Abdominal Wall Hernia in Complex Patients
incidences, risk factors and timing of repair

Joost Verhelst

Abdominal Wall Hernia in Complex Patients

incidences, risk factors and timing of repair

Joost Verhelst

Colofon

ISBN: 978-94-6233-350-5

Layout and printing: Gildeprint, Enschede, the Netherlands
Cover: Huib Nederhof, Rotterdam, the Netherlands

Printing of this thesis has been financially supported by:
Erasmus MC afdeling Heelkunde
Erasmus Universiteit Rotterdam
Soest Medical Group

Abdominal Wall Hernia in Complex Patients

incidences, risk factors and timing of repair

Buikwandbreuken bij complexe patiënten
incidentie, risico factoren en timing

Proefschrift

ter verkrijgen van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van
rector magnificus

Prof.dr. H.A.P. Pols
en volgens besluit van het College voor Promoties

De openbare verdediging zal plaatsvinden op
vrijdag 2 september 2016 om 09:30,
door

Joost Verhelst
geboren te Breda

Promotiecommissie

Promotor	Prof.dr. J.F. Lange
Overige leden	Prof.dr. F. Berrevoet
	Prof.dr. H.J.M. Verhagen
	Prof.dr. R.M.H. Wijnen
Copromotor	Prof.dr. J. Jeekel

Table of contents

Chapter 1

Introduction and outline of this thesis

Introduction and outline of this thesis

Abdominal wall hernia

The abdominal cavity is the space between the diaphragm and pelvic musculature and contains multiple abdominal organs. The abdominal wall represents the boundaries of this abdominal cavity. It consists of skin, subcutaneous fat, various layers of muscles, nerves, blood vessels, and connective tissues, retaining the organs in the abdominal cavity and protecting these from external trauma. To gain access to the abdominal cavity surgeons must cut through these tissues. The anterior abdominal wall consists of the rectus abdominis, external and internal oblique, and the transverse abdominal muscles. The rectus muscle inserts on the ribcage and on the pubic bone. The external, internal oblique and transverse abdominal muscles are situated laterally to the rectus abdominis muscle. The fascia of these three muscles join together in the midline and form the linea alba. The integrity and function of the abdominal wall can be compromised which can result in abdominal wall hernia. Hernia are gaps in the abdominal wall with or without a bulge and perceptible or palpable by clinical examination and/or radiological imaging. Abdominal wall hernia can be congenital or can be acquired by accidental or iatrogenic trauma. For example incisional hernia can be caused by a midline incision to gain access for abdominal surgery. Therefore, abdominal wall surgery is a broad term covering different type of hernia repair with different kind of approaches. However, there is also much overlap in treatment and approach of these different kind of abdominal wall hernias.

Abdominal wall surgery underwent a great evolution. The first hernia has already been described by the Egyptians, on a papyrus written around 1500 BC. In the 4th century B.C. Praxagoras reported to have attempted reduction of a strangulated hernia. In the first century A.D. Celsus described clinical signs and symptoms of strangulation. He was the first to describe a surgical technique for the treatment of hernia (1). Claudius Galenus described that deficiency in two external abdominal muscles can lead to hernias. In 1802 Sir Astley Cooper gave the first description of an incisional hernia repair. The anatomy and new surgical techniques were described in his book (2). After the introduction of general anaesthesia and subsequently of abdominal surgery, the incidence of acquired incisional hernia increased. In 1887 an American general surgeon from Boston: Marcy was the first to use foreign material, an animal tendon, as an alternative for tissue repair in hernia surgery. He performed high ligation of the hernia sac as well as closure of the internal ring to repair indirect inguinal hernias (3). This is a procedure that is still used widely today especially in pediatric patients. During the beginning of the 20th century several organic and metