface was also tested.

Enterocutaneous fistulas are a feared complication after intraabdominal mesh placement because their morbidity is severe and repair technically difficult. Although only few enterocutaneous fistulas have been reported in literature, the common opinion is that polypropylene mesh should never be in contact with intraabdominal organs to avoid this complication [*Morris-Stiff 1998*]. In chapter 6 a retrospective analysis of the outcome of incisional hernia repair with polypropylene mesh is described to assess the risk of enterocutaneous fistula formation, combined with an overview of literature concerning this topic.

Prevention and treatment of postoperative complications related to adhesions
To prevent the formation of adhesions, it was suggested that a mechanical barrier could be used peroperatively to temporarily separate the intraabdominal viscera from the abdominal wall or prosthetic mesh. A membrane containing hyaluronic acid has been developed for this purpose, which already has been shown effective in experimental studies. To assess the value of this material in clinical circumstances, a randomized controlled multicenter study was performed which is described in chapter 7.

Surgery is the only modality to confirm the presence of adhesions in the abdominal cavity and surgical lysis is the only therapy available. The reported results of adhesiolysis vary widely, and studies cannot be compared because the indication for adhesiolysis and duration of follow-up differ. In Chapter 8 the indication, method and success rate of adhesiolysis for intestinal obstruction, chronic abdominal pain and infertility are reviewed.

Chapter 9 contains the general discussion of this thesis.

1.2 Inguinal hernia

Definition and incidence
An inguinal hernia is defined as a protrusion of abdominal contents through a defect in the abdominal wall of the groin.

Although no exact figures are available, a prevalence varying from 10% to 15% in adults in the Western hemisphere has been estimated, with a male to female ratio of 12:1. Although the incidence of inguinal hernia rises with age, relatively young people are affected: an incidence between 5 and 8 % in patient 25 to 40 years of age has been reported [*Abrahamson 1997*]. Inguinal hernia repair is the most frequently performed surgical operation. In the United States approximately 700.000 procedures are performed annually [*Lichtenstein 1993*], and in the Netherlands 25.000 [*Health Care Information 1995*]. Consequently, inguinal hernias not only affect individual patients but also have a great impact on society. Failure of inguinal hernia repair leads to increased patient discomfort, reoperations and sick-leave, and therefore may result in a considerable economical burden [*Liem 1997b*].

Clinical picture, diagnosis and indications for inguinal hernia repair
The primary manifestation of an inguinal hernia is usually a bulge in the inguinal region. The patient may describe minor pain or vague discomfort. Severe pain only occurs in case of incarceration of bowel. In adults, the onset of inguinal hernia is usually rapid. At physical examination, a hernia can be observed if standing upright, while it may disappear in the supine position. Manipulation might be necessary to reduce the bulge and finally some hernias are not reducible anymore, either because of incarceration or because of adhesions. The most important tool in diagnosing an inguinal hernia is physical examination. If there is any doubt about the nature of the inguinal bulge ultrasonography or MRI can provide more evidence. If a hernia cannot be diagnosed by physical examination because of the absence of a clear bulge, herniography may be of help, although the accuracy of this procedure remains to be assessed [*Van den Berg 1993*].

Strangulation is a complication mainly of longer existing inguinal hernias. Abdominal contents become trapped in the abdominal wall defect, can not be reduced and become ischemic which results in bowel obstruction with severe abdominal pain. Although the incidence of incarceration is about 3 % and the incidence of strangulation no more than 1 %, morbidity and mortality increase considerably after emergency repair of incarcerated or strangulated hernias, and therefore it is generally advised to perform inguinal hernia repair timely [*Oishi 1991, Kulah 2001*]. The general opinion is that in case of an inguinal hernia, a repair should always be done.

Classification
Numerous classification systems for inguinal hernias have been described. Since the clinical significance is limited, these systems are rarely used in daily practice. The most important distinction is between a direct and an indirect hernia. A crucial role in this distinction is played by Hesselbach's triangle, which is bordered on the medial side by the rectus sheath, on the craniolateral side by the epigastric vessels and in the inferior side by the inguinal ligament.

An indirect inguinal hernia is situated lateral of Hesselbach's triangle and thus lateral of the epigastric vessels. The peritoneal sac protrudes through the internal inguinal ring and passes down the inguinal canal together with the spermatic cord. It is suggested that lack of the obliteration of the processus vaginalis is the primary factor leading to the development of an indirect inguinal hernia, and therefore can be defined as a congenital disease. Inguinal hernias in children are always indirect.

A direct inguinal hernia protrudes through the floor of the inguinal canal in Hesselbach's triangle, medial to the epigastric vessels. It is suggested to be acquired by repetitive straining, as with prostatism, constipation, coughing and heavy lifting, although solid evidence lacks. Defects in collagen synthesis might predispose to this type of hernia [*Wagh 1974*].

Other classifications have been described by *Casten* [*1967*], *Halverson* [*1970*], *Gilbert* [*1987*], *Robbins* [*1993*], *Nyhus* [*1993*] and *Rutkow* [*1993*] but since the clinical significance is limited and surgical treatment is identical for all different types in adults, these classifications will not be described in this thesis. The only exception might be the indirect hernia in young adults; it is thought reposition of the peritoneal sac and narrowing of the internal inguinal ring is a sufficient repair in these patients, but clinical reports on this subject lack.

Treatment and outcome

Numerous methods have been described for inguinal hernia repair. These can be divided in non-mesh or suture repairs and repairs with the use of prosthetic mesh.

Non-mesh repair

Bassini, an Italian surgeon, performed the first inguinal hernia repair with reconstruction of the inguinal canal to preserve the functional anatomy in 1894, and described this procedure in 1897 [*Bassini 1897*]. The operation involved high ligation of the hernia sac by opening the transversalis fascia and consequently suturing the internal oblique and transversus abdominis muscles, together with the upper leaf of the transversalis fascia, to the inguinal or Poupart's ligament and the lower leaf of the transversalis fascia. Interrupted silk sutures were used. His technique dramatically decreased postoperative mortality, morbidity and recurrence rate and his method has been the method of choice for about a hundred years.

In 1940 *McVay* popularized a method first described by *Lotheissen*, which described suturing the conjoint tendon to the pectineal (Cooper's) ligament instead of to the inguinal ligament [*McVay 1981, Lotheissen 1898*]. This method is based on the observation that the conjoint tendon originally is attached to Cooper's ligament.

Shouldice [*1953*] described a multi-layered repair based on *Bassini*'s repair, which is probably the most successful method of non-mesh repair. Stainless steel continuous sutures are applied. The transversalis fascia is also opened exposing the internal ring and widely dissected from the preperitoneal fat. The first layer of the repair involves suturing the lower flap of the transversalis fascia to the posterior side of the upper flap of this fascia and to the posterior side of the rectus abdominis muscle and of the aponeurosis of the transversus abdominis. The upper flap of the transversalis fascia is sutured to the base of the lower flap and to the inguinal ligament forming the second layer. The third layer consists of the conjoint tendon sutured to the inguinal ligament and lower flap of the external oblique aponeurosis. For the fourth layer, the

anterior rectus sheath and the lower aspect of the conjoint tendon from the front to the inner surface of the lower flap of the external oblique aponeurosis are sutured. Then the external oblique aponeurosis is closed over the spermatic cord.

This repair is technically complicated, time consuming and not always feasible, especially in patients with large direct hernias, who do not have sufficient transversalis fascia.

These three types of non-mesh repair represent the most widely used surgical procedures for inguinal hernia repair without the use of prosthetic material. Although many other methods have been described, the common problem of these procedures is that suturing and displacement of anatomic structures may cause excessive tension on the suture line and surrounding tissue, thus increasing the risk of recurrence of the hernia. More elaborate descriptions of these procedures and their modifications have been described in several textbooks [*Nyhus 2002*]. Recurrence rates of non-mesh repairs vary from 0.2 to 33 %, depending on the surgical method, experience, length of follow-up and type of hospital [*Beets 1997, De Wilt 1990, Hay 1995, IJzermans 1991, Janu 1997, Kux 1994, Paul 1994, Rand Corporation 1983, Simons 1996*].

Mesh repair

Abdominal wall hernia repair with the use of polypropylene mesh was initially described by *Usher* [*1958*]. Inguinal hernia repair employing polypropylene mesh to achieve a so-called 'tension-free' repair was first described by *Lichtenstein* and *Shulman* [*1986*]. This technique avoids tension on the sutured structures bordering the defect by refraining from approximating these structures. The Lichtenstein technique involves dissecting and inverting the hernia sac without opening it. Closure of the hernial orifice is not attempted. The defect is covered with a polypropylene mesh sized about 6 x 8 cm trimmed to fit the area. A non-absorbable suture is used to fix the mesh. The mesh is fixed medially to the rectus sheath and the lacunar ligament close to the pubic tubercle. On the inferior side the mesh is sutured to Poupart's ligament. A slit in the mesh on the lateral side at the internal ring allows emergence of the spermatic cord and vessels. The two lateral tails of the mesh are crossed to embrace the spermatic cord and vessels thus creating a new internal ring. The superior side of the mesh is loosely sutured to the rectus sheath and conjoint tendon. Then, the external oblique aponeurosis is closed over the mesh. This method is associated with a recurrence rate of less than one per cent [*McGillicuddy 1998, Lichtenstein 1989, Friis 1996*]. Randomized clinical trials concerning this subject have been done, and are mentioned in chapter 2 and 3 of this thesis [*McGillicuddy 1998, Friis 1996, Collaboration 2000a*].

Other types of repair with prosthetic mesh are for example *Gilbert*'s plug and patch repair [*Gilbert 1987*] which has been modified by *Robbins* and *Rutkow* [*1993*] and the *Rives*' repair involving placement of a larger mesh preperitoneally. [*Rives 1987*]. *Stoppa* [*1987*] described a repair with a very large preperitoneal mesh covering the lower half of the parietal peritoneum, which may be used in case of multiple recurrences. These repairs will not be discussed in this thesis.

Endoscopic repair

Endoscopic repair of inguinal hernia can be done totally extra peritoneally (TEP), a procedure first described by *McKernan* and *Laws* [*1993*] and transabdominally (TAPP), first reported by *Arregui* [*1991*].

Both procedures require the use of prosthetic mesh. It has been proven that endoscopic repair causes less recurrences if compared to open non-mesh repair, but if compared to open mesh repair no differences in recurrence rate exist [Liem 1997a, *Collaboration 2000b*]. The advantages of endoscopic procedures are less postoperative pain and more rapid return to normal activities, but since endoscopic procedures take longer to perform and may be related to rare but serious complications, the method of choice for inguinal hernia repair remains to be established [*Collaboration 2000b*]. In the Netherlands, the acceptance of endoscopic inguinal hernia repair is still low, only 16% of surgeons applies this method on a regular basis [*Knook 2001*].

Complications

The incidence of wound infections after inguinal hernia repair varies from 0.4% to 9% [*Bailey 1992, Gilbert 1993, Holmes 1994, Karran 1992, Mertens 1994*]. The wide variation of this incidence might be explained by a variation of surgical techniques and operative measures. The administration of antibiotic prophylaxis is generally advised if prosthetic mesh is used, although no strong evidence exists that it decreases the incidence of wound infections and serious complications like necrotizing fasciitis [*Platt 1990*]. Definitions of wound infection differ among studies which impedes interpretation of several studies at a time. Furthermore, retrospective studies tend to underestimate the rate of wound infection while prospective analyses record clinical events such as wound infection more accurately. There is great concern for infection of mesh, although it is an infrequent complication [*Anonymous 2002*].

Chronic pain is a common complication with an incidence of 2 to 5 per cent [*Starling 2002*]. However, few studies of inguinal hernia repair address chronic pain [*Callesen 1999, Cunningham 1996*]. Chronic pain may be related to peroperative nerve injury. The inguinal region receives sensory innervation from the iliohypogastric, ilioinguinal, genitofemoral and lateral femoral cutaneous nerves, all stemming from the eleventh thoracic through second lumbar nerve. In open inguinal hernia repair, the iliohypogastric nerve, the ilioinguinal nerve and the genital branch of the genitofemoral nerve are at stake. In endoscopic or laparoscopic repair the femoral branch of the genitofemoral nerve and the lateral femoral cutaneous nerves are at risk. *Starling* [*2002*] provides an excellent outline of this problem in Nyhus and Condon's Hernia. Although it has been suggested that the use of mesh and the development of chronic pain are related, no evidence can be found in literature. The EU Hernia Trialist Collaboration concluded that mesh appears to reduce the chance of persisting pain rather than to increase it [*Anonymous 2002*].

The incidence of testicular atrophy has not been frequently described. *Bendavid et al.* [*1995*] of the Shouldice Hospital described an incidence of 0.08 %. It was suggested that extensive dissection of the funiculus damaging the venous blood flow is responsible for this complication rather than the creation of a narrow internal inguinal ring [*Wantz 1995*].

General complications include pulmonary atelectasis and pneumonia which can be prevented by early postoperative reactivation. Exact data are lacking probably due to the low incidence of these sequelae. Urinary retention is more common, and has been related to prostatism and regional anesthesia. Both predispose to postponed micturition postoperatively that may evolve into urinary retention.

Non-mesh and mesh repairs have shown no significant difference in the incidence of complications in a systematic review [Collaboration 2*000a*].

1.3 Incisional hernia

Definition, incidence and risk factors

An incisional hernia is defined as a protrusion of abdominal contents through a defect in the abdominal wall located at the site of a former incision in the abdominal wall. The bowel contents remain covered by peritoneum and skin. Incisional hernia has been a common complication, reported in 2 – 19 % of patients after abdominal surgery [*Mudge 1985, Bucknall 1982, Luijendijk 1997, Regnard 1988, Israelsson 1993*].

Some incisional hernias develop within days after an abdominal operation while other hernias may develop many years after primary surgery. Incisional hernias that occur within days postoperatively have been suggested to originate from technical failure or raised intra-abdominal pressure due to persisting ileus or chronic pulmonary disease. In a later stage, wound healing disturbance and co-morbidity may be responsible for incisional herniation. The evidence on this subject is still incomplete, but it has been shown that there are several patient-related factors that predispose to the development of an incisional hernia. Male gender [*Wissing 1987*], increasing age [*Viljanto 1966*], pulmonary disease [*Wissing 1987, Gecim 1996*], prostatism [*Luijendijk 2000*] diabetes mellitus [*Sugerman 1996*], obstructive jaundice [*Armstrong 1984*] and aneurysmatic disease [*Stevick 1988, Luijendijk 2000*] have been indicated as risk factors in some studies, whereas this remained unconfirmed in others. Disturbances in collagen metabolism probably play a role in the development of incisional hernias [*Wagh 1974, Si 2002*]. Closure of the abdominal wound after surgery is a risk factor as well [*Niggebrugge 1999*].
Israelsson [*1993*] described the suture length to wound ratio as an important parameter for healing of midline incisions closed with a continuous suture technique. It was stated that this ratio should be ≥ 4 to reach a lower incidence of incisional hernias.

Clinical picture, diagnosis and indications for incisional hernia repair

Incisional hernias are often asymptomatic, especially in small hernias. However, if they cause symptoms, pain, discomfort and the presence of a bulge constitute the clinical picture. In large hernias, cutaneous ulceration and necrosis may develop. Strangulation of the hernia occurs in 2.4 % of patients with incisional hernia [*Read 1989*].

To ascertain the presence or absence of an incisional hernia, physical examination of the abdominal wall is mandatory. A weakness in the abdominal wall at the site of a scar with palpable fascial rims suggests the presence of a hernia. Bulging during Valsalva's manoeuvre or at getting up from a supine position may occur. An incisional hernia should be distinguished from local paralysis of the abdominal muscles which can occur postoperatively, and from diastasis of the rectus abdominis muscle. Diastasis of the rectus abdominis muscle, or divarication, occurs when this muscle is loosened from the linea alba. This may be related to pregnancy and obesity. When in doubt, ultrasonography or CT scanning can be of help to detect and locate a defect of the abdominal wall and assess the diameter of the defect.

Not all incisional hernias need to be repaired. It is generally thought safe to refrain from operating in case of minor symptoms [*Abrahamson 1997*]. Hernias with a small

fascial defect and a large protrusion and incisional hernias in patients who suffer from recurrent bowel obstruction are at risk for strangulation, and therefore should be considered as a definitive indication for surgery. For all other incisional hernias there is a relative indication for surgery without international, validated guidelines. When considering repair of incisional hernias, the benefits should be weighed against the recurrence rate which can be as high as 49 % [*Van der Linden 1988*].

Treatment and outcome

Numerous methods have been described for incisional hernia repair. These can be divided in non-mesh repairs and repairs with the use of prosthetic mesh.

Non-mesh repair

Before the introduction of prosthetic material for hernia repair, all incisional hernias were repaired by suturing the fascial edges. In spite of varying techniques and different suture materials, recurrence rates between 24 and 49 % were encountered in the larger studies [*Van der Linden 1988, Langer 1985, George 1986, Read 1989*].

Primary closure is performed in single or multiple layers. In single layer closure, all layers of the abdominal wall are approximated with one bite of suture. In multiple layer closure, different layers, for example the anterior and posterior rectus sheath are approximated and sutured separately. Both techniques are associated with high recurrence rates in large studies with long-term follow-up [*Langer 1985, George 1986, Gecim 1996*].

Mayo or overlap repair provides overlap of the fascial edges and fixated suturing. This method has shown a high recurrence rate of 31 to 78% [*Paul 1998, Luijendijk 1997*].

To prevent tension on the suture lines relaxing incisions have been advocated. These incisions are made in a vertical fashion and bilateral to the incisional hernia in the anterior sheath of the rectus abdominis muscle before closure of the defect. No studies involving larger numbers of patients have been reported assessing the value of this technique.

Rectus sheath techniques involve mobilizing of healthy tissue with subsequent primary closure to cover the defect in the abdominal wall. Different techniques have been described but no success rates have been reported. The components separation technique of *Ramirez* [*1990*] showed recurrence rates ranging from 4.5 to 8.6% in small series of large incisional hernias [*DiBello 1996, Girotto 1999, Shestak 2000*]. In some cases in these series, prosthetic material was used as well to reinforce the abdominal wall.

Mesh repair

Abdominal wall hernia repair with the use of polypropylene mesh was initially described by *Usher* [*1958*]. Since then, mesh repair was popularized and other types of mesh were developed. Three types of prosthetic mesh are currently used in hernia repair: polypropylene, expanded polytetrafluoroethylene and polyester. These meshes are all non-absorbable since the application of absorbable meshes leads to unacceptable high recurrence rates. There is much debate about which mesh to choose, because of different characteristics of these meshes, such as tissue ingrowth in the prosthesis, adhesion formation provoked by the mesh and

susceptibility to infection as well as disintegration of the mesh. In incisional hernia repair, different positions of the mesh are possible: intraperitoneal, preperitoneal or between rectus abdominis muscle and posterior fascia and the onlay method in which the prosthesis is placed on top of the anterior rectus fascia. It remains to be established which position is preferable. *Larson* and *Harrower* [*1978*] advised to place the mesh subfascially, but this is not supported by others.

Mesh repair is associated with lower, but still considerable recurrence rates of 4 – 17 % in different studies with a follow-up of 6 months to 7.6 years [*Leber 1998, Molloy 1991, Liakakos 1994, Sugerman 1996, McCarthy 1981, Matapurkar 1991, McLanahan 1997, Turkcapar 1998, Whiteley 1998, Ladurner 2001, Martin-Duce 2001, Schumpelick 1996*]. In 2000, the first randomized clinical trial comparing non-mesh repair and mesh repair was published by *Luijendijk et al.* [*2000*]. In this study, it was concluded that mesh repair is the method of choice for all non-emergency incisional hernia repairs, even in defects as small as 3 cm in diameter. Three year recurrence rates were 43 and 24 per cent for non-mesh versus mesh repair respectively.

Laparoscopic repair

Laparoscopic repair of incisional hernia with prosthetic mesh was introduced by *LeBlanc* and *Booth* [*1993*]. *Cassar* and *Munro* [*2002*] described 14 series of laparoscopic incisional hernia repair. In all studies, the mesh was placed intraperitoneally after installation of pneumoperitoneum, insertion of trocars as far as possible from the defect and careful adhesiolysis to create sufficient overlap of the mesh. It has been shown necessary to use full thickness sutures to fixate the mesh to the abdominal wall because only tackers or hernia staples have shown to provide inadequate fixation [*Riet 2002*]. Our own technique was described in the *Dutch Journal of Surgery* [*Vrijland 1998*]. The recurrence rate with the use of this technique varies between 0 and 9 per cent. The follow-up is still relatively short, but comparable to that of open mesh repair. [*Cassar 2002*]. The only randomized clinical trial on laparoscopic versus open incisional hernia repair shows similar recurrence rates, less morbidity and shorter hospital stay [*Carbajo 1999*]. Since this study is relatively small and other comparative studies can not confirm these results, more studies are necessary.

Complications

Since incisional hernia repair requires rather extensive dissection, postoperative bleeding and hematoma formation occurs in approximately 10% [*Luijendijk 2000*]. It is assumed that hematomas predispose to wound infections and since the use of drains does not reduce the incidence of hematomas, the only way to prevent hematoma formation and related wound complications is meticulous hemostasis and obliteration of dead space [*White 1998*]. A seroma is defined as a collection of serous fluid in the subcutaneous space which is related to extensive dissection as well. The incidence of seroma is 1 – 15 % in different studies [*Cassar 2002*]. This figure is not influenced by the placement of drains and therefore, there is still discussion about the use of drains in incisional hernia repair [*White 1998*].

Wound infection is a serious complication of incisional hernia repair which eventually may lead to recurrence of the incisional hernia [*Bucknall 1982, Luijendijk 2000*]. Bucknall et al. showed that an infected wound has a fivefold increased risk for

developing a ventral hernia. It is thought that recurrence of incisional hernia after incisional hernia repair occurs more frequently if infection occurs. Wound infection has been documented in 4 – 15 % after incisional hernia repair when mesh was used [*Cassar 2002, Houck 1989, White 1998*]. Details about the incidence of hematomas and seromas after non-mesh repair are lacking, but *Luijendijk et al.* [*2000*] showed no differences in complication rate between non-mesh and mesh repair in a randomized clinical trial. However, *Korenkov et al.* [*2002*] described a high infection rate after polypropylene mesh repair.

In mesh repair, wound infection may lead to an infection of the mesh. This is a serious complication, because sometimes removal of the mesh is required. Evidence exists that a polytetrafluoroethylene mesh requires removal more often than a polypropylene mesh in case of infection [*Cassar 2002*]. Some have suggested that the small pore size in polytetrafluoroethylene mesh enhances bacterial binding and therefore promotes chronic mesh infection. Another wound complication is wound sinus formation which was described to occur in 4 % of patients in one study [*Liakakos 1994*] and in 12 % of patients in another [*Molloy 1991*].

Antibiotic prophylaxis before surgery seems necessary to prevent wound complications, but a comparative study regarding this subject has never been executed.

Enterocutaneous fistula formation after mesh repair was first described by *Kaufman et al.* [*1981*]. The incidence of this complication is low, but it is a very serious complication requiring surgery and usually removal of the mesh [*Cassar 2002*]. Intraperitoneal placement of the mesh possibly increases the risk for enterocutaneous fistulas. In chapter 5 this complication is discussed more extensively.

Chronic pain is an issue in incisional hernia as well as in inguinal hernia. *Martin-Duce et al.* [*2001*] reported chronic pain in 28 per cent of patients after mesh repair of incisional hernias. In most studies chronic pain has not been reported. The origin and possible treatment of chronic pain after incisional hernia repair remain unclear.

General complications like pneumonia and urinary tract infections appear to occur at similar rates in mesh and non-mesh groups *Luijendijk et al.* [*2000*].

Carbajo et al. [*1999*] reported less complications after laparoscopic repair of incisional hernia in a small randomized clinical study which was confirmed by *Goodney et al.* [*2002*] in a meta-analysis. Other studies showed a higher complication rate after laparoscopic repair [*Cassar 2002*]. More clinical studies randomizing patients with incisional hernias for either open or laparoscopic surgery are necessary to establish the value of laparoscopic hernia repair. By the Erasmus Medical Center Rotterdam such a randomized clinical trial has been started.

1.4 Other types of ventral abdominal wall hernia

Umbilical hernia

Umbilical hernias occur when the fascia at the abdominal entry of the umbilical cord does not close completely. Hernias just below or just above the umbilicus in the midline are called paraumbilical hernias and are usually included in the group of umbilical hernias.

The incidence of umbilical hernias in children is high, but decreases with age because of spontaneous closure of the defect. The incidence of umbilical hernias in adults is unknown. Little is known about the cause of umbilical hernia in adults, but umbilical hernia in childhood is a risk factor [*Jackson 1970*]. Middle aged obese women with multiple pregnancies are at risk. Adults have a considerable risk of incarceration with associated morbidity and mortality, but detailed information on this subject lacks.

Non-mesh repair with non-absorbable sutures has been the method of choice [*Abrahamson 1997*]. Recently *Arroyo et al.* [*2001*] published a randomized clinical trial comparing non-mesh and mesh repair for umbilical hernias in adults with recurrence rates of 11 versus 1 per cent respectively. The mean follow-up was 64 months. The complication rate was comparable between both groups. The authors state that umbilical hernias should be treated with a mesh repair, regardless of the size of the hernia.

Epigastric hernia

An epigastric hernia may be defined as a fascial defect in the linea alba between the xyphoid process and the umbilicus. The prevalence of this hernia is between 0.5 and 10 per cent, as concluded from autopsy studies. Males are predominantly affected [*Abrahamson 1997*]. Probably the epigastric hernia is acquired, and results from excessive straining [*Askar 1978, Lang 2002*].

The majority of epigastric hernias, up to 75 per cent, is asymptomatic. Related symptoms are epigastric pain, abdominal distention, dyspepsia, nausea and vomiting. Incarceration, usually of the omentum, is common, but strangulation is rare.

The presence of epigastric hernia can be confirmed by clinical examination, although obesity can obscure epigastric hernia. In case of doubt, ultrasonography or CT-scanning may be of help.

Non-mesh repair is still advised, but recent randomized trials comparing different treatment modalities lack. Probably it is wise to consider mesh repair, especially in larger defects [*Abrahamson 1997*].

Spigelian hernia

The Spigelian hernia is called after Adriaan van der Spieghel, a Belgian anatomist and surgeon, who discovered the linea semilunaris. The linea semilunaris is the course of the lateral border of the rectus abdominis muscle, and in the muscular gap between the linea semilunaris and the medial borders of the oblique and transversus abdominis muscles the Spigelian aponeurosis is located, which is broadest just

caudal to the umbilicus. Spigelian hernias protrude through the Spigelian aponeurosis and usually in the lower abdomen [*Abrahamson 1997*]. They are rare and usually difficult to diagnose because of their intramural location and unspecific symptoms. An intermittent mass and local pain are the common symptoms of a Spigelian hernia [*Larson 2002*]. Clinical diagnosis can be confirmed by ultrasound, CT-scanning and ultimately herniography.

Generally, it is advised to perform non-mesh repair, but in larger hernias mesh repair should be considered. No comparative studies are available [*Larson 2002*].

CHAPTER 2

RANDOMIZED CLINICAL TRIAL OF NON-MESH *VERSUS* MESH REPAIR OF PRIMARY INGUINAL HERNIA

Br J Surg 2002;89:293-7

Abstract

Background: The optimum method for inguinal hernia repair has not yet been determined. The recurrence rate for non-mesh methods varies between 0.2 and 33%. The value of tension-free repair with prosthetic mesh remains to be confirmed. The aim of this study was to compare mesh and non-mesh suture repair of primary inguinal hernias with respect to clinical outcome, quality of life and cost in a multicentre randomized trial in general hospitals.

Methods: Between September 1993 and January 1996, all patients scheduled for repair of a unilateral primary inguinal hernia, were randomized to non-mesh or mesh repair. The patients were followed up at 1 week and at 1, 6, 12, 18, 24 and 36 months. Clinical outcome, quality of life and costs were registered.

Results: Three hundred patients were randomized of whom 11 were excluded. Three-year recurrence rates differed significantly: 7 per cent for non-mesh repair (n=143) and 1 per cent for mesh repair (n=146). There were no differences in clinical variables, quality of life and costs.

Conclusions: Mesh repair of primary inguinal hernia is superior to non-mesh repair with regard to hernia recurrence and is cost-effective. Postoperative complications, pain, and quality of life did not differ between groups.

2.1 Introduction

Inguinal hernia repair is the most frequently performed operation in The Netherlands [*Health Care Information 1995*]. Consequently, failure of inguinal hernia repair not only affects individual patients but also has a great influence on society. Failure leads to increased patient discomfort, reoperations and sick-leave, and thus may result in a considerable economical burden [*Liem 1997b*]. No consensus has been reached yet about the best operation of inguinal hernia repair, which should show good cost-effective clinical results [*MRC 1999, Barth 1998, McGillycuddy 1998*].

Recurrence rates after non-mesh suture repair of inguinal hernia vary between 0.2% and 33%, depending on the surgical method, experience, length of follow-up and type of hospital [*Beets 1997, De Wilt 1990, Hay 1995, IJzermans 1991, Janu 1997, Kux 1994, Paul 1994, Rand Corp. 1983, Simons 1996*]. Tension-free hernia repair, or repair with the use of mesh, was popularized by *Lichtenstein* and *Schulman* [*1986*]. This method was associated with a lower recurrence rate than suture repair in a non-randomized study of primary inguinal hernia repair [*Lichtenstein 1989*], and in two randomized studies [*McGillicuddy 1998, Friis 1996*].

The aim of this study was to establish the value of open mesh hernia repair for primary inguinal hernia in the general hospital setting, not only with respect to clinical outcome but also quality of life and cost. A multicentre randomized trial with long-term follow-up was conducted.

2.2 Patients and methods

Between September 1993 and January 1996, patients older than 18 years scheduled for repair of a primary unilateral inguinal hernia were randomized to non-mesh or mesh repair. Patients could only be enrolled once and were not included if they suffered from bilateral inguinal hernia. Patients were informed about the trial both verbally and in writing. Six hospitals participated in the study.

Randomization was achieved by calling an independent randomization centre, where computer-generated lists were available, stratified by hospital. The protocol was approved by the ethics committees of all participating hospitals.

Age, obesity, intermittent high abdominal pressure (cough, constipation, prostatism) and factors that may interfere with wound healing (diabetes, use of steroid medication, smoking) were noted. Obesity was defined as a Body Mass Index of 30 kg/m^2 or more. The type of inguinal hernia was also noted.

Evaluation of operation-related factors included surgical technique, type of anaesthesia, clinical setting or day-care, and whether the operation was performed by a surgeon or by a surgical resident. Drainage, wound hematoma, seroma, wound dehiscence and wound infection were also recorded. Wound infection was defined as discharge of pus from the wound.

At the induction of anaesthesia, a single dose of intravenous broad spectrum antibiotics was administered according to hospital protocol. Non-mesh repair was performed according to the surgeons' method of choice, provided that 2/0 polypropylene (Prolene, Ethicon, Johnson & Johnson, NJ, USA) sutures were used. Mesh repair was performed according to a strict protocol as described by *Lichtenstein and Shulman* [*1986*] using a polypropylene prosthetic mesh (Prolene, Ethicon, Johnson & Johnson, NJ, USA or Marlex, C.R. Bard, Inc., Billerica, MA, USA)

of 7.5 x 15 cm to avoid tension on the suture lines. The duration of surgery (from first incision to last skin suture), hospital stay and time off work were noted. Patients were followed up at 1 week and at intervals of 1, 6, 12, 18, 24 and 36 months. Awareness of hernia recurrence and complaints about the groin were noted and the groin was examined physically for recurrence of inguinal hernia. Hernia recurrence was defined as a bulge or weakness in the operative area exacerbated by a Valsalva manoeuvre and palpable outside the external ring. Hernia recurrence and death were the study endpoints. Patients who did not visit the outpatient department for follow-up at 36 months, were asked to complete a questionnaire, and were visited at home by a physician who was not aware of the method used for inguinal hernia repair. If recurrences were found after follow-up had terminated, they were not included in the statistical analysis in accordance with the protocol.

To assess quality of life (or current health state) before and after surgery, the Dutch version of the EuroQol EQ-5D and the EuroQol Visual Analogue Scale [*Brooks 1996, Kind 1999*] was administered for self-completion by patients before operation and 1 week, 1 month and 6 months after operation.

To determine the cost-effectiveness of both methods of inguinal hernia repair, a questionnaire about costs was completed 1 month and 6 months after surgery. This included questions about the need for help from a general practitioner, nurse or housekeeper, the need for pain medication and the duration of sick-leave. Cost-effectiveness also involved quality of life- and operation-related factors, such as duration of surgery, duration of hospital stay and time off work.

Statistical analysis was done with the Statistical Product and Service Solutions software (SPSS, Chicago, Illinois, USA). Percentages and continuous variables were compared using Fisher's exact test and Mann-Whitney *U* test respectively. Cumulative recurrence rates were calculated and compared using Kaplan-Meier curves and the log rank test. P-values given are two-sided; P = 0.05 was considered the limit of significance. The primary analysis was by intention to treat. A univariate regression analysis for the non-mesh repair group was performed.

2.3 Results

Three hundred patients were randomized. Eleven patients were excluded. In four patients another type of hernia was demonstrated at operation. One patient needed bilateral repair. The operation was cancelled for three patients. In spite of inclusion in the trial two patients underwent laparoscopic inguinal hernia repair and one patient withdrew consent before operation. Preoperative characteristics were well matched between the two groups (**Table 2.1**). Eight patients (3 per cent) were women.

Table 2.1

Comparison of study groups

Variable		Non-mesh repair group	Mesh repair group
Age[1]	[y]	53 (19-85)	58 (24-83)
BMI[1]	[kg/m^2]	25 (19-34)	25 (18-34)
Prostatism[2]	[n]	14/140	12/141
Constipation	[n]	11/143	10/146
Coughing	[n]	22/143	25/146
Diabetes	[n]	8/143	2/146
Use of steroids	[n]	2/143	4/146
Type of hernia			
Indirect	[n]	67	75
Direct	[n]	45	37
Combined	[n]	27	29
Not described	[n]	4	5

1) Values are: median (range). 2) Men only.

Intention to treat analysis.

Of the remaining 289 patients, 143 had been randomized to non-mesh repair and 146 to mesh repair. The type of inguinal hernia repair in the non-mesh repair group was Bassini-McVay in 75 patients (53 per cent), Shouldice in 36 (25 per cent), Bassini in 26 (18 per cent) and McVay in three (2%). Three patients received a mesh because the surgeon decided at operation that a mesh repair was preferable. These procedures were marked as conversions. In the mesh repair group, 125 patients received a *Prolene* mesh, whereas *Marlex* was used in 13 cases. In one occasion a resorbable polyglactin 910 mesh (Vicryl, Ethicon, Johnson & Johnson, NJ, USA) was used in error. Seven patients did not receive a mesh repair and these operations were marked as conversions.

Thirteen patients (4 per cent) died within the follow-up period from causes unrelated to inguinal hernia and more than 1 month after hernia repair.

Follow-up was complete for 254 patients (88 per cent). Thirty-five patients (12 per cent) were lost to follow-up: twelve patients withdrew from follow-up, twelve patients could not be traced, and eleven patients were followed up in writing at 36 months but

were not physically examinated at this time. All patients were included in the analysis with their follow-up censored at the time of last physical examination.

Recurrences

During the 3-year follow-up, nine recurrences were found in the non-mesh repair group and one in the mesh repair group. The only recurrence in the mesh group occurred in the patient who received a resorbable mesh in error. The 3-year cumulative recurrence rates in the non-mesh and mesh repair were 7 and 1 per cent respectively (P = 0.009, **Table 2.2**).

Table 2.2

Cumulative recurrence rates 1-36 months of follow up after primary inguinal hernia repair

Months after operation [mo]	Number at risk for recurrence [n]	Cumulative recurrence rate [%][1]
Non-mesh repair		
1	143	0
6	137	1 (1)
12	131	1 (1)
18	127	1 (1)
24	125	3 (2)
36	119	7 (2)
Mesh repair		
1	146	0
6	138	0
12	138	0
18	133	0
24	131	0
36	122	1 (1)

1) Values in parentheses are s.e.

Exclusion of the patient who received a resorbable mesh from the analysis (major trial violation) decreased the 3-year cumulative recurrence rate from 1 per cent to zero, increasing the difference between groups (P = 0.002). There were no recurrences after inguinal hernia operations that were converted peroperatively.

Univariate analysis

The non-mesh repair group was associated with a significantly higher recurrence rate. Risk factors were evaluated within this group. The recurrence rate was higher for older patients; 3-year recurrence rates for patients younger than 65 years of age and older patients were 3 and 16 per cent respectively (P = 0.01). Other patient characteristics and wound complications were not identified as significant risk factors.

Operation-related factors

Median duration of surgery was 45 min for both non-mesh repair (range 19-105) and mesh repair (range 20-120). Seventy-nine percent of patients were treated in a clinical setting and 21 percent in day-care; there was no difference between treatment groups. Median hospital stay was 2 days in both groups, with a range of 0-14 and 0-11 days respectively. Median time off work was 17 (range 0-56) days after non-mesh repair and 19 (range 2-113) days after mesh repair.

The type of anaesthesia did not differ between the groups (general 62 percent, epidural 23 percent, spinal 15 percent). The type of hernia encountered at operation was comparable between the two groups (**Table 2.1**). In the non-mesh group there was no recurrence of an indirect hernia, four recurrences of direct hernias and five recurrences of combined hernias. Surgeons and residents assisted by a surgeon operated on comparable numbers of patients (68 versus 78 and 78 versus 66 respectively). Of the ten patients with a recurrence, six were primarily treated by a surgeon and four by a resident (P not significant).

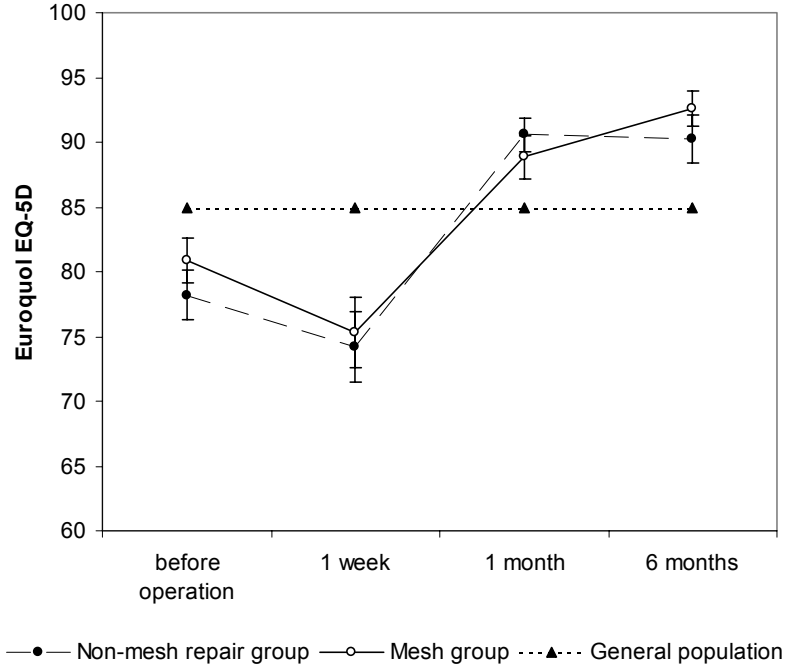
Complications

There was no significant difference between the non-mesh and the mesh repair group regarding postoperative wound infection (none of 143 versus one of 146; p = 0.32), wound dehiscence (none of 143 versus one of 146; p = 0.32), hematoma (17 of 143 versus 15 of 146, p = 0.66) and seroma (none of 143 versus 4 of 146, p = 0.62). In the non-mesh group one patient suffered from urinary retention and one patient from pneumonia. Apart from recurrences, there were no long-term complications.

Postoperative pain (week 1: 45 of 140 versus 58 of 140 (p = 0.11); 36 months: 9 of 125 versus 8 of 129 (p = 0.73)) and discomfort (week 1: 78 of 140 versus 72 of 140 (p = 0.42); 36 months: 13 of 125 versus 11 of 129, (p = 0.6)) were similar at all timepoints.

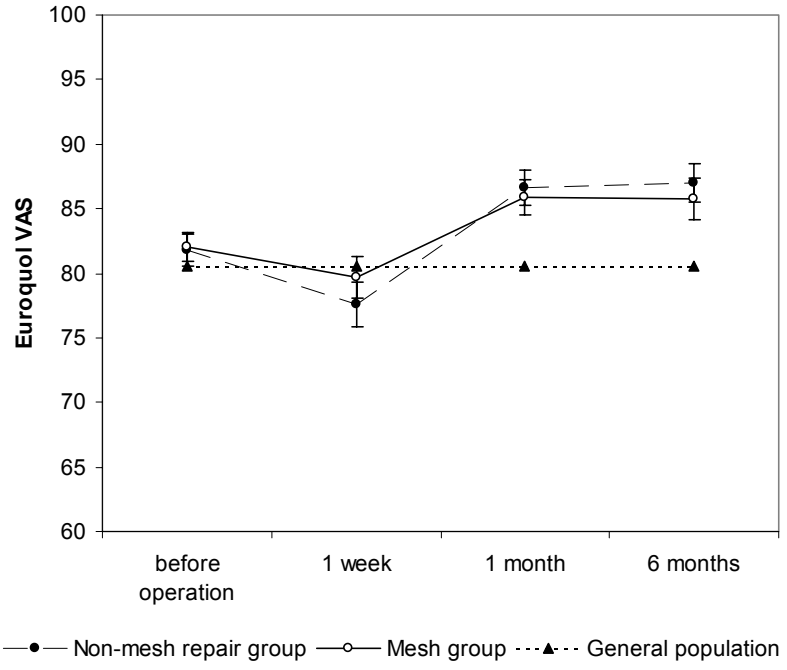
Quality of life

The response rate for the Euroqol questionnaire and VAS ranged from 49 to 74 percent for the non-mesh repair group and from 56 to 79 percent in the mesh group, varying between timepoints. The quality of life did not differ significantly between groups at any timepoint. There were no significant differences between mean (s.d.) values for EuroQol EQ-5D or EuroQol VAS measured in the general population (85(8) (*Kind 1999*) and 81(14) (*Van Agt 1994*) respectively) and either study group. (**Figures 2.1** and **2.2**).



Number of respondents per time point ranges from 90 to 111 per treatment group.

Figure 2.1 *Quality of life measured by Current Health State, EuroQol EQ-5D (minimum score 0, maximum score 100).*



Number of respondents per time point ranges from 101 to 119 per treatment group.

Figure 2.2 *Quality of life measured EuroQol Visual Analogue Scale (VAS) (minimum score 0, maximum score 100).*

Cost

The two groups paid a similar number of visits to the general practitioner (6 of 143 and 8 of 146) and required assistance of a nurse or a housekeeper in a comparable number of cases (4 of 143 versus 2 of 146). Use of analgesics was comparable (9 versus 7 patients).

No difference was noted in operation-related factors and quality of life. Cost-effectiveness was therefore determined by the costs of polypropylene mesh (€ 53) and by the number of recurrences requiring reoperation. Repair of a recurrent inguinal hernia costs approximately € 1600 in a Dutch hospital, including the specialists' fees, use of the operating room and a hospital stay of 2 days. To prevent the nine recurrences in the non-mesh group from developing, 143 meshes should have been used in hernia repair in this group, resulting in additional operating costs of € 7579 for the whole group. At least € 6821 would have been saved if mesh had been used for all repairs.

2.3 Discussion

Inguinal hernia repair performed by suturing and displacement of anatomic structures may lead to excessive tension on the suture line and surrounding tissue. Subsequently, tissue ischaemia and suture cut-out may occur, resulting in recurrence. The use of prosthetic mesh allows tension free repair of inguinal hernia and, in theory, better results. The current series proves the superiority of this method over non-mesh repair in the long term with regard to hernia recurrence; In addition, there was no increase in cost, complications or postoperative pain and quality of life was comparable.

The incidence of complications did not differ significantly between groups, results similar to the results of other randomized trials comparing mesh and non-mesh repair [*Barth 1998, McGillicuddy 1998, Friis 1996, Prior 1998*]. The reluctance of surgeons to use polypropylene mesh because of an assumed increase in the incidence of postoperative complications is thus unjustified.

Postoperative pain and discomfort, duration of surgery, hospital stay and time off work were comparable in the two groups, as has been shown previously [*Barth 1998, McGillicuddy 1998, Friis 1996, Prior 1998*], although *Barth et al.* [1998] reported a significantly longer duration of surgery in the non-mesh repair group and *Prior et al. [1998]* described significantly less postoperative pain in the mesh group.

Quality of life evaluation showed no differences between the two operative groups, and thus was only determined by the number of recurrences after inguinal hernia repair. The additional cost of mesh for mesh repair was less than the cost of operating on recurrences, confirming that mesh inguinal hernia repair is a cost-effective method.

In conclusion, mesh inguinal hernia repair was associated with a lower recurrence rate than non-mesh repair; indeed, a recurrence rate of zero is within reach. No differences were found in complication rate, postoperative pain and quality of life, and mesh repair proved to be cost-effective. Therefore, mesh repair is the method of choice for primary inguinal hernia repair.

CHAPTER 3

PROSTHETIC MESH REPAIR SHOULD BE USED FOR ANY DEFECT IN THE ABDOMINAL WALL

Current Medical Research and Opinion
accepted for publication

3.1 Introduction

Numerous methods have been described for repair of defects in the abdominal wall. Both inguinal and incisional hernias have been treated with primary closure of the defect until the introduction of prosthetic mesh. For hernia repair without prosthetic mesh, also referred to as conventional or non-mesh repair, recurrence rates have been described to vary between 0.2 and 33% for inguinal hernias [*Vrijland 2002a*] and between 24 and 54% for incisional hernias [*Luijendijk 2000*]. It has been suggested that non-mesh repair of hernias with approximation of the tissue leads to excessive tension on the suture line in the abdominal wall causing tissue ischemia and suture cut-out which finally results in high recurrence rates. In 1958, *Usher* [*1958*] described the use of polypropylene mesh for the tension-free repair of abdominal wall defects, avoiding the approximation of tissue. In 1986, *Lichtenstein and Shulman* [*1986*] described the currently most frequently used method of tension-free inguinal hernia repair using polypropylene mesh. The foreign body reaction provoked by the presence of the mesh induces collagen synthesis and therefore leads to a sound repair.

3.2 Inguinal hernia

Tension-free repair became a popular method of inguinal hernia repair because the procedure is quick, easy to perform and showed good results. *Friis* and *Lindahl* [*1996*] showed that mesh repair is superior to non-mesh repair in a randomized clinical trial. These results were confirmed by our own data [*Vrijland 2002*]. More trials have been executed to assess the value of repair with prosthetic material. The EU Hernia Trialists Collaboration identified 15 published and unpublished trials reporting on mesh versus non-mesh repair [*Collaboration 2000a*]. The data available showed less recurrences after mesh repair compared to non-mesh repair. This was true even if mesh repair was compared to Shouldice repair, which is the non-mesh repair that shows the most favourable results regarding recurrence rates amongst all types of non-mesh repair [*McGillicuddy 1998*] No differences were found in infection rate and other variables like postoperative pain and return to usual activity.

Endoscopic or laparoscopic inguinal hernia repair, which requires the use of mesh, became popular because of a claimed reduction of postoperative pain and early return to usual activity. *Liem et al.* [*1997a*] described less recurrences and more rapid recovery compared to conventional anterior repair. The EU Hernia Trialists Collaboration [*Collaboration 2000b*] included 34 (quasi-)randomized trials in a systematic review. It was confirmed that endoscopic and laparoscopic repair of inguinal hernias result in less recurrences if compared to open non-mesh repair. No difference was shown between endoscopic or laparoscopic repair and open mesh repair regarding recurrences.

3.3 Incisional hernia

For incisional hernia repair primary closure was performed until the introduction of prosthetic mesh. Presently, surgeons tend to use prosthetic mesh in large defects and primary closure in smaller defects. Mesh repair of incisional hernias showed favourable results regarding hernia recurrence compared to non-mesh repair in several non-randomized publications and in one controlled randomized trial reported by *Luijendijk et al.* [*2000*]. The latter study proved the superiority of retrofascial mesh repair over non-mesh or suture repair regarding recurrence rates. It is striking that this was true even for smaller hernias with a defect size of less than 10 cm^2. This was confirmed in a recent report on a randomized trial comparing mesh and non-mesh repair of umbilical hernias [*Arroyo 2001*]. Therefore, repair of small hernias with the use of mesh proved to be superior to non-mesh repairs.

Mesh repair of incisional hernia is not a difficult technique but some steps need special attention. It is of great importance to avoid suturing of the mesh under tension, and the overlap of the mesh and the fascia should be at least 2 cm. It might even be advisable to aim at an even more extensive overlap of mesh and fascia because shrinkage of mesh has been described. Infection usually does not lead to mesh removal in any case but can be treated conservatively. Since infection is proven to be a risk factor for recurrence, it is strongly advised to administer antibiotic prophylaxis peroperatively. The use of prosthetic mesh is still contra-indicated under infectious or contaminated conditions in which case second stage repair should be considered.

Laparoscopic repair of incisional hernias is a relatively new method with theoretical advantages. It was firstly described by *LeBlanc and Booth* [*1993*]. The general advantages of laparoscopy like less postoperative pain and morbidity and earlier return to usual activity could be applicable to laparoscopic incisional hernia repair. Another possible advantage is that the risk of wound infection is lower because of smaller incisions, and if infection occurs, there is less chance of the mesh becoming infected, because incisions are placed well away from the abdominal wall defect. Therefore, laparoscopic incisional hernia repair might lead to a reduction in recurrence rate. A randomized controlled trial is currently conducted to assess the value of this method.

3.4 Conclusion

In our opinion enough evidence has been obtained to claim that all defects in the abdominal wall, either inguinal, incisional or umbilical hernias, should be repaired with the use of prosthetic mesh. We strongly feel a mesh should be used independent of the size of the defect.

CHAPTER 4

INTRODUCTION TO PATHOPHYSIOLOGY AND PREVENTION OF POSTOPERATIVE ADHESIONS

4.1 Definition and pathofysiology

Adhesions can be defined as fibrous structures in the abdominal cavity that arise at injured peritoneal surfaces, and are a consequence of disturbed tissue repair after peritoneal trauma [*Haney 1994*]. Damage to the peritoneum may be caused by mechanical injury such as in surgery, by exposure to foreign materials, and by inflammatory disease [*Ellis 1997, Luijendijk 1996, Menzies 1993, van den Tol 1997*]. The equilibrium between mediators of the inflammatory response and fibrin formation and breakdown that is responsible for peritoneal repair may be disturbed after peritoneal trauma. This may result in inadequate breakdown of fibrin and eventually lead to the formation of a permanent fibrous structure between two peritoneal surfaces by invasion, proliferation and differentiation of fibroblasts and endothelial cells. Collagen synthesis and capillary formation transform the adhesion to its final state. Although great efforts have been made to reveal the dynamic process of peritoneal healing, and to determine the factors that cause disturbance of this process, considerable information is still lacking. An excellent overview of the peritoneal healing process known so far is described in the thesis of *Van den Tol* [*2001*] and in *Peritoneal Surgery* by *diZerega et al.* [*2000*].

4.2 Clinical consequences

The incidence, clinical signs and treatment of abdominal adhesions is described in chapter 8.

4.3 Prevention

To prevent the formation of adhesions, peritoneal trauma should be reduced. Reduction of damage is possible by avoiding unnecessary desiccation and hypothermia, limiting manipulation of the peritoneum and by reducing the use and spill of foreign materials intra-abdominally. Closing of the peritoneum during surgery is unnecessary and possibly harmful [*Luijendijk 1996, Ellis 1977, Hugh 1990, Duffy 1994, Irion 1996*]. It has been suggested that laparoscopy causes less peritoneal trauma than an open procedure and therefore provides a technique associated with reduced adhesion formation and related complications. This subject is further discussed in chapter 8.

In clinical studies, no beneficial effects of anti-inflammatory like corticosteroids, non-steroidal anti-inflammatory drugs and antihistamines has been shown. Fibrinolytic agents like citrate, heparin, dicoumarol and dextran neither showed a positive effect [*Farquhar 2000*]. Selective immunosuppression and mesenchymal seeding of stem cells on peritoneal defects show promising preclinical results for the prevention of adhesion formation [*Van den Tol 2001*]. No clinical results are available yet.

The only presently available anti-adhesive therapy is the use of a mechanical barrier. To separate peritoneal surfaces after a trauma reduces adhesion formation simply by avoiding contact between peritoneal surfaces. Ideally, such a barrier is absorbable and disappears after the peritoneal healing process has been completed. This process is final after approximately seven days and therefore a mechanical barrier should last for at least seven days [*Ellis 1965, Hubbard 1967*]. Non-absorbable barriers have proven their efficacy, but may cause chronic infection. [*Farquhar 2000*]. Seprafilm membrane is an absorbable mechanical barrier

consisting of hyaluronic acid and carboxymethylcellulose. These two substances are naturally occurring polymers that provide an adequate anti-adhesive barrier in animals [*Burns 1995*]. In humans the membrane proved its efficacy under non-infectious circumstances [*Becker 1996*].

4.4 Adhesions and mesh

In the first part of this thesis it was shown that mesh repair should be used for any defect of the abdominal wall. Since absorbable meshes only provide a temporary solution in hernia repair, a mesh used for hernia repair should be non-absorbable [*Tyrell 1989*]. Since repair with polypropylene mesh is strong and provokes limited inflammatory response and is associated with low infection rates, this material is our first choice in hernia repair, although there is no general agreement on this subject [*Tyrell 1989, Bellon 1998, Amid 1997, Klosterhalfen 2002*]. A great disadvantage of polypropylene mesh is the increased formation of adhesions if the mesh is placed intraperitoneally, which is often unavoidable in incisional hernia repair. Expanded polytetrafluoroethylene mesh (ePTFE) causes less formation of adhesions, but has a higher infection risk because of microporosity and a higher risk of recurrence, since ingrowth is less thorough than in polypropylene mesh and does not add to the strength of the repair. Polyester causes adhesion formation at a degree similar to that of polypropylene [*Amid 1997, Soler 1993, Cristoforoni 1996*]. However, recently it was stated that the structure of a mesh rather than its chemical composition is responsible for the formation of adhesions. A reticular structure, as present in polypropylene and polyester mesh, provoked more adhesions than a laminar structure, as present in ePTFE, in a rabbit model [*Bellon 2002*].

Another disadvantage is the supposed increase of enterocutaneous fistula formation after hernia repair, suggested to originate from the dense adhesion formation in reaction to the mesh, although little is known about the predisposing factors for this complication [*Kaufman 1981, Leber 1998, Losanoff 2002*].

CHAPTER 5

PERITONEAL ADHESIONS TO PROSTHETIC MATERIALS: CHOICE OF MESH FOR INCISIONAL HERNIA REPAIR

Surg Endosc 2000;14:960-3

Abstract

Background: In many cases, incisional hernia repair requires the use of prosthetic materials. The aim of this experimental study in a rat model was to assess the role of polyglactin 910 mesh and fluoropassivated polyester mesh in the prevention of formation of adhesions.

Methods: In the first experiment, the formation of peritoneal adhesions was assessed after insertion of polypropylene, polypropylene combined with polyglactin 910, or no mesh. In the second experiment, adhesion formation was compared after insertion of fluoropassivated polyester, polypropylene and no mesh.

Results: The first experiment showed no significant difference in adhesion formation between polypropylene mesh and the combined mesh; however, when no mesh was used, There were significantly fewer adhesions in both experiments ($p<0.01$). The second experiment showed a significant lower degree of adhesions and a lower Adhesion Index after insertion of fluoropassivated polyester mesh than when polypropylene mesh was used ($p=0.04$).

Conclusions: Adding polyglactin 910 mesh to polypropylene mesh to prevent the formation of adhesions is not an effective measure. Fluoropassivated polyester meshes could appear to provide a better alternative to the use of polypropylene meshes for incisional hernia repair in humans in terms of the formation of adhesions.

5.1 Introduction

Incisional hernias occur in 11 % of patients after laparotomy. Repair of these hernias frequently requires the use of prosthetic materials. Polypropylene mesh is commonly employed for this purpose [*Leber 1998, Molloy 1991*]. There is some concern among surgeons about the use of prosthetic material because of the risk of infection of the mesh, the formation of enterocutaneous fistulas and the development of adhesions between the viscera and the mesh. To prevent fistulas and adhesions, some authorities recommend that the parietal peritoneum be preserved during incisional hernia repair because it forms a barrier between the viscera and the mesh. When the parietal peritoneum cannot be kept intact, the surgeon may attempt to place the greater omentum between the abdominal contents and the prosthetic material.

However, in daily practice, it is often not feasible either to preserve the parietal peritoneum or to use the greater omentum. In these cases, some surgeons insert a resorbable polyglactin 910 mesh between the intestines and the polypropylene mesh or use a composite of polyglactin 910 and polypropylene meshes. Alternatively, ePTFE (expanded polytetrafluoroethylene, Gore-tex) meshes, which supposedly induces fewer adhesions, or human tissue such as dura can be employed; however, these alternatives are costly.

The search for new biomaterials for incisional hernia repair has resulted in the development of fluoropassivated polyester. Fluoropassivation of the polyester surface is expected to diminish the formation of adhesions. The cost of fluoropassivated polyester meshes is comparable to that of polypropylene meshes.

We performed two experimental studies in rats to evaluate the role of polyglactin 910 and fluoropassivated polyester in the prevention of the formation of adhesions.

5.2 Materials and methods

Animals

Female Wistar rats of reproductive age weighing 200-250 g were obtained from Harlan, Zeist, The Netherlands. They were bred under specific pathogen-free conditions and kept under standard laboratory conditions (temperature, 20-24°C, relative humidity, 50-60%, 12 h light and 12 h dark). The rats were given standard rat chow and water ad libitum. The experimental protocol adhered to rules laid down by the Dutch Animal Experimentation Act and was approved by the Committee on Animal Research of Erasmus University, Rotterdam.

Prosthetic material

The evaluated prosthetic materials were nonabsorbable polypropylene mesh in a double-filamented form (Prolene; Ethicon Inc., Somerville, NJ, USA), absorbable polyglactin 910 mesh (Vicryl, Ethicon Inc, Somerville, NJ) and nonabsorbable multi-filament fluoropassivated polyester mesh (Fluorosoft; Sulzer Vascutek Ltd., Renfrewshire, Scotland). Fluoropassivated polyester was developed to combine the strength, handling, and healing characteristics of polyester with the inertness and biocompatibility of expanded polytetrafluoroethylene (ePTFE, Gore-Tex; W.L. Gore, Flagstaff, AZ, USA). It is more resistant to bacterial binding than polypropylene [*Kelso 1997*]. The price of fluoropassivated polyester mesh is considerably lower than that of ePTFE mesh. In the Netherlands, ePTFE mesh costs $365-$820

depending on size and number of pieces required, whereas a fluoropassivated polyester mesh costs $100-$125 and a polypropylene mesh costs $35-$70.

Model

The experiment was executed in a validated uterus horn model in the rat, allowing semiquantitative scoring of adhesions according to *Van den* Tol et al. [*1997*] and *Bakkum et al.* [*1994*]. In the rat the uterus horn is a Y-shaped structure with two horns of approximately 4 cm length. Under ether anesthesia and aseptic but not sterile conditions, the abdomen was shaved and cleaned with alcohol. Laparotomy was performed using a lower midline incision of 5 cm. Bilaterally, 1.5 cm downwards from the abdominal incision, a mesh of 1.5 x 1.0 cm was positioned between the uterus horn and the abdominal wall and then sutured to the abdominal wall with three 5.0 Surgilene sutures at 0.7 cm intervals *(**Fig 5.1**)*.

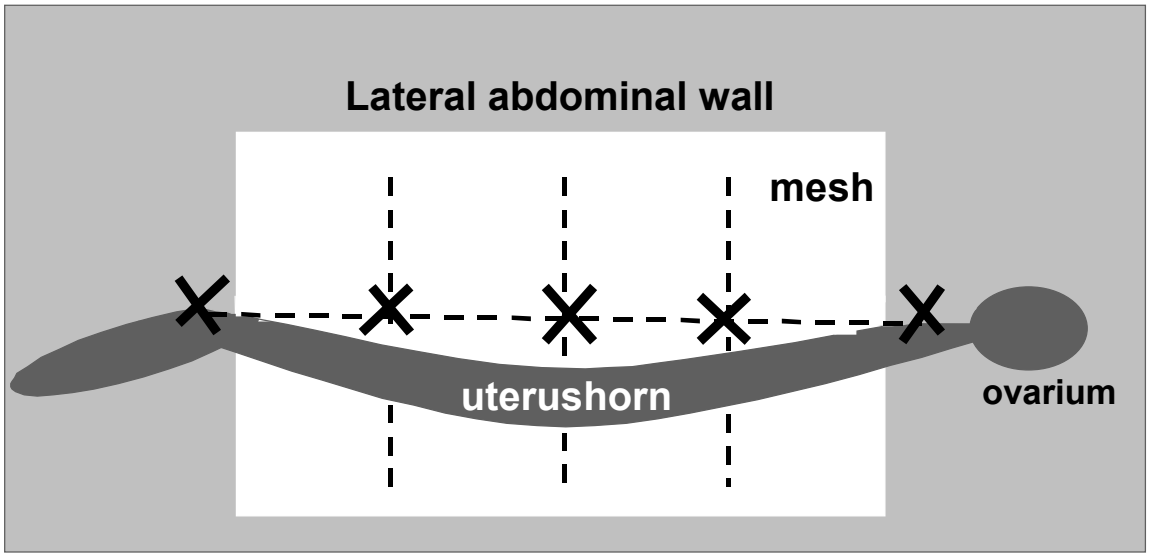


Figure 5.1 *The mesh was fixed to the lateral abdominal wall with three sutures 0.7 cm apart. Then the uterus horn that was previously rubbed with gauze was tightened to the abdominal wall without strong tension*

Standard surgical trauma to induce adhesion formation [*Thompson 1965*] was inflicted on the uterus horn by rubbing it with a surgical gauze using a device enabling the application of a constant pressure of 120 g/cm^2. The uterine horn was rubbed ten times over its total length, then tightened to the lateral abdominal wall with two 5.0 Surgilene sutures. If a mesh was inserted between abdominal wall and uterus horn, it was fixed with the three 5.0 Surgilene sutures. This procedure was performed bilaterally.

Experimental design

Experiment I

In the first experiment, 20 rats of identical arrival date were included. Three groups were formed after random selection of rats according to an allocation list. Group Ia consisted of 8 rats treated with a polypropylene mesh. Group Ib consisted of 8 rats treated with a polypropylene mesh combined with a polyglactin 910 mesh placed between the polypropylene mesh and the uterus horn. Group Ic was a control group that underwent the same procedure without the insertion of prosthetic material (n = 4).

Experiment II

The second experiment was performed with 24 rats of identical arrival date. The experiment involved three groups with rats selected at random according to an allocation list: group IIa was treated with a polypropylene mesh. Group IIb was treated with a fluoropassivated polyester mesh. The control group (IIc) was not treated with any prosthetic material. All three groups consisted of 8 rats.

Evaluation of adhesion formation

Sixty days after operation, the rats were killed by ether overdose for assessment of postsurgical adhesion formation. This period was chosen to ascertain that the polyglactin 910 mesh had disappeared. The adhesions were scored macroscopically in terms of extent (quantity) and type (quality) by two independent observers. The extent of adhesion formation was quantified by dividing the area to be scored into eight by means of the three sutures by which the defect was closed (***Fig. 5.2***).

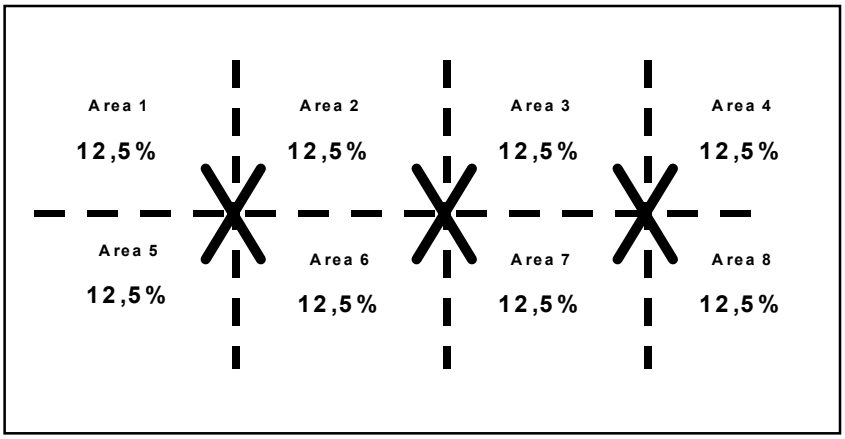


Figure 5.2 *The extent of adhesion formation was quantified by dividing the treated area to be scored into eight areas of 12.5% each by means of the three sutures to fix the mesh.*

When adhesions were present in one of the 8 areas, a score of 12.5% was recorded. In each rat, both areas on the lateral abdominal wall were assessed. The type of adhesions formed was classified as described by *Zühlke et al*. [*1990*]. (***Table 5.1***). The Adhesion Index (AI) is an overall measure of adhesion formation and is defined as the product of extent and quality of adhesions.

Table 5.1

Macroscopic classification of abdominal adhesions according to *Zühlke et al.* [*Zühlke1990*]

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

Statistical analysis

Statistical analysis was performed by the Mann-Whitney-U test for independent samples. Comparisons were made between treatment groups (Ia versus Ib and IIa versus IIb) and between treatment and control groups (Ia + Ib versus Ic and IIa + IIb versus IIc). Statistical significance was defined as $p<0.05$. Data were expressed as mean ± SE adhesion percentage, mean ± SE adhesion grade and mean ± SE Adhesion Index.

5.3 Results

In group I, no significant difference was shown between group Ia and group Ib either in extent or quality of the formed adhesions (**Table 5.2**). The control group (Ic) had a significant lower value than groups Ia and Ib in terms of extent of adhesions ($p = 0.004$), quality of adhesions ($p < 0.001$) and AI ($p < 0.001$).

Table 5.2

Comparison of groups in experiment 1
PP, polypropylene; PP/PG, polypropylene combined with polyglactin 910 (PG)

Group	Mesh	n	Mean % of adhesions (+ SE)	Zühlke (+ SE)	Adhesion Index (+ SE)
Ia	PP	8	66 (7.4)	2.5 (0.1)	170 (24)
Ib	PP/PG	8	78 (7.4)	2.5 (0.1)	196 (23)
Ic	No Mesh	4	32 (11.7)	1 (0)	33 (12

Table 5.3

Comparison of groups in experiment 3
PP, polypropylene; FP, fluoropassivated polyester

Group	Mesh	n	Mean % of adhesions (+ SE)	Zühlke (+ SE)	Adhesion Index (+ SE)
IIa	PP	8	80 (5.1)	3.0 (0.2)*	243 (28)*
IIb	FP	8	73 (6.0)	2.3 (0.1)*	173 (21)*
IIc	No Mesh	8	29 (4.5)	1.0 (0.2)	36 (8)

*) p = 0.04

As **Table 5.3** shows, no significant difference between group IIa and group IIb in terms of extent of adhesions. However, the quality of the adhesions differed slightly; group IIb had a lower mean adhesion grade than group IIa (p=0.04). The Adhesion Index was significantly lower in group IIb than in group IIa (p=0.04). Groups IIa and IIb had both significantly more and denser adhesions compared to group IIc (p=0.001) as well as a significantly higher AI (p=0.001).

5.4 Discussion

Tension-free repair of incisional hernias with prosthetic material lowered the recurrence rate of 30-46% initially reported after primary repair [*George 1986*, *Hesselink 1993, Langer 1985, Manninen 1991*] to rates that have varied from 2.2 to 10% in recent studies [*Mudge 1985, Turkcapar 1998*]. In the surgical treatment of inguinal hernias, a similar tendency towards tension-free repair has been seen over the past few years. Due to these advances and the growing use of endoscopic techniques to treat inguinal and incisional hernias, the choice of which prosthetic material to use has become a topic of debate in the surgical community.

The ideal mesh maintains adequate and permanent closure of the abdominal wall defect, has a low infection rate, causes few adhesions and induces no enterocutaneous fistulas. Polypropylene meets these demands to some extent, but alternatives are being sought to improve the results of incisional hernia repair and reduce its complication rate. The belief of many surgeons that polyglactin 910 can prevent adhesion formation if it is added to a polypropylene mesh was not supported by our study. Polyglactin 910 can not be used without an other mesh for incisional hernia repair because the mesh is absorbed in <60 days and thus does not provide a permanent solution. Therefore, from a clinical point of view, there was no reason for us to include a group treated with a polyglactin 910 mesh only. However, *Jenkins et al.* [*1983*] described limited adhesion formation after insertion of this material in Sprague-Dawley rats. These rats underwent midline laparotomy and excision of a 4 by 4 cm segment of abdominal wall musculature. The defect was repaired by suturing patches of prosthetic material to the abdominal margins. According to the authors, the fibrous sheath that remained after the polyglactin mesh had resolved had surprising resistance to rupture, but no favorable results have been described in humans.

Although the extent of adhesion formation was not diminished after the insertion of fluoropassivated polyester mesh, the quality and the Adhesion Index were slightly lower. These results suggest that fluoropassivated polyester may provide a better alternative for polypropylene in incisional hernia repair in humans in terms of preventing adhesion formation; however, further research on its use in humans should be undertaken. *Soares* [*1996*] investigated fluoropassivated polyester and found sufficient resistence to rupture, good healing of the abdominal wall and a local and systemic response to the foreign material similar to that seen with ePTFE.

Fluoropassivated polyester meshes cost considerably less than ePTFE meshes, but they appear to have the same properties. Polypropylene meshes are in a similar price range, but they are associated with greater adhesion formation.

Clinical experience in hernia repair with fluoropassivated polyester is still limited. At the University Hospital of Rotterdam a prospective randomized clinical trial has been set up to compare laparoscopic and open incisional hernia repair. Fluoropassivated polyester will be used for both repairs.

It has yet to be determined whether fluoropassivated polyester causes fewer wound infections and enterocutaneous fistulas than other materials now used for incisional hernia repair. This question will be addressed by clinical follow-up of the patients included in the laparoscopic versus open incisional hernia repairs.

5.5 Addendum to the original publication

The fluoropassivated polyester mesh that was introduced in this study was designed as a vascular prosthesis and was adapted for hernia repair. It was suggested to combine the strength and pliability of a polyester mesh with the low infection rate of polypropylene and reduced adhesion formation, comparable to ePTFE mesh, both properties caused by the fluoropassivated coating on the polyester mesh. Since the experiment showed favourable results, we were planning on further experiments with this mesh, to investigate its use in hernia surgery. Unfortunately, the manufacturer of the mesh decided to withdraw the mesh for the purpose of hernia surgery for economical reasons.

CHAPTER 6

INTRAPERITONEAL POLYPROPYLENE MESH REPAIR OF INCISIONAL HERNIA IS NOT ASSOCIATED WITH ENTEROCUTANEOUS FISTULA

Br J Surg 2000;87:348-52

Abstract

Background: Incisional hernia repair with prosthetic material is followed by fewer recurrences than primary repair. Polypropylene is the most commonly used prosthetic material but may cause enterocutaneous fistulas. The aim of this study was to determine whether enterocutaneous fistulas developed after incisional hernia repair with polypropylene mesh and to evaluate clinical outcome after incisional hernia repair.

Methods: A retrospective analysis of the outcome of incisional hernia repair with polypropylene mesh between 1982 and 1998 was conducted. Follow-up data were obtained from medical records and questionnaires.

Results: Polypropylene incisional hernia repair was performed in 136 patients. Median follow-up was 34 months. No enterocutaneous fistulas developed. Wound infection occurred in 6 per cent. Wound sinus formation occurred in two patients. No mesh was removed because of infection and no persisting infection of the mesh occurred.

Conclusions: Enterocutaneous fistula formation appears very rare after incisional hernia repair with polypropylene mesh, regardless of intraperitoneal placement, omental coverage or closing of the peritoneum.

6.1 Introduction

Incisional hernias develop in 2 –19 per cent of patients after abdominal surgery [*Mudge 1985, Bucknall 1982, Luijendijk 1996, Regnard 1988, Israelsson 1993*]. After primary repair, until recently the method of choice, recurrence occurs in up to 46 per cent [*George 1986, Manninen 1991, Langer 1985, Hesselink 1993, Wissing 1987*]. Tension-free repair with prosthetic material lowered the reported recurrence rate to between 2.2 and 10 per cent [*Mudge 1985, Turkcapar 1998*] but is not recommended when contact between the mesh and bowel is unavoidable.

Plastic prostheses were first used in 1958 [*Usher 1958*] and proved to be easy to use, pliable, and showed no desintegration with ageing. Polypropylene mesh has become the most widely used prosthetic material for repair of incisional hernias [*Leber 1998, Molloy 1991*]. This mesh is available in a monofilamented (Marlex; Davol, Cranston Rhode Island, USA) and a double-filament (Prolene, Ethicon, Somerville, New Jersey, USA) form.

An early report by *Usher et al.* [*1958*] suggested that placing the mesh in direct contact with omentum or bowel could be done safely. However, enterocutaneous fistula was first described in 1981 as a late complication of intraperitoneal placement of a polypropylene mesh in a patient [*Kaufman 1981*]. After reports of other enterocutaneous fistulas following mesh repair of incisional hernias, this technique was no longer recommended [*Leber 1998, Kaufman 1981, Miller 1997, Seelig 1995*].

However, enterocutaneous fistula formation was not mentioned by *Molloy et al.* [*1991*], *Liakakos et al.* [*1994*] and *Sugerman et al.* [*1996*]. as a long term complication after incisional hernia repair with mesh. Therefore, it remains unclear what the potential danger is of intraperitoneal non-resorbable mesh used without omental or peritoneal coverage of the bowel. Series of incisional hernia repairs with polypropylene mesh have been described by other authors [*Leber 1998, Molloy 1991, Liakakos 1994, Sugerman 1996, White 1998*] but the possible association between intraperitoneal placement of polypropylene mesh and fistula formation has not been discussed extensively.

The aim of this retrospective study was to determine whether or not enterocutaneous fistulas occurred after repair of incisional hernias with polypropylene mesh, and to assess whether it can be considered safe to perform intraperitoneal polypropylene mesh repair with or without coverage of bowel with omentum or peritoneum.

6.2 Patients and methods

Patients undergoing incisional hernia repair with the use of mesh between September 1982 and August 1998 were identified by the Department of Medical Registration. The medical records of these patients were examined and data regarding incisional hernia repair with mesh were entered into a database (SPSS-data entry; SPSS, Chicago, Illinois, USA).

A mild wound infection was defined as redness surrounding the laparotomy wound, a moderate infection produced pus and a severe infection was defined as wound dehiscence and wound edge necrosis. Wound sinus was defined as a non-healing defect of the wound extending into the subcutaneous tissue.

Statistical analysis of possible recurrence-related factors was performed with Kaplan-Meier curves and comparisons between curves were made by the log rank test. Other comparisons were made according to the Pearson chi-square test.

Follow-up data were acquired either from the medical record if patients had been visiting the outpatient clinic or from a questionnaire sent to the patient's general practitioner. This questionnaire contained questions about whether the patient had visited the general practitioner since the incisional hernia repair and if this visit was related to the hernia repair.

A Medline search on incisional hernia repair with cross-references identified other series of incisional hernia repair. The results of these series were summarized and compared with the present results in **Table 6.2.**

6.3 Results

Incisional hernia repair with the use of prosthetic material was performed in 171 patients between 1 September 1982 and 1 August 1998. A polypropylene mesh was inserted in 136 patients (80 per cent) and a polytetrafluoroethylene patch (Gore-Tex; W.L. Gore, Phoenix, Arizona, USA) in 16, in 13 patients a Vicryl (Ethicon) mesh was added to a polypropylene mesh and in six only Vicryl was used to close the defect.

Only the patients who had solely polypropylene meshes were included in this analysis (n = 136). This group consisted of 69 men and 67 women with a mean (sd) age of 62 (12) years. Laparotomy had been performed in the midline in 71 per cent of these 136 patients, was oblique (appendicectomy and cholecystectomy) in 18 per cent and transverse in 11 per cent. An upper midline incision was the most common location of incisional hernias (38 per cent). Some 72 per cent of incisional hernias were primary, 16 per cent were recurrent, 7 per cent had recurred for the second time and 5 per cent had recurred more than twice. The median (sd) diameter of the fascial defect was 6 (5) cm.

At induction of anaesthesia for surgical repair of the incisional hernia, 82 per cent of all patients received antibiotic prophylaxis. Only 4 per cent of all incisional hernia repairs with polypropylene were performed as an emergency operation for incarceration. A serosal lesion of the bowel occurred in 7 patients (5 per cent) and bowel perforation occurred in three (2 per cent). Major peroperative bleeding did not occur in any patient. In most patients (84 per cent), the mesh was placed subfascially. The omentum was placed between mesh and bowel in 27 patients (20 per cent) and in 39 patients (29 per cent) the peritoneum could remain closed or was closed during the repair. In 57 patients (42 per cent) it was not possible to place omentum between the mesh and bowel or to close the peritoneum.

In 13 patients (10 per cent) the surgical report was inconclusive about interposition of peritoneum or omentum. The mesh was fixed with non-resorbable sutures in 90 per cent. In six patients the surgical procedures were performed under contaminated conditions, because of accidental bowel perforation (n = 3), planned bowel resection (n = 2) or restoration of continuity after ileostomy (n = 1). No patient was operated on for a burst abdomen. Prophylactic antibiotics were administered in 82 per cent of all repairs. Every patient with contamination during incisional hernia repair received antibiotics peroperatively.

In 49 per cent of surgical procedures a drain was left behind, which was removed after a median (sd) time of 2 (1) days. Antibiotic prophylaxis was administered peroperatively in all patients with drains. The median (sd) operative time was 100 (42) min and duration of stay in hospital was 7 (7) days.

Six patients (4 per cent) were lost to follow up. Recurrence of incisional hernia occurred in 19 patients (3-year recurrence rate of 18 per cent) after a median (sd) follow-up of 10 (38) months. **Table 6.1** shows the results of analysis of factors possibly related to the development of recurrence. Patients without recurrence (n = 111) had a median (sd) duration of follow-up of 34 (30) months.

Table 6.1

Overview of patient-related factors related to recurrence rate

	3-year recurrence [%]			P*
Age ≤70	12	vs.	33	.01
Antibiotics Yes versus no	18	vs.	0	.02
Size hernia≤ 6 versus >6 cm	13	vs.	25	.12
Primary versus recurrent hernia	15	vs.	24	.21
Placement subfascial versus suprafascial	20	vs.	12	.46
Sutures Resorbable versus non-resorbable	25	vs.	18	.54
Wound infection yes versus no	19	vs.	0	.17
Total	18			

*) Log rank test comparing Kaplan-Meier curves

No enterocutaneous fistulas were encountered during follow-up. Early postoperative complications consisted of wound infection (2 mild, 1 moderate and 5 severe), haematoma (n = 2), ileus (n = 2) and bleeding from the surgical wound (n = 3). In 2 patients reoperations were necessary, the first because of a bowel perforation not identified during initial surgery and the second because of loosening of the inserted mesh resulting in wound dehiscence. Removal of the mesh was not necessary in these patients. In two patients a wound sinus developed in the operative field, both of whom underwent emergency repair with a suprafascially placed mesh and received antibiotic prophylaxis. Both sinuses were treated conservatively. Six seromas (4 per cent) were reported, all of which were treated conservatively. In four of these patients the mesh was placed subfascially and in two suprafascially; a drain was placed in three of the patients.

6.4 Discussion

An overview of other series of incisional hernia repair as well as our results is given in **Table 6.2**. In 567 patients only 3 enterocutaneous fistulas were reported (0.5 %).

Table 6.2

Overview of published series of incisional hernia repair

	Leber et al. 1998	Molloy et al. 1991	Liakakos et al.1994	Sugerman et al. 1996	White et al. 1998*	Vrijland et al.
No. of patients	135	50	49	98	99	136
Mean hernia diameter [cm]	9.8	n.a.	n.a.	173 †	9.9	6.0 ‡
Antibiotics	n.a.	50 (100)	49 (100)	98 (100)	90 (91)	112(82)
Subcutaneous drain	n.a.	50 (100)	'almost all'	98 (100)	56 (57)	67 (49)
Position of mesh	Various	Supra-fascial	Onlay	Supra-fascial	Onlay (50 Inlay (28) Other (22)	Subf. 114 (84) Supraf. 22 (16)
Non resorbable sutures	n.a.	Yes	Yes	Yes	n.a.	(90)
Wound infection	7 (5)	4 (8)	2 (4)	17 (17)	16 (16)	8 (6%)
Seroma formation	N = n.a. (< 3)	2 (4)	n.a.	n.a.	21 (21)	6 (4)
Enterocutaneous fistula formation	2 (1)	0	0	0	1 (1)	0
Recurrence	N=n.a.(17)	4 (8)	4 (8)	4 (4)	n.a.	(18)
Wound sinus	n.a.	6 (12)	2 (4)	n.a.	n.a.	2 (1)
Mean follow up	6.7 y.	45 mo.	7.6 y.	20 mo.	1-144 mo.	34 mo‡

Values in parentheses are percentages
* Not solely polypropylene repair
† Mean surface area [cm^2]
‡ median. n.a., data not available

A number of authors [*Leber 1998, Kaufman 1981, Miller 1997, Seelig 1995, White 1998*] have described enterocutaneous fistula formation after incisional hernia repair. Kaufman et al. [*1981*] described a single patient with a burst abdomen due to wound infection and necrosis of the abdominal wall after operation. The defect in the abdominal wall was closed with the use of polypropylene during an emergency operation. Afterwards an enterocutaneous fistula developed.

Miller and Junger [*1997*] described the development of a fistula after laparoscopic repair of an inguinal hernia that recurred for the seventh time. An enterocutaneous fistula developed although the peritoneum was closed after positioning the mesh. According to the authors, close contact between the mesh and bowel resulted in low-grade infection of the mesh whereafter the mesh eroded through the visceral

peritoneum into the ileum causing a local infection and consequently an ileocutaneous fistula.

Seelig et al. [*1995*] described one patient who suffered from a burst abdomen that was successively closed with a Vicryl mesh, a polypropylene mesh and another polypropylene mesh because of incisional hernia recurrence. After 9 months an enterocutaneous fistula developed. *Leber et al.* [*1998*] observed two entero-cutaneous fistulas in a group of 135 patients who underwent incisional hernia repair with polypropylene mesh. No specific details about these patients were reported but it was suggested that development of enterocutaneous fistula was correlated with previous wound infection. *White et al.* [*1998*] reported one enterocutaneous fistula after mesh repair but no details were described.

In the present study no fistula occurred in a group of 136 patients. The results show that enterocutaneous fistula formation need not to be feared in elective incisional hernia repair with polypropylene mesh. In 42 per cent of incisional hernia repairs the polypropylene mesh was placed intraperitoneally without coverage of the bowel by omentum or peritoneum. In 49 per cent of repairs the omentum was placed between the mesh and bowel or the peritoneum was or remained closed. The goal of these procedures is to prevent fistula formation. *Leber et al.* [*1998*] suggested a beneficial effect of these procedures whereas *Molloy et al.* [*1991*] and *Larson and Harrower* [*1978*] placed the mesh intraperitoneally without omental or peritoneal coverage of the intestines. Both described no complications.

The use of prosthetic materials for incisional hernia repair has significantly lowered the reported recurrence rates; the 3-year recurrence rate was 18 per cent in this series. This percentage is higher than that reported by other authors [*Mudge 1985, Turkcapar 1998, Molloy 1991, Liakakos 1994, Sugerman 1996*].

Advanced age predisposed to a higher recurrence rate after incisional hernia repair. Impaired wound healing in older patients [*Halasz 1968, Mendoza 1970*] is a probable cause of the significant difference in recurrence between patients over 70 years of age and younger patients.

Whether prophylactic antibiotics are necessary has been subject to discussion. The wound infection rate after incisional hernia repair with prosthetic material was 6 per cent (n = 8) and removal of the mesh was not necessary in any patient. Six out of 8 wound infections were reported in the group that received antibiotics pre-operatively. *Houck et al.* [*1989*] described an infection rate of 15% and *White et al.* [*1998*] reported wound infections in 14 per cent although prophylactic antibiotics were administered almost routinely. No correlation could be shown between placement of drains and infection rate in the present study. Two patients suffered from wound sinuses which were both treated conservatively. *Molloy et al.* [*1991*] described a wound sinus formation of 12 per cent, of which two-thirds needed surgical intervention.

A significant difference in recurrence was found between patients who received antibiotics and those who did not, and therefore prophylactic antibiotics should be used in every incisional hernia repair. No relation was found between subfascial insertion of the mesh or insertion of a drain and the development of seroma.

To minimise seroma formation *Larson and Harrower* [*1978*] advised subfascial placement of the prosthetic mesh. Most authors prefer suprafascial placement of the mesh to prevent long-term complications [*Leber 1998, Molloy 1991, Sugerman 1996,*

White 1998], but this may predispose to seroma formation. However, the present results suggested no relation between insertion of a subcutaneous drain and a decrease in seroma formation.

6.5 Conclusion

Polypropylene mesh can be placed safely intraperitoneally but this should be performed under antibiotic cover.

CHAPTER 7

FEWER INTRAPERITONEAL ADHESIONS WITH USE OF HYALURONIC ACID-CARBOXYMETHYLCELLULOSE MEMBRANE

A RANDOMIZED CLINICAL TRIAL

Ann Surg 2002;235:193-9

Abstract

Objective: To assess the effectiveness of bioresorbable Seprafilm membrane in preventing abdominal adhesions in a prospective clinical randomized multicenter trial.

Summary background data: Adhesions occur frequently after abdominal operations and are a common cause of bowel obstruction, chronic abdominal pain and infertility. To reduce the formation of adhesions, a mechanical barrier composed of hyaluronic acid and carboxymethylcellulose was developed, preventing adherence of tissues after abdominal surgery.

Methods: Between April 1996 and September 1998, all patients requiring a Hartmann procedure for sigmoid diverticulitis or obstructed rectosigmoid were randomized to either intraperitoneal placement of the antiadhesions membrane under the midline during laparotomy and in the pelvis, or as a control. Direct visual evaluation of the incidence and severity of adhesions was performed laparoscopically at second-stage surgery for restoration of the continuity of the colon.

Results: A total of 71 patients were randomized; of these, 42 could be evaluated. The incidence of adhesions did not differ significantly between the two groups, but the severity of adhesions was significantly reduced in the Seprafilm group both for the midline incision and for the pelvic area. Complications occurred in similar numbers in both groups.

Conclusions: Seprafilm antiadhesions membrane appears effective in reducing the severity of postoperative adhesions after major abdominal surgery, although the incidence of adhesions was not diminished. The authors recommend using Seprafilm when relaparotomy or second-look intervention is planned. Long-term studies are needed to assess the cost-effectiveness and value of Seprafilm in preventing bowel obstruction, chronic abdominal pain, and infertility.

7.1 Introduction

Adhesions after abdominal surgery are abnormal attachments between tissues or organs. The formation of adhesions may result from mechanical peritoneal damage, intra-abdominal ischemia and presence of foreign materials in the abdominal cavity such as glove powder, microorganisms, gauze lint, sutures and prosthetic mesh. [*Ellis 1997, Jenkins 1983, Luijendijk 1996*]. Adhesions occur in 68 - 100% of patients who underwent one or more laparotomies. [*Ellis 1997, Luijendijk 1996, Menzies 1990*].

Although intra-abdominal adhesions are asymptomatic in most patients, adhesions can cause intestinal obstruction, chronic abdominal pain, infertility and an increased rate of complications during subsequent operations [*Ellis 1999*]. Adhesions are the most common cause of intestinal obstructions in the Western world [*Menzies 1990*].

Another clinical problem, possibly caused by adhesions, is chronic abdominal pain [*Kresch 1984, Goldstein 1980*]. Infertility is a known sequela of intra-abdominal adhesions [*OLSG 1991, Trimbos-Kemper 1985*] The increased complication rate can be caused by a longer duration of surgery, postoperative bleeding and a higher risk of bowel perforations [*Ellis 1999, Chapron 1999*]. The incidence of these complications increases with the number of previous laparotomies or laparoscopies [*Mecke 1996*].

Substantial costs are associated with adhesion-related clinical problems [*Jeekel 1997, Wilson 1998*]. Hospital admissions for adhesiolysis were responsible for an estimated $1,180 million in expenditures in the United States [*Ray 1993, Ray 1998*].

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 [*Raftery 1973*]. 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 [*Becker 1996*].

The incidence of adhesions after (partial) colectomy is high, so this procedure provides a suitable model for studies of adhesion prevention [*Beck 1999, Nieuwenhuijzen 1998*]. 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 anti-adhesions membrane in reducing the number, incidence and severity of adhesions in patients with diverticulitis or obstruction of the rectosigmoid.

7.2 Methods

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 damaged mechanically 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 antiadhesions 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 intra-peritoneal 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.* [*1990*]. (**Table 7.1**).

Table 7.1 (= Table 5.1)

Macroscopic classification of abdominal adhesions [*Zühlke et al. 1990*]

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

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 7.2**) and the type was assessed according to *Zühlke et al.* [*1990*].

Table 7.2

Score of extent of adhesions in the pelvic area

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

Evaluations were recorded on videotape allowing postoperative masked reevaluation by two independent observers. Severity of formation of adhesions 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.

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 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 Diakonessenhuis (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).

7.3 Results

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 7.3**).

Table 7.3

Preoperative data

		Seprafilm group	Control group
Age (years, 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

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 7.4**)

Table 7.4

Intraoperative data

		Seprafilm group	Control group
Length of midline incision [cm] (mean ± st. dev.)		20 ± 4.2	20 ± 6.8
Resected colon segment (n)	sigmoid	20	18
	other	1	3
Length of resected segment [cm] (range)		18 (10-60)	15 (10-45)
Closure rectal stump (n*)	sutured	6	8
	stapled	18	17
Drain placed	yes	10	10
	no	11	11
Peritoneum sutured	yes	3	0
	no	18	21
Duration of surgery [min] (range)		103 (75-180)	100 (60-260)
Adhesions present (n)	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

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 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 7.5**).

Table 7.5

Incidence of postoperative adhesions assessed during evaluation at laparoscopy

		Seprafilm group (n)	Control group (n)	p-value
Adhesions to the midline incision				
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	

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 (**Fig. 7.1**).

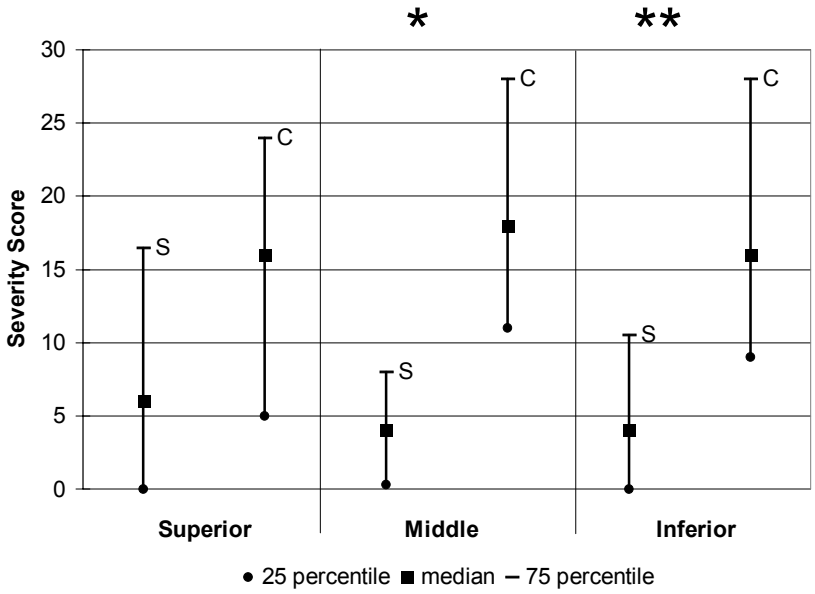


Figure 7.1 *Severity of adhesions per site (extent x type), superior, middle and inferior part of midline incision (median, 25 percentile, 75 percentile)*
S = Seprafilm group; C = Control group; * p < 0.0001; ** p = 0.002.

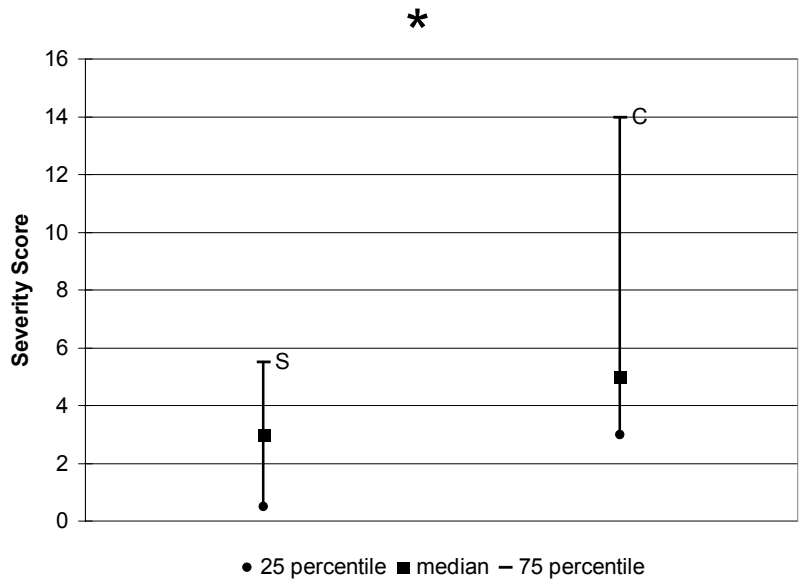


Figure 7.2 *Severity of adhesions in the pelvis (extent x type) (median, 25 percentile, 75 percentile)*
S = Seprafilm group; C = Control group; * p = 0.042.

In addition, the pelvic area showed a significant difference between groups regarding the severity of adhesions (**Fig. 7.2**). 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).

The median severity of adhesions for the total midline incision showed a significant difference: 18 (25^{th} – 75^{th} percentile: 7 - 44) for the Seprafilm group and 50 (25^{th} - 75^{th} 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 (25^{th}- 75^{th} percentile: 8 - 25) for the Seprafilm group and 53 (25^{th}- 75^{th} percentile: 46 - 66) for the control group. Severity score in the pelvis was 0 (25^{th} - 75^{th} percentile: 0 - 2) in the Seprafilm group and 5 (25^{th} - 75^{th} percentile: 2 – 10) in the control group. These severity scores were not significantly different from the values scored at restorative surgery by the surgeon.

7.4 Discussion

Adhesions develop in the vast majority of patients after abdominal surgery [*Ellis 1997, Luijendijk 1996, Menzies 1990*]. 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 [*Becker 1996*].

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 that received Seprafilm compared with the group who served as controls. This finding corresponds to the results of *Becker et al.* [*1996*] 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 [*Holmdahl 1997*]. 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 [*IABSG 1989, Becker et al. 1996*]. found no relation between blood loss and antiadhesions 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 preexistent 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 antiadhesions methods, and time between initial surgery and evaluation of reformation *[OLSG 1991, Trimbos-Kemper 1985, Diamond 1984].*

Seprafilm is not easy to handle, and some experience is needed to apply it 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 antiadhesions 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.

7.5 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 antiadhesions barrier after colorectal surgery if relaparotomy is expected.

CHAPTER 8

ABDOMINAL ADHESIONS: INTESTINAL OBSTRUCTION, PAIN AND INFERTILITY, A REVIEW

Surgical Endoscopy
accepted for publication

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 open and laparoscopic surgery for adhesions should be executed with long-term follow-up to assess the success rates of adhesiolysis and compare the morbidity and mortality.

8.1 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 [*Ellis 1997, Lehmann-Willenbrock 1990, Luijendijk 1996, Menzies 1993*]. Exposing the peritoneum to foreign material such as powder, gloves or intra-abdominal prosthetic meshes is another source of adhesions [*Ellis 1997, Jenkins 1983, Luijendijk 1996*]. 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 rarely cause intestinal obstruction [*Menzies 1990, Menzies 1993*].

Adhesions are responsible for the majority of bowel obstructions in the Western world [*Al-Took 1999, Barkan 1995, Menzies 1993*]. Chronic abdominal pain and infertility are other manifestations of abdominal adhesions [*Kresch 1984, Marana 1995, OLSG 1991*].

One third of patients who has undergone open general surgery of the abdomen, is re-admitted to the hospital for causes related to abdominal adhesions [*Ellis 1999*]. Gynaecologic procedures carry a similar faith; more than one third of women is hospitalised for adhesive disease after gynaecologic surgery [*Lower 2000*]. The costs of surgery for abdominal adhesions exceeds one billion dollars annually in the USA [*Ray 1993, Ray 1998*] and therefore adhesive disease is a considerable societal burden [*Ivarsson 1997, Jeekel 1997, Wilson 1998*].

8.2 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 [*Al-Took 1999, Beck 1999, Cox 1993, Cross 1987, Ellis 1997, McEntee 1987, Nieuwenhuijzen 1998, Zbar 1993*]. Bowel obstruction due to adhesions can occur as early as within one month after surgery, but intervals up to 20 years have been reported [*Ellis 1997*]. The highest number of re-operations for intestinal obstruction occurs after colorectal surgery [*Barkan 1995*]. Bowel perforation or opening the bowel have been suggested to be associated with an increased risk of small bowel obstruction due to adhesions [*Zbar 1993*].

Management of small bowel obstruction caused by adhesions is controversial because surgery can induce new adhesions, whereas conservative treatment does not remove the cause of the obstruction [*Barkan 1995*]. Conservative treatment involves nasogastric intubation, intravenous fluid administration and clinical observation. Strangulation of bowel requires immediate surgery but intestinal ischemia can be difficult to determine clinically. Tachycardia, fever, focal tenderness, increased white blood cell counts and elevated lactate levels can indicate intestinal ischemia but are not very specific [*Landercasper 1993*]. When intestinal ischemia is unlikely, a conservative approach can be continued for 24 to 48 hours. *Meagher et al.* [*1993*] have suggested that surgery is unavoidable in patients with small bowel obstruction after previous appendectomy or surgery on the Fallopian tubes or ovaries.

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.* [*1995*] observed recurrences in 53% of patients after an initial episode of bowel obstruction irrespective of conservative or operative treatment. *Landercasper et al.* [*1993*] 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 [*Ellis 1997, Kaltiala 1972 Leffal 1970*].

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 [*Kieffer 1993*]. One third of the English surgeons occasionally use this method [*Scott-Coombes 1993*].

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 [*Scott-Coombes 1993*]. 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* [*2002*] 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% 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 [*Suter 2000*].

Laparoscopic adhesiolysis is associated with a considerable risk of bowel perforation [*Francois 1994, Freys 1994, Jansen 1997, Leon 1998, Lin 1999, Reich 1992*]. Bowel perforation can occur during the establishment of pneumoperitoneum or during adhesiolysis itself. Diathermic lesions of the bowel are of particular concern because perforation does not occur immediately. One third of complications in laparoscopic surgery was reported to occur during establishment of pneumoperitoneum [*Chapron 1999, Hashizume 1997*]. 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 [*Bonjer 1997, Hasson 1971*]. This technique is of great value in laparoscopic adhesiolysis because bowels adherent to the anterior abdominal wall prone to iatrogenic perforation are common 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 is four days in the majority of patients [*Chapron 1999*]. It is assumed delayed perforation of bowel occurs because of thermal lesions.

8.3 Adhesiolysis for chronic abdominal pain

Chronic abdominal pain is another sequela 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 [*Sulaiman 2001*]. In patients with continuous pain, other causes of abdominal pain such as gastritis, galbladder stones, diverticulosis, 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*. [*1992*] performed laparoscopy using local anaesthesia enabling the patient to indicate which adhesions were causing pain upon stretching.

The success rate of adhesiolysis varies from 38 to 87%, while failure occurs in 13 to 54 % (**Table 8.1**). 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. The randomized clinical trial of *Peters* [*1992*] showed that patients with light or moderate pain do not benefit from adhesiolysis. In case of severe adhesions involving the intestinal tract adhesiolysis may be beneficial.To prevent adhesions, Ringer's lactate was occasionally left behind in the abdomen [*Chan 1985, Mueller 1995, Nezhat 1996, Schietroma 2001, Steege 1991*]. The extent of adhesiolysis was not described clearly in the reviewed studies.

Table 8.1

Outcome of adhesiolysis in patients with chronic abdominal pain with no other cause than adhesions

	N	Cured/ Improved	Unchanged/ Worse	No response	Follow up [mo]	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

The extent of adhesions did not correlate to pre-operative symptoms [*Freys 1994, Rapkin 1986, Stout 1991*]. The site of chronic abdominal pain correlated well with the location of adhesions according to *Stout et al.*[*1991*] whereas *Rapkin et al*. [*1986*] did not find this correlation.

Pathophysiology of chronic abdominal pain is still poorly understood [*Punch 1993*] and psychosocial factors are supposed to play a role in chronic abdominal pain [*Howard 1996*].

The success rate of adhesiolysis decreases with time. [*Kolmorgen 1991, Lavonius 1999, Saravelos 1995, Steege 1991, Sutton 1990, Tschudi 1993, Wipfli-Funke 1995*]. The highest reported recurrence rate was 26% [*Saravelos 1995*]. The longest pain-free interval was 2 years [*Kolmorgen 1991*]. A longer duration of pre-operative symptoms predisposes for a lower success rate [*Mecke 1988*].

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 [*OLSG 1991*] and the severity of adhesions increases with time [*Ugur 1996*]. This offers an explanation for the recurrence of pain. The temporary relief of pain might also be explained by the placebo effect [*Beecher 1961*].

8.4 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% [*NAPSG 1995*].

If a second look laparoscopy is performed after adhesiolysis, there is debate about the interval between these operations. Some gynaecologists advocate an early second look after one week to prevent transformation of fibrinous attachments into permanent adhesions [*Barbot 1987, Daniell 1983, McLaughlin 1984, Surrey 1982, Swolin 1975, Trimbos-Kemper 1985*]. Others postpone second look laparoscopy for three to twelve months to assess whether pregnancy occurs leaving secondary surgery unnecessary [*Serour 1989*].

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 8.2**)

Table 8.2

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	?	Dexa-methasone, 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	?	Dexa-methasone promethazineDextran, Ringer's solution	1 week - 2 years	[60% improve-ment, 35% comparable, 5% worse]	Laparotomy	?
Serour et al 1989	22	Sharp/electro-surgery	Ringer's solution, Hydro-cortisone	9-12 months	12 (55%):	Laparoscopy	?
Surrey et al. 1982	31	Electrosurgery	Dextran, Heparine, Hydro-cortisone	6 weeks	22 (71%)	Laparotomy	16 (52%)
Trimbos-Kemper et al 1985	41	Electrosurgery via laparotomy	steroids, dextran	8 days	? (70%)	Laparotomy	20 (48%)

8.5 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 [*Francois 1994, Freys 1994, Holtz 1982*]. In experimental studies, laparoscopy caused less adhesions than laparotomy [*Filmar 1987, Gamal 2001, Jacobi 2001, Luciano 1992, Schafer 1998, Tittel 2001*]. *Lundorff et al*. [*1991*] also observed less adhesions after laparoscopic tubal surgery than after open surgery. *DeWilde* et al. [*1991*] 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 CO_2 laser surgery and electrosurgery did not differ at second look laparoscopy [*Luciano et al. [1992*] reported no differences in effectiveness between Nd:YAG laser, CO_2 laser and electrosurgery in an animal study, although it was concluded Nd:YAG laser was 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 [*Becker 1996, Lundorff 2001, Vrijland 2002b*]. Absorbable and non-absorbable mechanical barriers are considered effective in surgery for subfertility [*Farquhar 2000*]. Adjuvants like dexamethasone, Ringer's lactate and dextran never proved effective in a clinical study [*Farquhar 2000*].

8.6 Conclusion

The best treatment of adhesions is 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.

CHAPTER 9

DISCUSSION

9.1 Repair of hernias of the abdominal wall

Inguinal hernia repair is the most frequently performed operation in the Netherlands [*Health Care Information 1995*], while incisional hernia is one of the most common complications of open abdominal surgery. [*Bucknall 1982, Mudge 1985*]. Therefore, hernias of the abdominal wall are a major health care issue. Hence, innovations in the treatment of abdominal wall hernias which lower morbidity and recurrence rates have considerable economic impact.

Until recently, the standard method of the repair of hernias of the abdominal wall was closure of the defect with sutures. This type of hernia repair is referred to as conventional, tension, suture or non-mesh repair. Recurrence rates of such a repair vary between 0.2 and 33 % for inguinal hernias while Shouldice repair appears preferable [*Beets 1997, de Wilt 1990, Hay 1995, IJzermans 1991, Janu 1997, Kux 1994, Paul 1994, Simons 1996, Collaboration 2000a*]. The recurrence rate after incisional hernia repair varies between 24 and 54 % independent of the employed technique, although reports on smaller patient groups have recorded fewer recurrences [*Luijendijk 2000, Cassar 2002*]. Theoretically, non-mesh repair of hernias with approximation of the tissue edges by sutures causes excessive tension which is associated with tissue ischemia and cutting through of sutures. Both precede recurrence of a hernia of the abdominal wall.

The use of prosthetic mesh for closure of defects in the abdominal wall, first described by *Usher* [*1958*] changed hernia surgery completely. A tension-free repair became possible by covering the defect with a mesh instead of closing the defect under tension. The mesh is sutured to the fascial edges without approximating them. Consequently, the tension on the suture lines is reduced and therefore, recurrences are less likely. Polypropylene mesh was the first material used in hernia surgery, and is the most widely employed mesh until now [*Leber 1998, Molloy 1991*]. Recurrence rates decreased dramatically after the introduction of mesh in inguinal hernia repair, [*Lichtenstein 1986, McGillycuddy 1998, Friis 1996*] as confirmed by our own results in a randomized clinical trial described in chapter 2 of this thesis [*Vrijland 2000a*]. The same is true for incisional hernias [*Luijendijk 2000, Cassar 2002*], and for umbilical hernias [*Arroyo 2001*].

The inguinal hernia repair according to Shouldice was still under discussion. It was suggested that this method caused fewer recurrences than other non-mesh repairs and therefore might show comparable results to mesh repairs. Recently, *Nordin et al*. [*2002*] published a randomized trial of Lichtenstein versus Shouldice hernia repair in general surgical practice, showing that mesh inguinal hernia repair is superior to a Shouldice repair as well. Also, a mesh repair was easier to learn and required less time than a Shouldice repair.

Chapter 3 of this thesis is an editorial claiming that prosthetic mesh repair should be used for any defect in the abdominal wall. Although recurrences were reduced, possible adverse consequences of prosthetic material such as disintegration of the mesh, chronic infection, adhesion formation and enterocutaneous fistula formation need to be addressed.

9.2 The choice of prosthetic mesh for hernia repair

The choice of prosthetic mesh for inguinal hernia repair remains difficult. Ideally, a mesh is strong and pliable and shows good tissue ingrowth to secure long-term repair. A mesh should not provoke a strong foreign body reaction, it should be chemically inert, and it should be effective even in the presence of infection. Furthermore, the cost of the mesh should be low.

Three materials are commonly used in hernia repair: polypropylene, expanded polytetrafluoroethylene (ePTFE) and polyester. *Morris-Stiff* and *Hughes* [*1998*] could not confirm the superiority of one type of mesh over the other for hernia repair, but some aspects of mesh material determine the surgeon's choice [*Amid 1997*].

A polypropylene mesh is manufactured as a macroporous mesh. This macroporosity not only allows bacteria to invade the mesh, but also allows free access to macrophages to eliminate bacteria and facilitates migration of fibroblasts to ensure a strong ingrowth. In case of mesh infection, local drainage usually suffices and it is generally accepted that the mesh does not need to be removed, although discussion continues [*Korenkov 2002*]. The mesh is relatively pliable, but restriction of abdominal wall motility and paraesthesia of the abdominal wall were described. A new low-weight mesh with large pores made of polypropylene and polyglactin was suggested to preserve abdominal wall function [*Welty 2001*].
Shrinkage of the mesh has been described, and therefore an overlap with the fascia of 3 to 5 cm is advised [*Klinge 1998*]. Seroma formation occurs frequently, but has little clinical consequences [*Cassar 2002*]. Adhesion formation is an important disadvantage of polypropylene mesh, and is considerably more severe than in ePTFE mesh as shown in animal studies [*Morris-Stiff 1998*]. It has been suggested that polypropylene mesh provokes the development of enterocutaneous fistulas but evidence is contradictory. The cost of polypropylene mesh is low.

ePTFE is a microporous mesh with pores of less than 10 microns that may harbour bacteria but are too small to allow easy access to macrophages and fibroblasts. Proliferation of bacteria can therefore not be stopped by macrophages and this may result in an infection of the mesh. Ingrowth of tissue in ePTFE mesh is less than in polypropylene mesh, which might reduce the strength of the repair [*Simmermacher 1994*]. The ePTFE mesh is pliable and shrinkage has not been described. Seroma formation occurs frequently but without clinical consequences. Adhesion formation is considerably less if compared to polypropylene mesh. The cost of this mesh is about ten times higher than that of polypropylene mesh.

Polyester meshes have microporous components, which make them as susceptible to infections as ePTFE mesh. In addition, polyester meshes are often multifilamentous, which increases their susceptibility to infection [*Klinge 2002*]. Polyester meshes are very flexible and rarely cause seromas. Their incorporation in tissue and provocation of adhesion formation is comparable to that of polypropylene mesh. The recurrence rate is higher than that after polypropylene and ePTFE according to *Leber et al*. [*1998*], maybe due to early disintegration of the mesh. Shrinkage of polyester mesh has not been described. Polyester mesh is in the same price range as polypropylene mesh.

At our hospital, polypropylene mesh is the material of choice in hernia surgery. In inguinal hernia repair, mesh usually does not come into close contact with abdominal contents and therefore most of the disadvantages of a polypropylene mesh do not

play a role in the choice of mesh for inguinal hernia surgery. In incisional hernia repair, there is a risk of adhesion formation because close contact between abdominal contents and mesh can not always be prevented. This is particularly true for open repair of large defects of the abdominal wall but also for laparoscopic repair of an incisional hernia of any size. In laparoscopic repair of incisional hernia, which increases patient comfort and probably reduces wound infections, the mesh is placed intraabdominally and is then fixated to the anterior abdominal wall. Preperitoneal repair of incisional hernia is not yet feasible and therefore contact between mesh and abdominal contents is unavoidable.

However, since ePTFE is costly, appears associated with a higher rate of mesh infections, and limits immigration of fibroblasts and since the infection and recurrence rates of polyester seem of concern, many surgeons tend to use polypropylene mesh. However, polypropylene does not meet all the qualities of the ideal mesh. Especially adhesion formation is of great concern, as well as the formation of enterocutaneous fistulas.

9.3 Mesh, adhesions and enterocutaneous fistulas

Prevention of adhesions starts with reducing surgical trauma as stated in chapter 4. Leaving the peritoneum or hernial sac intact provides a natural barrier between the mesh and the abdominal contents. Unfortunately, leaving these structures intact in incisional hernia repair is often impossible because of the disturbed anatomy in the abdominal wall as a consequence of an incisional hernia. It has been advocated to close the peritoneum after mesh placement, but this provokes adhesion formation as well [*Ellis 1977, Duffy 1994*].

To prevent the formation of adhesions to a mesh, different preventive measures have been explored. One of them is placing a resorbable polyglactin 910 mesh between the polypropylene mesh and the abdominal contents. Theoretically, the abdominal contents adhere to the resorbable mesh and after resorption of the resorbable polyglactin mesh the adhesions disappear. We designed an experiment, described in chapter 5 to assess adhesion formation after lining a polypropylene mesh with polyglactin mesh. After sixty days, the polyglactin mesh had disappeared, but no decrease of adhesion formation was noted. However, *Dasika* and *Widman* [*1998*] described a significant decrease of adhesion formation in a comparable experiment. An explanation for the failure of polyglactin in reducing adhesion formation, might be the reticular structure of the polyglactin mesh [*Bellon 2002*]. *Bellon et al.* suggested that only a laminar mesh structure secures rapid mesothelialisation without defects and therefore leads to a reduction in adhesion formation.

As stated in chapter 6, enterocutaneous fistula formation was suggested to originate from dense adhesion formation. Fistula formation has never been examined in animal studies, and is a rare complication after incisional hernia repair as is shown in chapter 6. In 42 % of the incisional hernia repairs described, the mesh was placed intraperitoneally without the intestines being covered by peritoneum or omentum. Antibiotic prophylaxis is advocated to prevent mesh infection, but cannot prevent enterocutaneous fistula formation. The risk of enterocutaneous fistula formation in elective incisional hernia repair appears to be low. Although the pathogenesis of

enterocutaneous fistulas has not been elucidated, opening the bowel during the repair of the incisional hernia is considered a risk factor.

9.4 New means to prevent adhesions to mesh

In chapter 7, the effectiveness of reducing the formation of adhesions by placement of a resorbable mechanical barrier between the abdominal wall and the abdominal contents has been reported. Although the recorded effect of the Seprafilm membrane was less than in a previously described study [*Becker 1996*], a possible explanation of this difference is the inclusion of patients with fecal peritonitis, while infection was absent in the study described by *Becker et al*. Since intraabdominal infection lowers tissue–type plasminogen activator, which plays a role in fibrinolysis and therefore prevents adhesion formation, it is suggested that peritonitis is associated with increased adhesion formation [*Van Goor 1994*]. Seprafilm has been proven not to affect the fibrinolytic response in the abdominal cavity [*Reijnen 2002*], and hence it seems safe and advisable to use this membrane in the presence of peritonitis as well.

Preventing adhesion formation in the presence of mesh can theoretically be done with mechanical barriers like Seprafilm. Recently, some animal studies were published showing a beneficial effect on adhesion formation in the presence of mesh [*Hooker 1999, Dinsmore 1999, Baptista 2000, Dinsmore 2000, Kramer 2002*, *Van 't Riet* 2003]. A composite of Seprafilm and polypropylene mesh showed to be superior to a composite of polypropylene and ePTFE [*Greenawalt 2000*].

To demonstrate the value of Seprafilm or other mechanical barriers in the prevention of adhesion formation to prosthetic mesh in humans, a clinical study should be designed that allows two-stage surgery to evaluate the adhesion formation. It is generally considered unethical to do second stage surgery only for evaluation. Since there are no other means to assess the presence of adhesions and their clinical significance, it might prove impossible to assess the value of mechanical barriers in prevention of adhesions to mesh in patients. However, it seems advisable to apply such a barrier, especially if subsequent surgery can be expected.

In laparoscopic surgery, Seprafilm cannot be applied since it sticks together if it is moist, and therefore it is impossible to introduce it through a trocar. Alternatives for Seprafilm in laparoscopic surgery are Sepracoat (Genzyme), Intergel (Ethicon) and Adept (Shire) but only few have confirmed the efficacy of these agents [*Lundorff 2001, Ozmen 2002, Van den Tol 2001*]. Intergel proved to reduce adhesions in a clinical study [*Lundorff 2001*].

I SUMMARY

The repair of hernias of the abdominal wall has gradually changed during the past fifty years from closing the defect with sutures to covering the defect with prosthetic mesh. The aim of employing mesh was to reduce recurrence rates which have remained high after non-mesh techniques. The disadvantages of the use of mesh are not totally clear yet; chronic pain and inflammation caused by the presence of mesh, disintegration of the mesh causing long-term recurrences and serious complications like infection of mesh of mesh have been mentioned and used as arguments against the use of mesh in hernia repair. Since mesh repair has become more and more popular because of the impressive decrease in recurrence rate, attention arose for the adverse consequences of the employment of mesh and the development of strategies to prevent these adverse consequences. This thesis focuses on mesh repair of abdominal wall hernia, on intraabdominal adhesions and enterocutaneous fistula formation.

In **chapter 1** an overview of hernias of the ventral abdominal wall is described. The incidence, clinical implications and treatment options and their complications are described, based on the available literature regarding this subject. Recurrence rates of non-mesh repairs are high: Inguinal hernia recurrence varies from 0.2 to 33 %, and incisional hernia recurrence varies from 24 to 49 %.

In **chapter 2** a randomized clinical trial of non-mesh versus mesh repair of primary inguinal hernia is described. Not only clinical outcome was examined, but quality of life and cost were subject of investigation as well. From this trial it was concluded that mesh repair is superior to non-mesh repair with regard to hernia recurrence and that mesh repair is cost-effective. No differences were found regarding postoperative complications, pain and quality of life.

Chapter 3 is an editorial about the preferential method of hernia repair for abdominal wall hernias in general. The superiority of mesh repair over any technique of non-mesh repair for inguinal hernias is assessed. For incisional hernia, the evidence of superiority of mesh techniques is still limited, but one randomized clinical trial supports this view. The role of endoscopic hernia repair still remains to be assessed, yet no evidence exists that these minimally invasive techniques of inguinal and incisional hernia do have the theoretical advantages that have been suggested.

Adhesions are fibrous structures in the abdominal cavity that arise at injured peritoneal surfaces. Injury to the peritoneum may be caused by surgery, exposure to foreign materials and infection. **Chapter 4** is an introduction to adhesions. Intraperitoneal mesh placement appears a provoking factor for adhesion formation although often unavoidable in incisional hernia repair. Enterocutaneous fistulas may evolve from adhesions under certain circumstances and are among the most serious complications of mesh repair.

Polypropylene mesh is the most widely used mesh in hernia surgery. In **chapter 5**, adhesion formation in the presence of a polypropylene mesh is compared to adhesion formation of a polypropylene mesh covered with an absorbable polyglactin 910 mesh, in an animal study. A newly developed mesh with an inert surface was also tested. It appeared from this study that adding polyglactin absorbable mesh to polypropylene mesh to prevent the formation of adhesions is not an effective

measure. The newly developed mesh showed significantly better results, but was withdrawn for hernia surgery by the manufacturer.

Enterocutaneous fistulas are a feared complication after intraabdominal mesh placement because their morbidity is severe and surgical repair technically difficult. In **chapter 6**, a retrospective analysis of the outcome of incisional hernia repair with polypropylene mesh is described to assess the risk of enterocutaneous fistula formation, combined with an overview of literature concerning this topic. It is concluded that enterocutaneous fistula formation is very rare after incisional hernia repair with polypropylene mesh, regardless of intraperitoneal placement, omental coverage or closure of the peritoneum.

To prevent the formation of adhesions, it was suggested that a mechanical barrier could be used peroperatively to temporarily separate the intraabdominal viscera from the abdominal wall or prosthetic mesh. A membrane containing hyaluronic acid, Seprafilm, has been developed for this purpose. This material has already shown its effectiveness in experimental studies. To assess the value of this material in clinical circumstances, a randomized controlled multicenter study was performed which is described in **chapter 7**. This clinical trial included a second stage evaluation of adhesion formation in patients requiring a Hartmann procedure with second stage restoration of continuity. Based on this trial it was concluded that Seprafilm is effective in reducing the severity of postoperative adhesions.

Surgery is the only modality to confirm the presence of adhesions in the abdominal cavity and surgical lysis is the only therapy available. The reported results of adhesiolysis vary widely, and published studies cannot be compared because the indication for adhesiolysis and duration of follow up differ widely. In **chapter 8**, indication, method and success rate of adhesiolysis for intestinal obstruction, chronic abdominal pain and infertility are reviewed. It is concluded that prevention of adhesions is the most effective measure to prevent adhesion related disease. Adhesiolysis is a treatment option with varying results and serious complications. More research is needed to determine the ideal anti-adhesive agent.

Chapter 9 entails the general discussion of this thesis. It is stated that mesh repair is superior to non-mesh repair in uncomplicated abdominal wall hernias. The available meshes as well as the features of the ideal mesh are discussed. Mechanical barriers may prevent adhesion formation to mesh, although more research is necessary.

II CONCLUSIONS

- Mesh repair of primary inguinal hernia is superior to non-mesh repair with regard to hernia recurrence and shows comparable results as non-mesh repair regarding postoperative complications, pain and quality of life. (Chapter 2)

- Mesh repair of primary inguinal hernia is cost-effective. (Chapter 2)

- The value of endoscopic techniques for abdominal wall hernia repair appears beneficial but remains to be established. (Chapter 3)

- Polyglactin 910 absorbable mesh does not provide an adequate mechanical barrier between mesh and abdominal contents to prevent adhesions. (Chapter 5)

- Enterocutaneous fistula formation is a rare complication after incisional hernia repair, regardless of direct contact between mesh and bowel. (Chapter 6)

- Prophylactic antibiotics decrease recurrence rate of incisional hernia repair. (Chapter 6)

- Seprafilm is effective in reducing the severity of postoperative adhesions. (Chapter 7)

III SAMENVATTING

De techniek van het herstel van buikwandhernia's zoals lies- en littekenbreuken is in de afgelopen vijftig jaar aan verandering onderhevig geweest. Tot voor kort was de meest toegepaste techniek het primair sluiten van het defect van de breuk met hechtingen, een operatie waarop veel variaties beschreven zijn. De verandering van techniek is ingezet doordat kunststof materiaal beschikbaar kwam dat geschikt was voor implantatie in het lichaam. Met dit materiaal kan het defect van een breuk van de buikwand bedekt worden waarbij het niet nodig is de randen van het defect onder spanning naar elkaar toe te trekken. Dit wordt een spanningsvrije correctie genoemd. Het doel van het gebruik van een kunststofmat is het reduceren van recidieven (het opnieuw optreden van een buikwandbreuk), zoals die regelmatig voorkomen bij het primair sluiten van een defect. De nadelen van het gebruik van een kunststofmat zijn nog niet geheel duidelijk. Genoemd - en gebruikt als argumenten tegen het gebruik van een kunststofmat bij de correctie van buikwand-breuken - zijn: chronische pijn en ontsteking veroorzaakt door de aanwezigheid van de mat, desintegratie van de mat waardoor recidieven op lange termijn ontstaan, en ernstige complicaties zoals infectie van het weefsel rondom de mat. Omdat het gebruik van matten aan populariteit gewonnen heeft vanwege de reductie van recidieven, is er aandacht gekomen voor de negatieve gevolgen van het gebruik van een mat en voor mogelijkheden om deze gevolgen te voorkomen. Dit proefschrift richt zich op het herstel van buikwandhernia's met toepassing van kunststof materiaal en enkele daaraan gerelateerde complicaties zoals verklevingen in de buik oftewel intra-abdominale adhesies en verbindingen tussen darm- en buikhuid oftewel enterocutane fistels.

In **hoofdstuk 1** wordt een overzicht gegeven van hernia's van de voorste buikwand. Het vóórkomen, de klinische overwegingen en de behandelingsmethoden, alsmede de gerelateerde complicaties worden beschreven, gebaseerd op de literatuur die beschikbaar is over dit onderwerp. Recidief percentages van het primair sluiten van buikwanddefecten zijn hoog: liesbreuken vertonen recidiefpercentages tot 33% en littekenbreuken tot 49%.

In **hoofdstuk 2** wordt een gerandomiseerde klinische studie bij volwassenen beschreven die het primair sluiten van liesbreuken vergelijkt met het bedekken van het defect met een kunststofmat. Niet alleen de klinische resultaten werden bestudeerd, maar ook de kwaliteit van leven en de kosten werden vergeleken. Uit dit onderzoek is gebleken dat de correctie van liesbreuken met een mat duidelijk te verkiezen is boven het primair sluiten van een liesbreuk, en dat deze ingreep kosteneffectief is. Er werden geen verschillen gevonden tussen de twee bestudeerde groepen betreffende postoperatieve complicaties, postoperatieve pijn en kwaliteit van leven.

In **hoofdstuk 3** wordt ingegaan op de voorkeursmethode voor de correctie van buik-wandhernia's. Voor liesbreuken is er inmiddels uitvoerig bewijs dat correctie met kunststofmat betere resultaten geeft dan elke vorm van primaire correctie. Voor littekenbreuken zijn er aanwijzingen dat hetzelfde geldt, alhoewel dit op dit moment slechts door één gerandomiseerde klinische studie onderbouwd wordt. Een verondersteld voordeel van endoscopie (ofwel minimaal invasieve chirurgie via een kijkbuis) bij de correctie van buikwandhernia's is nog niet eenduidig bewezen. Wel

wordt er gesuggereerd dat endoscopie gepaard gaat met sneller herstel en minder pijn na een breukcorrectie en dat de kans op wondinfecties kleiner is.

Adhesies zijn bindweefselstrengen in de buikholte die ontstaan ter plaatse van beschadigd buikvlies dat organen of buikwand bedekt. Buikvlies of peritoneum kan worden beschadigd door chirurgisch ingrijpen, blootstelling aan lichaamsvreemde materialen en/of infectie. **Hoofdstuk 4** is een inleiding op het onderwerp adhesies en beschrijft dat het in de buikholte plaatsen van een kunststofmat het ontstaan van adhesies bevordert. Het in de buikholte plaatsen van een mat is meestal niet te vermijden bij de correctie van een littekenbreuk. Onder bepaalde omstandigheden kan zich vanuit een adhesie een enterocutane fistel ontwikkelen, wat een zeer ernstige complicatie van correctie van buikwandbreuken met een mat is.

Bij hernia-chirurgie wordt er het meest frequent gebruik gemaakt van een onoplosbare kunststof mat van polypropeen. In **hoofdstuk 5** wordt de vorming van adhesies bij toepassing van een enkelvoudige polypropeenmat vergeleken met die bij toepassing van een samengestelde mat. In dat laatste geval is op de polypropeenmat een oplosbare polyglactine mat aangebracht. Dit is een strategie die regelmatig wordt toegepast om adhesies te voorkomen bij het plaatsen van een polypropeenmat in de vrije buikholte. De hieraan ten grondslag liggende gedachte is dat de verklevingen zullen ontstaan aan de oplosbare mat, en dat de adhesies los zijn van het polypropyleen oppervlak als deze mat vervolgens oplost. Uit een in dit proefschrift beschreven dierstudie is gebleken dat het afdekken van een polypropeenmat met een oplosbare mat geen effect heeft op de vorming van adhesies en dus niet nuttig is. In ditzelfde onderzoek werd ook nog een nieuw ontwikkelde mat bestudeerd. Deze liet minder adhesievorming zien.

Een enterocutane fistel is een gevreesde complicatie die op kan treden na het in de buik plaatsen van een kunststofmat. Zo'n fistel is een verbinding tussen een darm en de buikhuid waarbij voortdurend maagdarminhoud via een opening in de buikhuid kan aflopen. Dit kan een zeer invaliderende situatie opleveren, waarvoor bij een aantal patiënten een ingrijpende operatie noodzakelijk is waarbij de mat uit de buikwand verwijderd moet worden. In **hoofdstuk 6** wordt een retrospectieve analyse beschreven waarin de lange termijn resultaten van litteken-breukcorrectie met mat beschreven worden om het risico van het ontstaan van een enterocutane fistel te bepalen. Tevens wordt een overzicht van de beschikbare literatuur op dit terrein gegeven. Uit dit onderzoek blijkt dat enterocutane fistelvorming na littekenbreukcorrectie met een kunststofmat zeer zeldzaam is, en onafhankelijk van plaatsing in de buik, bedekking met omentum of sluiten van het peritoneum.

Om het ontstaan van adhesies te voorkomen, kan in theorie een mechanische barrière gebruikt worden om de buikorganen tijdelijk af te schermen van de buikwand of van een mat die in de buikholte geplaatst is. Voor dit doel is een membraan ontwikkeld met de naam Seprafilm, dat binnen 3 weken oplost. Het bevat alleen materialen die natuurlijk in het lichaam voorkomen. Dit materiaal heeft in dierstudies reeds bewezen het ontstaan van adhesies te verminderen. Om het nut van dit membraan in de klinische situatie te testen werd een gerandomiseerde studie uitgevoerd als beschreven in **hoofdstuk 7**. In deze klinische studie wordt het evalueren van adhesievorming na het gebruik van Seprafilm mogelijk gemaakt door patiënten deel te laten nemen die een operatie in twee fasen moesten ondergaan. Patiënten die een Hartmann procedure moesten ondergaan konden deelnemen. Bij een Hartmann procedure wordt een stoma van de dikke darm aangelegd dat in

latere instantie weer opgeheven kan worden. Bij de eerste operatie werd geloot voor het al dan niet gebruiken van Seprafilm aan het eind van de operatie. Tijdens de tweede operatie kon het effect van Seprafilm geëvalueerd worden. Uit dit onderzoek is gebleken dat Seprafilm de ernst van postoperatieve adhesies doet afnemen.

Adhesies ofwel verklevingen tussen organen in de buik kunnen verantwoordelijk zijn voor verschillende ziektebeelden. Verklevingen kunnen afsnoering van darmen veroorzaken waardoor een ileus ontstaat. Verklevingen kunnen soms een verklaring vormen voor chronische buikpijn of voor onvruchtbaarheid. Er is geen niet-invasieve diagnostische methode beschikbaar om vast te stellen of het inderdaad verklevingen zijn die de klachten veroorzaken. Chirurgie, bij voorkeur met een kijkoperatie, is de enige manier om het bestaan van adhesies vast te stellen en de enige manier om verklevingen in de buik te behandelen. Adhesiolyse is het losmaken van verklevingen. De beschreven resultaten van deze operatie in de wetenschappelijke literatuur zijn zeer verschillend. In **hoofdstuk 8** worden de indicatie, de methode en het succes van adhesiolyse voor de verschillende ziektebeelden beschreven. Geconcludeerd wordt dat preventie van het ontstaan van adhesies een grote rol moet spelen, onder meer door het ontwikkelen en onderzoeken van middelen die verklevingen kunnen voorkomen. Tevens wordt duidelijk dat de resultaten van adhesiolyse niet altijd bevredigend zijn en dat de ingreep wel zeer ernstige complicaties tot gevolg kan hebben.

Hoofdstuk 9 bevat de algemene discussie van deze dissertatie. Er wordt gesteld dat het herstellen van ongecompliceerde buikwandbreuken met een kunststofmat beter is dan zonder mat. De beschikbare kunststofmatten en de aspecten van een ideale mat worden besproken. Het gebruik van een mechanische barrière om het ontstaan van verklevingen aan de mat te voorkomen is een veelbelovende techniek, maar op dit gebied zal meer onderzoek gedaan moeten worden.

IV LIST OF PUBLICATIONS

Vrijland WW, van den Tol MP, Luijendijk RW, Hop WCJ, Busschbach JJV, De Lange DCD, van Geldere D, Rottier AB, Vegt PA, IJzermans JNM, Jeekel J
Randomized clinical trial of non-mesh versus mesh repair of primary inguinal hernia
Br J Surg 2002;89:293-7

Vrijland WW, Jeekel J
Prosthetic mesh should be used for any defect in the abdominal wall
Current Medical Research and Opinion: accepted for publication

Vrijland WW, Bonthuis F, Steyerberg EW, Marquet RL, Jeekel J, Bonjer HJ
Peritoneal adhesions to prosthetic materials: choice of mesh for incisional hernia repair
Surg Endosc 2000;14:960-3

Vrijland WW, Jeekel J, Steyerberg EW, den Hoed PT, Bonjer HJ
Intraperitoneal polypropylene mesh repair of incisional hernia is not associated with enterocutaneous fistula
Br J Surg 2000;87:348-52

Vrijland WW, Tseng LNL, Eijkman HJM, Hop WCJ, Jakimowicz JJ, Leguit P, Stassen LPS, Swank DJ, Haverlag R, Bonjer HJ, Jeekel J
Fewer intraperitoneal adhesions with use of hyaluronic acid-carboxymethylcellulose. A randomized clinical trial
Ann Surg 2002;235:193-9

Vrijland WW, Jeekel J, Swank DJ, van Geldorp HJ, Bonjer HJ
Postoperative abdominal adhesions: the role of adhesiolysis
Surgical Endoscopy: accepted for publication

V REFERENCES

Abrahamson J. Hernias. [edited by] Zinner MJ. Maingot's Abdominal Operations, 10th ed. Appleton & Lange, Stamford, Connecticut, USA. 1997;14:479-580

Al-Took S, Platt R, Tulandi T. Adhesion-related small-bowel obstruction after gynecologic operations. Am J Obstet Gynecol 1999;180:313-5

Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia 1997;1:15-21

Anonymous. Repair of groin hernia with synthetic mesh. Meta-analysis of randomized controlled trials. Ann Surg 2002;235:322-32

Arregui ME. Laparoscopic preperitoneal herniorraphy. Paper presented at: Annual Meeting of the Society of American Endoscopic Surgeons; April 18-20, 1991; Montery CA

Arroyo A, Garcia P, Perez F, Andreu J, Candela F, Calpena R. Randomized clinical trial comparing suture and mesh repair of umbilical hernia in adults. Br J Surg 2001;88:1321-3

Askar OM. A new concept of the aetiology and surgical repair of paraumbilical and epigastric hernias. Ann R Coll Surg Engl 1978;60:42

Bailey IS, Karran SE, Tyn K, Brough P, Ranaboldo C, Karran SJ. Community surveillance of complications after hernia surgery. BMJ 1992;304:739

Bakkum EA, Van Blitterswijk CA, Dalmeijer RA, Trimbos JB. A semiquantitative rat model for intraperitoneal postoperative adhesion formation. Gynecol Obstet Invest 1994;37:99-105

Baptista ML, Bonsack ME, Delaney JP. Seprafilm reduces adhesions to polypropylene mesh. Surgery 2000;128:86-92

Barbot J, Parent B, Dubuisson JB, Aubriot FX. A clinical study of the CO2 laser and electrosurgery for adhesiolysis in 172 cases followed by early second-look laparoscopy. Fertil Steril 1987;48:140-2

Barkan H, Webster S, Ozeran S. Factors predicting the recurrence of adhesive small-bowel obstruction. Am J Surg 1995;70:361-5

Barth RJ Jr, Burchard KW, Tosteson A, Sutton JE Jr, Colacchio TA, Henriques HF, Howard R, Steadman S. Short-term outcome after mesh or Shouldice herniorraphy: a randomized prospective study. Surgery 1998;123:121-6

Bassini E. Nuovo metodo per la cura radicale dell'ernia inguinale. Atti Congr Associ Med Ital 1887;2:179

Beck DE, Opelka FG, Bailey HR, Rauh SM, Pashos CL. Incidence of small-bowel obstruction and adhesiolysis after open colorectal and general surgery. Dis Colon Rectum 1999;42:241-8

Becker JM, Dayton MT, Fazio VW, Beck DE, Stryker SJ, Wexner SD, Wolff BG, Roberts PL, Smith LE, Sweeney SA, Moore M. Prevention of postoperative adhesions by a sodium hyaluronate-based bioresorbable membrane: a prospective, randomized, double-blind multicenter study. J Am Coll Surg 1996;183:297-306

Beecher HK. Surgery as placebo. J Am Med Assoc 1961;176:1102-7

Beets GL, Oosterhuis KJ, Go PM, Baeten CG, Kootstra G. Longterm followup (12-15 years) of a randomised controlled trial comparing Bassini-Stetten, Shouldice, and high ligation with narrowing of the internal ring for primary inguinal hernia repair. J Am Coll Surg 1997;185:352-7

Bellon JM, Contreras LA, Bujan J, Palomares D, Carrera-San Martin A. Tissue response to polypropylene meshes used in the repair of abdominal wall defects. Biomaterials 1998;19:669-75

Bellon JM, Jurado F, Garcia-Honduvilla N, Lopez R, Carrera-San Martin A, Bujan J. The structure of a biomaterial rather than its chemical composition modulates the repair process at the peritoneal level. Am J Surg 2002;184:154-9

Bonjer HJ, Hazebroek EJ, Kazemier G, Giuffrida MC, Meijer WS, Lange JF. Open versus closed establishment of pneumoperitoneum in laparoscopic surgery. Br J Surg 1997;84:599-602

Brooks R, with the EuroQol Group. EuroQol: the current state of play. Health Policy 1996;37:53-72

Bucknall TE, Cox PJ, Ellis H. Burst abdomen and incisional hernia: a prospective study of 1129 major laparotomies. Br Med J 1982;284:931-3

Burns JW, Skinner K, Colt J, Sheidlin A, Bronson R Yaacobi Y, Goldberg EP. Prevention of tissue injury and postsurgical adhesions by precoating tissues with hyaluronic acid solutions. J Surg Res 1995;59:644-52

Callesen T, Bech K, Kehlet H. Prospective study of chronic pain after groin hernia repair. Br J Surg 1999;86:1528-31

Carbajo MA, Martin del Olmo JC, Blanco JI, de la Cuesta C, Toledano M, Martin F, Vaquero C. Laparoscopic treatment vs open surgery in the solution of major incisional and abdominal wall hernias with mesh. Surg Endosc 1999;13:250-2

Cassar K, Munro A. Surgical treatment of incisional hernia. Br J Surg 2002;89:534-45

Casten DF. Functional anatomy of the groin area as related to the classification and treatment of groin hernias. Am J Surg 1967;114:894-9

Chan CL, Wood C. Pelvic adhesiolysis - the assessment of symptom relief by 100 patients. Aust N Z J Obstet Gynaecol 1985;25:295-8

Chapron C, Pierre F, Harchaoui Y, Lacroix S, Beguin S, Querleu D, Lansac J, Dubuisson JB. Gastrointestinal injuries during gynaecological laparoscopy. Hum Reprod 1999;14:333-7

Collaboration EH. Laparoscopic compared with open methods of groin hernia repair: systematic review of randomized controlled trials. Br J Surg 2000(b);87:860-7

Collaboration EH. Mesh compared with non-mesh methods of open groin hernia repair: systematic review of randomized controlled trials. Br J Surg 2000(a);87:854-9

Cox MR, Gunn IF, Eastman MC, Hunt RF, Heinz AW. The operative aetiology and types of adhesions causing small bowel obstruction. Aust N Z J Surg 1993;63:848-52

Cross KS, Johnston JG. Small bowel obstruction: a review of 456 cases in a west of Ireland region. J R Soc Med 1987;80:149-50

Cunningham J, Temple WJ, Mitchell P, Nixon JA, Preshaw RM, Hagen NA. Cooperative hernia study. Pain in the postrepair patient. Ann Surg 1996;224:598-602

Daniell JF, Pittaway DE. Short-interval second-look laparoscopy after infertility surgery. A preliminary report. J Reprod Med 1983;28:281-3

Dasika UK, Widman WD. Does lining polypropylene with polyglactin mesh reduce intraperitoneal adhesions? Am Surg 1998;64:817-9

De Wilt JHW, IJzermans JNM, Hop WCJ, Jeekel J. De behandeling van recidief van hernia inguinalis. Ned Tijdschr Geneeskd 1990;134:531-4

DeCherney AH, Mezer HC. The nature of posttuboplasty pelvic adhesions as determined by early and late laparoscopy. Fertil Steril 1984;41:643-6

DeWilde RL. Goodbye to late bowel obstruction after appendectomy. Lancet 1991;338:1012

Diamond MP, Daniell JF, Martin DC, Feste J, Vaughn WK, McLaughlin DS. Tubal patency and pelvic adhesions at early second-look laparoscopy following intraabdominal use of the carbon dioxide laser: initial report of the intraabdominal laser study group. Fertil Steril 1984;42:717-23

DiBello JN Jr, Moore JH Jr. Sliding myofascial flap of the rectus abdominus muscles for the closure of recurrent ventral hernias. Plast Reconstr Surg 1996;98:464-9

Dinsmore RC, Calton WC Jr, Harvey SB, Blaney MW. Prevention of adhesions to polypropylene mesh in a traumatized bowel model. J Am Coll Surg 2000;191:131-6

Dinsmore RC, Calton WC Jr. Prevention of adhesions to polypropylene in a rabbit model. Am Surg 1999;65:383-7

DiZerega GS. Peritoneal Surgery, New York: Springer-Verlag 2000

Duffy DM, di Zerega GS. Is peritoneal closure necessary? Obstet Gynecol Surv 1994;49:817-22

Ellis H, Harrison W, Hugh TB. The healing of peritoneum under normal and pathological conditions. Br J Surg 1965;52:471-6

Ellis H, Heddle R. Does the peritoneum need to be closed at laparotomy? Br J Surg 1977;64:733-6

Ellis H, Moran BJ, Thompson JN, Parker MC, Wilson MS, Menzies D, Mc Guire A, Lower AM, Hawthorn RJ, O'Brien F, Buchan S, Crowe AM. Adhesion-related hospital readmissions after abdominal and pelvic surgery: a retrospective cohort study. Lancet 1999;353;1476-80

Ellis H. The clinical significance of adhesions: focus on intestinal obstruction. Eur J Surg Suppl 1997;577:5-9

Farquhar C, Vandekerckhove P, Watson A, Vail A, Wiseman D. Barrier agents for preventing adhesions after surgery for subfertility. Cochrane Database Syst Rev 2000;2:CD000475

Filmar S, Gomel V, McComb PF. Operative laparoscopy versus open abdominal surgery: comparative study on postoperative adhesion formation in the rat model. Fertil Steril 1987;48:486-9

Fischer CP, Doherty D. Laparoscopic approach to small bowel obstruction. Seminars in laparoscopic surgery 2002;1:40-5

Fitzgibbons RJ and Gerson A. Lippincott Williams and Wilkins 2002, Philadelphia PA

Francois Y, Mouret P, Tomaoglu K, Vignal J. Postoperative adhesive peritoneal disease. Laparoscopic treatment. Surg Endosc 1994;8:781-3

Freys SM, Fuchs KH, Heimbucher J, Thiede A. Laparoscopic adhesiolysis. Surg Endosc 1994;1202-7

Friis E, Lindahl F. The tension-free hernioplasty in a randomised trial. Am J Surg 1996;172:315-9

Gamal EM, Metzger P, Szabo G, Brath E, Peto K, Olah A, Kiss J, Furka I, Miko I. The influence of intraoperative complications on adhesion formation during laparoscopic and conventional cholecystectomy in an animal model. Surg Endosc 2001;15:873-7

Gecim IE, Kocak S, Ersoz S, Bumin C, Aribal D. Recurrence after incisional hernia repair: results and risk factors. Surg Today 1996;26:607-9

George CD, Ellis H. The results of incisional hernia repair: a twelve year review. Ann R Coll Surg Engl 1986;68:185-7

Gilbert AI, Felton LL. Infection in inguinal hernia repair considering biomaterials and antibiotics. Surg Gynecol Obstet 1993;177:126-30

Gilbert AI. Overnight hernia repair: updated considerations. South Med J 1987;80:191-5

Girotto JA, Ko MJ, Redett R Muehlberger T, Talamini M, Chang B. Closure of chronic abdominal wall defects: a long-term evaluation of the components separation method. Ann Plast Surg 1999;42:385-94

Goldstein DP, deCholnoky C, Emans SJ, Leventhal JM. Laparoscopy in the diagnosis and management of pelvic pain in adolescents. J Reprod Med 1980:251-6

Greenawalt KE, Butler TJ, Rowe EA, Finneral AC, Garlick DS, Burns JW. Evaluation of sepramesh biosurgical composite in a rabbit hernia repair model. J Surg Res 94:92-8

Halasz NA. Dehiscence of laparotomy wounds. Am J Surg 1968;116:210-4

Hallfeldt KK, Kantelhardt T, Waldner H, Schweiberer L. [Laparoscopic adhesiolysis in therapy of chronic abdominal pain]. Zentralbl Chir 1995;120:387-91

Halverson K, Mc Vay B. Inguinal and femoral hernioplasty: a 22 year study of the author's methods. Arch Surg 1970;101:127-35

Hashizume M, Sugimachi K. Needle and trocar injury during laparoscopic surgery in Japan. Surg Endosc 1997;11:1198-1201

Hasson HM. A modified instrument and method for laparoscopy. Am J Obstet Gynecol 1971;110:886-887

Hay JM, Boudet MJ, Fingerhut A, Poucher J, Hennet H, Habib E, Veyrieres M, Flamant Y. Shouldice inguinal hernia repair in the male adult: the gold standard? A multicenter controlled trial in 1578 patients. Ann Surg 1995;222:719-727

Health Care Information (SIG). Trends in Surgery 1984 – 1993. Apeldoorn, SIG Zorginformatie, 1995

Hesselink VJ, Luijendijk RW, de Wilt JH, Heide R, Jeekel J. An evaluation of risk factors in incisional hernia recurrence. Surg Gynecol Obstet 1993;176:228-34

Holmdahl L. The role of fibrinolysis in adhesion formation. Eur J Surg Suppl 1997;577:24-31

Holmes J, Readman R. A study of wound infections following inguinal hernia repair. J Hosp Infect 1994;28:153-6

Holtz G, Kling OR. Effect of surgical technique on peritoneal adhesion reformation after lysis. Fertil Steril 1982;37:494-6

Hooker GD, Taylor BM, Driman DK. Prevention of adhesion formation with use of sodium hyaluronate based bioresorbable membrane in a rat model of ventral hernia repair with polypropylene mesh—a randomized controlled study. Surgery 1999;125:211-6

Houck JP, Rypins EB, Sarfeh IJ, Juler GL, Shimoda KJ. Repair of incisional hernia. Surg Gynecol Obstet 1989;169:397-9

Howard FM. Laparoscopic evaluation of women with chronic pelvic pain. J Am Assoc Gynecol Laparosc 1994;1:325-31

Howard FM. The role of laparoscopy in the evaluation of chronic pelvic pain: pitfalls with a negative laparoscopy. J Am Assoc Gynecol Laparosc 1996;4:85-94

Hubbard TB, Khan MZ, Carag VR, Albites VE, Hricko GM. The pathology of peritoneal repair: its relation to the formation of adhesions. Ann Surg 1967;165:908-16

Hugh TB, Nankivell C, Meagher AP, Li B. Is closure of the peritoneal layer necessary in the repair of midline surgical abdominal wounds? World J Surg 1990;14:231-3

IJzermans JNM, de Wilt JHW, Hop WCJ, Jeekel J. Recurrent inguinal hernia treated by classical hernioplasty. Arch Surg 1991;126:1097-100

Interceed (TC7) Adhesion Barrier Study Group. Prevention of postsurgical adhesions by Interceed (TC7), an absorbable adhesion barrier: a prospective, randomized multicenter clinical study. Fertil Steril 1989;51:933-938

Irion O, Luzuy F, Beguin F. Nonclosure of the visceral and parietal peritoneum at casarean section: a randomised controlled trial. Br J Obstet Gynaecol 1996;103:690-4

Israelsson LA, Jonsson T. Suture length to wound length ratio and healing of midline laparotomy incisions. Br J Surg 1993;80:1284-6

Ivarsson ML, Holmdahl L, Franzen G, Risberg B. Cost of bowel obstruction resulting from adhesions. Eur J Surg 1997;163:679-84

Jackson OJ, Moglen LH. Umbilical hernia: a retrospective study. Calif Med 1970;113-8

Jacobi CA, Sterzel A, Braumann C, Halle E, Stosslein R, Krahenbuhl L, Muller JM. The impact of conventional and laparoscopic colon resection (CO2 or helium) on intraperitoneal adhesion formation in a rat peritonitis model. Surg Endosc 2001;15:380-6

Jansen FW, Kapiteyn K, Trimbos-Kemper T, Hermans J, Trimbos JB. Complications of laparoscopy: a prospective multicentre observational study. Br J Obstet Gynaecol 1997;104:595-600

Janu PG, Sellers KD, Mangiante EC. Mesh inguinal herniorrhaphy: a ten-year review. Am Surg 1997;63:1065-9

Jeekel H. Cost implications of adhesions as highlighted in a European study. Eur J Surg Suppl 1997;579:43-45

Jenkins SD, Klamer TW, Parteka JJ, Condon RE. A comparison of prosthetic materials used to repair abdominal wall defects. Surgery 1983;94:392-398

Jung D, Mendel V, Heymann H. [Therapeutic possibilities in adhesions]. Zentralbl Chir 1986;111:1482-8

Kaltiala EH, Lenkkeri H, Larmi JK. Mechanical intestinal obstruction. An analysis of 577 cases. Ann Chir Gynaecol 1972;61:87-90

Karran SJ, Karran SE, Toyn K, Brough P. Antibiotic prophylaxis in clean surgical cases and the role of community surveillance. Eur J Surg Suppl 1992;567:31-2

Kaufman Z, Engelberg M, Zager M. Fecal fistula: a late complication of Marlex mesh repair. Dis Colon Rectum 1981;24:543-4

Kelso K, Blackett B. Bacterial adherence to Prolene (Ethicon), Fluorosoft and Fluoromesh (Sulzer Vascutek); A product comparison data on file at Sulzer Vascutek. 1997

Kieffer RW, Neshat AA, Perez LM, Boudet RA, Seel DJ. Indications for internal stenting in intestinal obstruction. Mil Med 1993;158:478-9

Kind P, Hardman G, Macran S. UK population norms for the EQ-5D. University of New York, Centre for Health Economics, Discussion paper 172, November 1999

Klinge U, Junge K, Spellerberg B, Piroth C, Klosterhalfen B, Schumpelick V. Do multifilament alloplastic meshes increase the infection rate? Analysis of the polymeric surface, the bacteria adherence, and the in vivo consequences in a rat model. J Biomed Mater Res 2002;63:765-71

Klinge U, Klosterhalfen B, Muller M, Ottinger AP, Schumpelick V. Shrinking of polypropylene mesh in vivo: an experimental study in dogs. Eur J Surg 1998;164:965-9

Klingensmith ME, Soybel DI, Brooks DC. Laparoscopy for chronic abdominal pain. Surg Endosc 1997;10:1085-7

Klosterhalfen B, Junge K, Hermanns B, Klinge U. Influence of implantation interval on the long-term biocompatibility of surgical mesh. Br J Surg 2002;89:1043-8

Knook MT, Stassen LP,Bonjer HJ. Impact of randomized trials on the application of endoscopic techniques for inguinal hernia repair in the Netherlands. Surg Endosc 2001;15:55-8

Kolmorgen K, Schulz AM. [Results of laparoscopic lysis of adhesions in patients with chronic pelvic pain]. Zentralbl Gynakol 1991;113:291-5

Korenkov M, Sauerland S, Arndt M, Bograd L, Neugebauer EAM, Troidl H. Randomized clinical trial of suture repair, polypropylene mesh or autodermal herniplasty for incisional hernia. Br J Surg 2002;89:50-6

Kramer K, Senninger N, Herbst H, Probst W. Effective prevention of adhesions with hyaluronate. Arch Surg 2002;137:278-82

Kresch AJ, Seifer DB, Sachs LB, Barrese I. Laparoscopy in 100 women with chronic pelvic pain. Obstet Gynecol 1984;64:672-4

Kulah B, Kulacoglu, Oruc MT, Duzgun AP, Moran M, Ozmen MM, Coskun F. Presentation and outcome of incarcerated external hernias in adults. Am J Surg 2001;181:101-4

Kux M, Fuchsjager N, Schemper M, Shouldice is superior to Bassini inguinal herniorrhaphy. Am J Surg 1994;168:15-8

Ladurner R Trupka A, Schmidbauer S, Hallfeldt K. The use of an underlay polypropylene mesh in complicated incisional hernias: successful French surgical technique. Minerva Chir 2001;56:111-17

Landercasper J, Cogbill TH, Merry WH, Stolee RT, Strutt PJ. Long-term outcome after hospitalization for small-bowel obstruction. Arch Surg 1993;128:765-70

Lang B, Lau H, Lee F. Epigastric hernia and its etiology. Hernia 2002;6:148-50

Langer S, Christiansen J. Long-term results after incisional hernia repair. Acta Chir cand 1985;151:217-9

Larson GM, Harrower HW. Plastic mesh repair of incisional hernias. Am J Surg 1978;135:559-63

Lavonius M, Gullichsen R, Laine S, Ovaska J. Laparoscopy for chronic abdominal pain. Surg Laparosc Endosc 1999;9:42-4

Leber GE, Garb JL, Alexander AI, Reed WP. Long-term complications associated with prosthetic repairs of incisional hernias. Arch Surg 1998;133:378-82

LeBlanc KA, Booth WV. Laparoscopic repair of incisional abdominal hernias using expanded polytetrafluoroethylene: preliminary findings. Surg Laparosc & Endosc 1993;3:39-41

Leffal SB. Clinical aids in strangulated intestinal obstruction. Am J Surg 1970;120:756-8

Lehmann-Willenbrock E, Mecke H, Riedel HH. Sequelae of appendicectomy, with special reference to intra-abdominal adhesions, chronic abdominal pain, and infertility. Gynecol Obstet Invest 1990;29:241-5

Leidig P, Krakamp B. [Laparoscopic lysis of adhesions - a simple method of diagnosis and therapy of abdominal pain caused by adhesions]. Leber Magen Darm 1992;22:27-8

Leon EL, Metzger A, Tsiotos GG, Schlinkert RT, Sarr MG. Laparoscopic management of small bowel obstruction: indications and outcome. J Gastrointest Surg 1998;2:132-40

Liakakos T, Karanikas I, Panagiotidis H, Dendrinos S. Use of Marlex mesh in the repair of recurrent incisional hernia. Br J Surg 1994;81:248-49

Lichtenstein IL, Shulman AG, Amid PK. The tension-free hernioplasty. Am J Surg 1989;157:188-93

Lichtenstein IL, Shulman AG, Amid, PK. The cause, prevention, and treatment of recurrent groin hernia. Surg Clin North Am 1993;73:529-44

Lichtenstein IL, Shulman AG. Ambulatory (outpatient) hernia surgery including a new concept: introducing tension-free repair. Int Surg 1986;71:1-4

Liem MS, Van der Graaf Y, Van Steensel CJ, Boelhouwer RU, Clevers GJ, Meijer WS, Stassen LP, Vente JP, Weidema WF, Schrijvers AJ, Van Vroonhoven TJ. Comparison of conventional anterior surgery and laparoscopic surgery for inguinal hernia repair. N Engl J Med 1997a;336:1541-7

Liem MSL, Halsema JAM, Van der Graaf Y, Schrijvers AJP, Van Vroonhoven ThJMV. Cost-effectiveness of extraperitoneal laparoscopic inguinal hernia repair: a randomised comparison with conventional herniorraphy. Ann Surg 1997b;226:668-75

Lin P, Grow DR. Complications of laparoscopy. Strategies for prevention and cure. Obstet Gynecol Clin North Am 1999; 26:23-38

Losanoff JE, Richman BW, Jones JW. Entero-colocutaneous fistula: a late consequence of polypropylene mesh abdominal wall repair: case report and review of the literature. Hernia 2002;6:144-7

Lotheissen G. Zur radikol operation der Schenkelhernien. Zentralbl Chir 1898;23:548

Lower AM, Hawthorn RJS, Ellis H, O'Brien F, Buchan S, Crowe AM. The impact of adhesions on hospital readmissions over ten years after 8849 open gynaecological operations: an assessment from the Surgical and Clinical Adhesions Research Study. Br J Obstet Gynaecol 2000;107:855-62

Luciano AA, Frishman GN, Maier DB. A comparative analysis of adhesion reduction, tissue effects, and incising characteristics of electrosurgery, CO_2 laser, and Nd:YAG laser at operative laparoscopy: an animal study. J Laparoendosc Surg 1992;2:287-92

Luijendijk RW, de Lange DC, Wauters CC, Hop WC, Duron JJ, Pailler JL, Camprodon BR, Holmdahl L, van Geldorp HJ, Jeekel J. Foreign material in postoperative adhesions. Ann Surg 1996;223:242-8

Luijendijk RW, Hop WC, Van den Tol MP, De Lange DC, Braaksma MM, IJzermans JN, Boelhouwer RU, De Vries BC, Salu MK, Wereldsma JC, Bruijninckx CM, Jeekel J. A comparison of suture repair with mesh repair for incisional hernia. N Engl J Med 2000;343:392-8

Luijendijk RW, Lemmen MH, Hop WC, Wereldsma JC. Incisional hernia recurrence following 'vest-over-pants' or vertical Mayo repair of primary hernias of the midline. World J Surg 1997;21:62-6

Lundorff P, Hahlin M, Kallfelt B, Thorburn J, Lindblom B. Adhesion formation after laparoscopic surgery in tubal pregnancy: a randomized trial versus laparotomy. Fertil Steril 1991;55:911-5

Lundorff P, van Geldorp H, Tronstadt SE, Lalos O, Larsson B, Johns DB, diZerega GS. Reduction of post-surgical adhesions with ferric hyaluronate gel: a European study Human Reproduction 2001;16:1982-8

Manninen MJ, Lavonius M, Perhoniemi. VJ Results of incisional hernia repair; a retrospective study of 172 unselected hernioplasties. Eur J Surg 1991;157:29-31

Marana R, Rizzi M, Muzii L, Catalano GF, Caruna P, Mancuso S. Correlation between the American Fertility Society Classification of adnexal adhesions and distal tubal occlusion, salpingoscopy, and reproductive outcome in tubal surgery. Fertil Steril 1995;65:924-9

Martin-Duce A, Noguerales F, Villeta R, Hernandez P, Lozano O, Keller J, Granell J. Modifications to Rives technique for midline incisional hernia repair. Hernia 2001;5:70-2

Matapurkar BG, Gupta AK, Agarwal AK. A new technique of 'Marlex peritoneal sandwich' in the repair of large incisional hernias. World J Surg 1991;15:768-70

McCarthy JD, Twiest MW. Intraperitoneal polypropylene mesh support of incisional herniorraphy. Am J Surg 1981;142:707-11

McEntee G, Pender D, Mulvin D, McCullough M, Naeeder S, Farah S, Badurdeen MS, Ferraro V, Cham C, Gillham N, Matthews P. Current spectrum of intestinal obstruction. Br J Surg 1987;74:976-80

McGillicuddy JE. Prospective randomised comparison of the Shouldice and Lichtenstein hernia repair procedures. Arch Surg 1998;133:974-8

McKernan JB, Laws HL. Laparoscopic repair of inguinal hernias using a totally extraperitoneal prosthetic approach. Surg Endosc 1993;7:26

McLanahan D, King LT, Weems C, Novotney M, Gibson K. Retrorectus prosthetic mesh repair of midline abdominal hernia. Am J Surg 1997;173:445-9

McLaughlin DS. Evaluation of adhesion reformation by early second-look laparoscopy following microlaser ovarian wedge resection. Fertil Steril 1984;42:531-7

McVay CB, Halverson K. Preperitoneal hernioplasty. In Beahrs OH, Beart RW Jr (eds), General Surgery Therapy. New York NY,: John Wiley and Sons;1981:10

Meagher AP, Moller C, Hoffmann DC. Non-operative treatment of small bowel obstruction following appendicectomy or operation on the ovary or tube. Br J Surg 1993;80:1310-1

Mecke H, Heuchmer R, Lehmann-Willenbrock E. [Complications in 5,000 pelviscopies at the Kiel University Gynecologic Clinic]. Geburtshilfe Frauenheilkd 1996;56:449-52

Mecke H, Semm K, Lehmann-Willenbrock E. [Pelviscopic adhesiolysis. Successes in the treatment of chronic abdominal pain caused by adhesions in the lower and middle abdomen]. Geburtshilfe Frauenheilkd 1988;48:155-9

Mendoza CB, Postlethwait RW, Johnson WD. Veterans Administation cooperative study of surgery for duodenal ulcer. II. Incidence of wound disruption following operation. Arch Surg 1970;101:396:8

Menzies D, Ellis H. Intestinal obstruction from adhesions - how big is the problem? Ann R Coll Surg Engl 1990;72:60-3

Menzies D. Postoperative adhesions: their treatment and relevance in clinical practice [review]. Ann R Coll Surg Engl 1993;75:147-53

Mertens R, Van den Berg JM, Veerman-Brenzikofer ML, Kurz X, Jans B, Klazinga N. International comparison of resuts of infection surveillance The Netherlands versus Belgium. Infect Control Hosp Epidemiol 1994;15:572-3

Miller K, Junger W. Ileocutaneous fistula formation following laparoscopic polypropylene mesh hernia repair. Surg Endosc 1997;7:772-3

Miller K, Mayer E, Moritz E. The role of laparoscopy in chronic and recurrent abdominal pain. Am J Surg 1996;172:353-7

Molloy RG, Moran KT, Waldron RP, Brady MP, Kirwan WO. Massive incisional hernia: abdominal wall replacement with Marlex mesh. Br J Surg 1991;78:242-4

Morris-Stiff GJ, Hughes LE. The outcome of nonabsorbable mesh placed within the abdominal cavity: literature review and clinical experience. J Am Coll Surg 1998;186: 352-67

MRC Laparoscopic Groin Hernia Trial Group. Laparoscopic versus open repair of groin hernia: a randomized comparison. The Lancet 1999;354:185-90

Mudge M, Hughes LE. Incisional hernia: a 10 year prospective study of incidence and attitudes. Br J Surg 1985;72:70-1

Mueller MD Tschudi J, Herrmann U, Klaiber C. An evaluation of laparoscopic adhesiolysis in patients with chronic abdominal pain. Surg Endosc 1995;9:802-4

Nezhat CR, Nezhat FR, Swan AE. Long-term outcome after laparoscopic adhesiolysis in women with chronic pelvic pain after hysterectomy. J Am Assoc Gynecol Laparosc 1996;3:S33-4

Nezhat FR, Crystal RA, Nezhat CH, Nezhat CR. Laparoscopic adhesiolysis and relief of chronic pelvic pain. JSLS 2000;4:281-5

Nieuwenhuijzen M, Reijnen MM, Kuijpers JH, van Goor H. Small bowel obstruction after total or subtotal colectomy: a 10-year retrospective review. Br J Surg 1998;85:1242-5

Niggebrugge AH, Trimbos JB, Hermans J, Steup WH, Van de Velde CJ. Influence of abdominal wound closure on complications after surgery: a randomized study. Lancet 1999;353:1563-7

Nordic Adhesion Prevention Study Group. The efficacy of Interceed (TC7) for prevention of reformation of postoperative adhesions on ovaries, Fallopian tubes, and fimbriae in microsurgical operation for fertility: a multicenter study. Fertil Steril 1995;63:709-14

Nordin P, Bartelmess P, Jansson C, Svensson C, Edlund G. Randomized trial of Lichtenstein versus Shouldice hernia repair in general surgical practice. Br J Surg 2002;89:45-9

Nyhus LM. Individualization of hernia repair; a new era. Surgery 1993;114:1-2

Oishi SN, Page CP, Schwesinger WH. Complicated presentations of groin hernias. Am J Surg 1991;162:568-70

Operative Laparoscopy Study Group. Postoperative adhesion development after operative laparoscopy: evaluation at early second look procedures. Fertil Steril 1991;55:700-4

Ozmen MM, Arslar AK, Terzi MC, Albayrak L, Berberoglu M. Prevention of adhesions by bioresorbable tissue barrier following laparoscopic intraabdominal mesh insertion. Surg Laparosc Endosc Percutan Tech 2002;12:342-6

Paul A, Korenkov M, Peters S, Kohler L, Fischer S, Troidl H. Unacceptable results of the Mayo procedure for repair of abdominal incisional hernias. Eur J Surg 1998;164:361-7

Paul A, Troidl H, Williams JI, Rixen D, Langen R. Randomised trial of modified Bassini versus Shouldice inguinal hernia repair. Br J Surg 1994;81:1531-4

Peters AA, Trimbos-Kemper GC, Admiraal C, Trimbos JB, Hermans J. A randomized clinical trial on the benefit of adhesiolysis in patients with intraperitoneal adhesions and chronic pelvic pain. Br J Obstet Gynaecol 1992;99:59-62

Platt R, Zaleznik DF, Hopkins CC, Dellinger EP, Karchmer AW, Bryan CS, Burke JF, Wikler MA, Marino SK, Holbrook KF et al. Perioperative antibiotic prophylaxis for herniorraphy and breast surgery. N Engl J Med 1990;322:153-60

Prior MJ, Williams EV, Shukla HS, Phillips S, Vig S, Lewis M. Prospective randomized controlled trial comparing Lichtenstein with modified Bassini repair of inguinal hernia. J R Coll Surg Edinb 1998;43:82-6

Punch MR, Roth RS. Adhesions and chronic pain: an overview of pain and a discussion of adhesions and pelvic pain. Prog Clin Biol Res 1993;381:101-20

Raftery AT. Regeneration of parietal and visceral peritoneum: an electron microscopical study. J Anat 1973;115:379-92

Raj SG, Hulka JF. Second-look laparoscopy in infertility surgery: therapeutic and prognostic value. Fertil Steril 1982;38:325-9

Ramirez OM, Ruas E, Dellon AL. “Components separation” method for closure of abdominal wall defects: an anatomic and clinical study. Plast Reconstr Surg 1990;86:519-26

Rand Corp. (Santa Monica, California): Conceptualization and Measurement of Physiologic Health for adults. Rand Corp. Publications. 1983;15:3-120

Rapkin AJ. Adhesions and pelvic pain: a retrospective study. Obstet Gynecol 1968;68:13-5

Ray NF, Denton WG, Thamer M, Henderson SC, Perry S. Abdominal adhesiolysis: inpatient care and expenditures in the United States in 1994. J Am Coll Surg 1998;186:1-9

Ray NF, Larsen JW Jr, Stillman RJ, Jacobs RJ. Economic impact of hospitalizations for lower abdominal adhesiolysis in the United States in 1988. Surg Gynecol Obstet 1993;176:271-6

Read RC, Yoder G. Recent trends in the management of incisional herniation. Arch Surg 1989;124:485-8

Regnard JF, Hay JM, Rea S, Fingerhut A, Flamant Y, Maillard JN. Ventral incisional hernias: incidence, date of recurrence, localization and risk factors. Ital J Surg Sci 1988;18:259-65

Reich H. Laparoscopic bowel injury. Surg Laparosc Endosc 1992;2:74-8

Reijnen MMPJ, Holmdahl L, Kooistra T, Falk P, Hendriks T, van Goor H. Time course of peritoneal tissue plasminogen activator after experimental colonic surgery: effect of hyaluronan-based antiadhesive agents and bacterial peritonitis. Br J Surg 2002;89:103-9

Riet M, Steenwijk PJ, Kleinrensink GJ, Steyerberg EW, Bonjer HJ. Tensile strength of mesh fixation methods in laparoscopic incisional hernia repair. Surg Endosc 2002; [epub ahead of print July 2002].

Rives J. Major incisional hernias. In: Chevrel JP (ed), Surgery of the abdominal wall. New York NY: Springer-Verlag, 1987:116

Robbins AW, Rutkow IM. The mesh-plug hernioplasty. Surg Clin North Am 1993;73:501-12

Rutkow IM, Robbins AW. Demographic, classificatory and socioeconomic aspects of hernia repair in the United States. Surg Clin North Am 1993;73:413-26

Saravelos HG, Li TC, Cooke ID. An analysis of the outcome of microsurgical and laparoscopic adhesiolysis for chronic pelvic pain. Hum Reprod 1995;10:2895-901

Schafer M, Krahenbuhl, Buchler MW. Comparison of adhesion formation in open and laparoscopic surgery. Dig Surg 1998;15:148-52

Schietroma M, Carlei F, Altilia F, Carloni A, Mattucci S, Agnifili A, Maira E, Antonellis M. The role of laparoscopic adhesiolysis in chronic abdominal pain. Minerva Chir 2001;56:461-5

Schmidbauer S, Hallfeldt KK. Laparoscopic adhesiolysis in the treatment of chronic abdominal pain. Surgery 2001;129:513-4

Schumpelick V, Conze J, Klinge U. Preperitoneal mesh-plasty in incisional hernia repair. A comparative retrospective study of 272 operated incisional hernias. Chirurg 1996;67:1028-35

Scott-Coombes DM, Vipond MN, Thompson JM. General surgeons' attitudes to the treatment and prevention of abdominal adhesions. Ann R Coll Surg Engl 1993;75:123-8

Seelig MH, Kasperk R, Tietze L, Schumpelick V. Enterocutane fistel nach Marlex-netz-implantation; eine seltene komplikation nach narbenhernienreparation. Chirurg 1995;66:739-41

Serour GI, Badraoui MH, el Agizi HM, Hamed AF, Abdel-Aziz F. Laparoscopic adhesiolysis for infertile patients with pelvic adhesive disease. Int J Gynaecol Obstet 1989;30:249-52

Shestak KC, Edington HJ, Johnson RR. The separation of anatomic components technique for the reconstruction of massive midline abdominal wall defects: anatomy, surgical technique, applications, and limitations revisited. Plast Reconstr Surg 2000;105:731-8

Shouldice EE. The treatment of hernia. Ontario Med Rev 1953;20:670

Si Z, Bhardwaj R, Rosch R, Mertens PR, Klosterhalfen B, Klinge U, Rhanjit B, Rene PM. Impaired balance of type I and type III procollagen mRNA in cultured fibroblasts of patients with incisional hernia. Surgery 2002;131:324-31

Simmermacher RKJ, Schakenraad JM, Bleichrodt RP. Reherniation after repair of the abdominal wall with expanded polytetrafluoroethylene. J Am Coll Surg 1994;178:613-6

Simons MP, Kleijnen J, van Geldere D, Hoitsma HF, Obertop H. Role of the Shouldice technique in inguinal hernia repair: a systematic review of controlled trials and a meta-analysis. Br J Surg 1996;83:734-8

Soares BM, Guidoin RG, Marois Y, Martin L, King MW, Laroche G, Zhang Z, Charara J, Girard JF. In vivo characterisation of a fluoropassivated gelatin-impregnated polyester mesh for incisional hernia repair. J Biom Mat Res 1996;32:293-305

Starling JR. Neuralgia (inguinodynia) after inguinal hernorraphy. Nyhus and Condon's hernia, 5th ed., Fitzgibbons RJ and Greenberg AG (eds). Lippincott, Williams & Wilkins, Philadelphia USA 29:317-26

Steege JF, Stout AL. Resolution of chronic pelvic pain after laparoscopic lysis of adhesions. Am J Obstet Gynecol 1991;165:278-83

Stevick CA, Long JB, Jamasbi B, Nash M. Ventral hernia following abdominal aortic recontruction. Am Surg 1988;54:287-9

Stoppa R. Hernia of the abdominal wall. In: Chevrel JP (ed), Surgery of the abdominal wall. Berlin Germany: Springer-Verlag, 1987: 155

Stout AL, Steege JF, Dodson WC, Hughes CL. Relationship of laparoscopic findings to self-report of pelvic pain. Am J Obstet Gynecol 1991;164:73-9

Sugerman HJ, Kellum JM, Reines HD, DeMaria EJ, Newsome HH, Lowry JW. Greater risk of incisional hernia with morbidly obese than steroid-dependent patients and low recurrence with prefascial polypropylene mesh. Am J Surg 1996;171:80-4

Sulaiman H, Gabella G, Davis C, Mutsaers SE, Boulos P, Laureny GJ, Herrick SE. Presence and distribution of sensory nerve fibers in human peritoneal adhesions. Ann Surg 2001;234:256-61

Surrey MW, Friedman S. Second-look laparoscopy after reconstructive pelvic surgery for infertility. J Reprod Med 1982;27:658-60

Suter M, Zermatten P, Halkic N, Martinet O, Bettschart V. Laparoscopic management of mechanical small bowel obstruction: are there predictors of success or failure? Surg Endosc 2000;14:478-83

Sutton C, MacDonald R. Laser laparoscopic adhesiolysis. J Gynecol Surg 1990;6:155-9

Swolin K. Electromicrosurgery and salpingostomy: long-term results. Am J Obstet Gynecol 1975;121:418-9

Thompson JN, Whawell SA. Pathogenesis and prevention of adhesion formation. Br J Surg 1965;52:471-6

Tittel A, Treutner KH, Titkova S, Ottinger A, Schumpelick V. New adhesion formation after laparoscopic and conventional adhesiolysis: a comparative study in the rabbit. Surg Endosc 2001;15:44-46

Toy FK, Bailey RW, Carey S, Chappuis CW, Gagner M, Josephs LG, Mangiante EC, Park AE, Pomp A, Smoot RT, Uddo JF, Voeller GR. Prospective, multicenter study of laparoscopic ventral hernioplasty. Preliminary results. Surg Endosc 1998;12:955-8

Trimbos-Kemper TC, Trimbos JB, van Hall EV. Adhesion formation after tubal surgery: results of the eighth-day laparoscopy in 188 patients. Fertil Steril 1985;43:395-400

Tschudi J, Mueller M, Klaiber C. [Does laparoscopic lysis of adhesions make sense]? Schweiz Med Wochenschr 1993;123:1128-30

Turkcapar AG, Yerdel MA, Aydinuraz K, Bayar S, Kuterdem E Repair of midline incisional hernias using polypropylene grafts. Surg Today 1998;28:59-63

Tyrell J, Silberman H, Chandrasoma P, Niland J, Shull J. Absorbable versus permanent mesh in abdominal operations. Surg Gynecol Obstet 1989;168:227-32

Ugur M, Turan C, Mungan T, Aydogdu T, Sahin Y, Gokmen O. Laparoscopy for adhesion prevention following myomectomy. Int J Gynaecol Obstet 1996;53:145-9

Usher FC. Use of Marlex mesh in the repair of incisional hernias. Am Surg 1958;24:969-74

Van Agt HM, Essink-Bot ML, Krabbe PF, Bonsel GJ. Test-retest reliability of health state valuations collected with the EuroQol questionnaire. Soc Sci Med 1994;39:1537-44

Van den Berg JC, Strijk SP, Rosenbuch G. Is peritoneography indicated for the diagnosis of inguinal and abdominal wall hernias? Radiologe 1993;33:352-5

Van den Tol MP, Van Stijn I, Bonthuis F, Marquet RL, Jeekel J. Reduction of intraperitoneal adhesion formation by use of non-abrasive gauze. Br J Surg 1997;84:1410-5

Van den Tol MP. Influence of peritoneal trauma on postoperative adhesion formation and intra-abdominal tumour recurrence. Thesis. 2001

Van der Linden FT, van Vroonhoven TJ. Long-term results after surgical correction of incisional hernia. Neth J Surg 1988;40:127-9

Van Goor H, de Graaf JS, Grond J, Sluiter WJ, van der Meer J, Bom VJ. Fibrinolytic activity in the abdominal cavity of rats with faecal peritonitis. Br J Surg 1994;81:1046-9

Van't Riet M, De Vos van Steenwijk PJ, Bonthuis F, Marquet RL, Steyerberg EW, Jeekel J, Bonjer HJ. Prevention of adhesion to prosthetic mesh: comparison of different barriers using an incisional hernia model. Ann Surg 2003;237:123-8

Viljanto J, Vanttinen E. Incisional hernias as a function of age. Ann Chir Gynecol Fenn 1966;57:246-9

Vrijland WW, Den Hoed PT, Jeekel J, Bonjer HJ. Laparoscopische littekenbreukcorrectie. (Nieuwsbrief Werkgroep Endoscopische Chirurgie) Nederlands tijdschrift voor Heelkunde 1998;175-7

Vrijland WW, Tseng LNL, Eijkman HJM, Hop WCJ, Jakimowicz JJ, Leguit P, Stassen LPS, Swank DJ, Haverlag R, Bonjer HJ, Jeekel J. Fewer intraperitoneal adhesions with use of hyaluronic acid-carboxymethylcellulose membrane: a randomized clinical trial. Ann Surg 2002b;235:193-9

Vrijland WW, Van den Tol MP, Luijendijk RW, Hop WC, Busschbach JJ, De Lange DC, van Geldere D, Rottier AB, Vegt PA. Randomized clinical trial of non-mesh versus mesh repair of primary inguinal hernia. Br J Surg 2002a;89:1-7

Wagh PV, Leverich AP, Sun CN, White HJ, Read RC. Direct inguinal herniation in men: a disease of collagen. J Surg Res 1974;17:425-33

Wantz GE. Atlas of hernia surgery. New York, NY, USA. Raven;1991:101

Wantz GE. Testicular atrophy and chronic residual neuralgia as risks of inguinal hernioplasty. Surg Clin North Am 1993;73:571-81

Welty G, Klinge U, Klosterhalfen B, Kasperk R, Schumpelick V. Functional impairment and complaints following incisional hernia repair with different polypropylene meshes. Hernia 2001;5:142-7

White TJ, Santos MC, Thompson JS. Factors affecting wound complications in repair of ventral hernias. Am Surg 1998;64,276-80

Whiteley MS, Ray-Chaudhuri SB, Galland RB. Combined fascia and mesh closure of large incisional hernias. J R Coll Surg Edinb 1998;43:29-30

Wilson MS, Hawkswell J, McCloy RF. Natural history of adhesional small bowel obstruction: counting the cost. Br J Surg 1998;85:1294-8

Wipfli-Funke A, Riedel HH. Success of laparoscopic - pelviscopic adhesiolysis in treating chronic abdominal pain. J Am Assoc Gynecol Laparosc 1995;2:S60

Wissing JC, van Vroonhoven ThJ, Eeftinck Schattenkerk M, HF Veen, Ponsen RJ, Jeekel J. Fascia closure after midline laparotomy: results of a randomized trial. Br J Surg 1987;74:738-41

Zbar RI, Crede WB, McKhann CF, Jekel JF. The postoperative incidence of small bowel obstruction following standard, open appendectomy and cholecystectomy: a six-year retrospective cohort study at Yale-New Haven Hospital. Conn Med 1993;57:123-7

Zühlke HV, Lorenz EMP, Straub EM, Savvas V. Pathophysiologie und Klassifikation von Adhäsionen. Langenbecks Arch Chir Suppl II Verh Dtsch Ges Chir 1990;345:1009-16

VI DANKWOORD

Tijdens mijn co-schap chirurgie sprak **Prof. dr. J. Jeekel** mij aan over mijn plannen voor de toekomst. Toen ik te kennen gaf dat chirurgie me wel wat leek, beloofde hij een onderzoeksplek voor me te zoeken voor als ik zover was. Nog geen jaar later kon ik beginnen, in eerste instantie als coördinator van de Seprafilm trial.
Professor Jeekel, uw liberale begeleiding zorgde ervoor dat ik het op mijn eigen manier kon doen. Gelukkig was u altijd beschikbaar voor overleg als ik niet meer wist hoe het verder moest, en vaak kon ik zo maar binnenlopen. Ik beschouw het als een eer dat ik uw 50^{e} promovendus ben en ik vertrouw erop dat ik niet de laatste ben.

Prof. dr. H.J. Bonjer, toen ik als onderzoeker begon heette je nog Jaap. Met jouw hulp is er samenhang in dit boekje gekomen. Jouw ideeën en creativiteit, maar ook je, niet altijd even genuanceerde, kritische commentaar hebben mij vaak een duwtje in de rug gegeven. Jouw visie, ambitie en energie zijn een voorbeeld, en niet alleen in wetenschappelijke zin. Ik ben blij dat ik mijn opleiding onder jouw hoede mag voltooien.

Prof. dr. H. W. Tilanus: mijn eerste schreden op het klinische pad heb ik onder uw leiding gezet en ik ben zeer vereerd dat u in mijn kleine commissie plaats heeft willen nemen. Heel hartelijk dank voor het beoordelen van het manuscript.

Prof. dr. Th.J.M. Helmerhorst wil ik hartelijk danken voor de participatie in de kleine commissie en de beoordeling van het manuscript.

Prof. dr. J.B.M.Z. Trimbos wil ik bedanken voor de beoordeling van het manuscript en evenzo **Dr. H. van Goor** die bereid gevonden is Professor Trimbos te vervangen op 19 maart.

Dr. P. Leguit en **dr. Dick van Geldere** wil ik hartelijk danken voor de deelname aan de grote commissie en voor de samenwerking bij de Seprafilmstudie respectievelijk de liesbreukenstudie.

Prof. dr. V. Schumpelick: Ich möchte mich bei Ihnen bedanken für Ihre Anwesenheit und Opposition während der Verteidigung meiner Doktorarbeit.

Dr. Wim Hop: zowel bij de liesbreukenstudie als bij de Seprafilmstudie bent u onmisbaar geweest. De hulp bij de statistische bewerking van alle zo zorgvuldig door Anneke van Duuren verzamelde gegevens was een hele toer en heeft uiteindelijk geleid tot twee mooie publicaties.
Ewout Steyerberg, jij hebt mij geholpen bij de statistiek van hoofdstuk 5 en 6. Als jij het liet zien, leek het net of SPSS heel gemakkelijk is. **Jan van Busschbach**, de kwaliteit-van-leven studie in hoofdstuk 2 is door jou geanalyseerd. Ondanks ontbrekende gegevens liet jij de moed niet zakken en zijn we tot een mooie beschrijving gekomen. Hartelijk dank!

Anneke van Duuren: dank voor al je hulp. Jij verzamelde niet alleen de data van de liesbreuk- en Seprafilmtrial, maar deed ook een groot gedeelte van de 'huis-, tuin- en keukenstatistiek' die nodig was om tot een goede beschrijving van de studies te komen. Daarnaast was je samen met **Conny Vollebregt** de stabiele factor in 'de onderzoekskamer' waar naast het doen van onderzoek ook wel eens frivolere activiteiten ontplooid werden.

Fred Bonthuis: dank voor je hulp bij het uitvoeren van het dierexperimentele werk en de vele gesprekken al doende, zowel over het werk als over lekker eten.
Richard Marquet: dank voor je hulp en je suggesties bij het dierexperimentele werk, het indienen van aanvragen voor proefdieren en voor de discussies op een breder wetenschappelijk vlak. Ik heb het zeer gewaardeerd om bij jullie in het lab te gast te mogen zijn.

Bij het verrichten van klinisch onderzoek komen een groot aantal co-auteurs kijken die diverse rollen spelen in het proces van opzetten, uitvoeren en uitwerken en vastleggen van een studie. Naast de personen die hierboven al genoemd zijn, wil ik de volgende personen bedanken:

Petrousjka van den Tol, **Roland Luijendijk** en **Diederik de Lange** voor het ontwerpen en deels uitvoeren van hoofdstuk 2, de liesbreukstudie, alsmede het beoordelen van het manuscript.
Dr. A.B. Rottier en **Dr. P.A. Vegt** voor het deelnemen aan deze studie en de nauwgezette beoordeling van het manuscript.
Dr. Jan IJzermans was vanaf het begin betrokken bij de liesbreukstudie. Pas toen het manuscript voor dat artikel echt perfect was, mocht het opgestuurd worden. Dank voor je weloverwogen commentaar.

Ted den Hoed, jij hebt een belangrijke bijdrage geleverd aan hoofdstuk 6, waarvoor mijn dank. Heel blij was ik dit jaar met de acceptatie van het hemangiomen artikel, eindelijk!

Larissa Tseng, jij bent begonnen met de Seprafilmtrial en je hebt enorm veel energie gestoken in het schrijven van het protocol en de lobby om chirurgen deel te laten nemen. Ook later heb je altijd belangstelling getoond en geholpen met de video-evaluatie, waarvoor dank. **Heert Eijkman**, kort, maar stormachtig was jouw trialcoördinatorschap. Dank voor de introductie in het klinische onderzoekersleven.
Dr. J.J. Jakimowicz, **Dr. Laurents Stassen** en **Dingeman Swank**, heel hartelijk dank voor het includeren van patiënten en het beoordelen van het manuscript van hoofdstuk 7. Dingeman, ook hartelijk dank voor je bijdrage aan hoofdstuk 8. Ik hoop dat jouw promotie dit jaar ook met succes afgerond wordt.
Robert Haverlag, dank voor je uitgebreide relativering van het begrip ‘onderzoek doen’. Jouw rol in de Seprafilmstudie heb je me nooit helemaal duidelijk kunnen maken, maar de video-evaluatie was erg gezellig.

Dr. H.J. van Geldorp, dank voor uw inbreng in en beoordeling van hoofdstuk 8.

Collegae van ‘de onderzoekskamer’ **Marc Romijn**, **Philippe Wittich**, **Bas Wijnhoven, Marijel Braaksma**, **Manon Gosselink**, **Gerrit Slooter**, **Eric Hazebroek** en **Martijne van ’t Riet** wil ik allemaal hartelijk bedanken voor de gezellige tijd en het delen van successen en tegenslagen op onderzoeksgebied. Philippe, Eric en Martijne, deel uit maken van de ‘Bonjer group’ was mede dank zij jullie altijd een groot plezier, met name tijdens buitenlandse trips. Martijne, ik vind het leuk dat jij de Colibristudie over hebt genomen en de onderzoekslijn hebt voortgezet. Heel veel succes met het voltooien van je eigen boekje.

Elma van Rossen, **Arend Aalbers**, **Amir Mearadji** en **Helma van Grevenstein,** het was altijd leuk om in het lab te komen, zeker als er weer eens een evenement georganiseerd moest worden. Dank voor de gezelligheid.

Mireille Knook, 'endoscopische liesbreukkoningin', discussiëren over liesbreuken zullen we wel altijd blijven doen. Jammer dat ons experimentele werk nooit tot een publicatie geleid heeft. Wel was het aanleiding voor veel gezelligheid. Als vriendin en adviserend net-iets-oudere collega ben je onmisbaar.

Antoinette Herben en **Jacqueline Feteris** wil ik bedanken voor de vlotte hulp die ik altijd van jullie kreeg. Dank voor het bewaren van kalmte als ik die zelf kwijt was.

Lieve **Caroline** en **Evelyn**, met achternamen als de Vrey, Vrijland en Waasdorp was het onvermijdelijk dat wij naast elkaar in dezelfde practicumgroep zaten. Ik vind het bijzonder dat wij 12 jaar later hier zij aan zij staan. Heel hartelijk dank voor jullie steun en interesse al die jaren. Ik vind het een eer dat jullie mijn paranymphen willen zijn. **Sacha**, al lang geleden heb jij beloofd dat als ik zou gaan promoveren, jij de voorkant van mijn proefschrift zou ontwerpen. Ik ben heel trots op het resultaat, dankjewel!

Het eerste gedeelte van mijn opleiding heb ik gevolgd in het Medisch Centrum Rijnmond Zuid, lokatie Zuider, maar voor mij nog altijd het **Zuiderziekenhuis**. De maatschap chirurgie, mijn collega-assistenten, de dames van het secretariaat en de (IC-) verpleegkundigen, het OK-personeel, het personeel van de polikliniek chirurgie en alle andere mensen waar ik mee gewerkt heb, wil ik van harte bedanken voor de goede tijd. Dank voor de goede werksfeer en de interesse in mijn bezigheden. Het personeel van de bibliotheek van het Zuider wil ik in het bijzonder bedanken voor de vloed aan artikelen die jullie op mijn verzoek opgezocht en gekopieerd hebben.

Papa, jij hebt de technische uitvoering van dit proefschrift voor je rekening genomen, en daar ben ik je heel dankbaar voor. En passant heb je ook nog gericht commentaar gegeven, alhoewel je eigen expertise toch op een heel ander vlak ligt. Jij en **Mama** hebben mij altijd gestimuleerd en geholpen om te worden wat ik wilde.

Maarten, **Marieke**, **Luc**, **Anne** en **Rutger**, dank voor jullie interesse en steun al die tijd dat ik met dit boekje bezig was. Ik ben blij dat het af is, en ik weet zeker dat jullie dat met me eens zijn.

De firma's **Johnson & Johnson Medical BV, Bard Benelux b.v.** en **Tyco Healthcare Nederland B.V.** wil ik hierbij hartelijk danken voor hun bijdragen voor het uitgeven van dit proefschrift.

VII CURRICULUM VITAE AUCTORIS

Wietske Willemijn Vrijland was born on January 5th, 1971 in Enschede.
After graduating from high school at the Ichthus College in Enschede in 1990, she attended medical school at the Faculty of Medicine of the Erasmus University Rotterdam. During her undergraduate years she worked as a student assistant at the Neurology Department of the University Hospital Rotterdam-Dijkzigt and at the Department of Cardiochemistry of the Erasmus University. In 1997, she obtained her medical degree. In 1998 she obtained a research position at the Department of General Surgery of the University Hospital Rotterdam-Dijkzigt (Prof.dr. J. Jeekel).
In 2000 she started her training at the Department of Surgery of the Zuiderziekenhuis, Rotterdam (Dr. K.J. Brouwer) and from 2003 she continued her training at the Department of General Surgery of the University Hospital Rotterdam-Dijkzigt (Prof.dr. H. J. Bonjer).

Ah! Vanitas Vanitatum! Which of us is happy in this world?
Which of us has his desire? Or, having it, is satisfied? –
Come children, let us shut up the box and the puppets,
for our play is played out.

Vanity Fair
William Makepeace Thackeray
1848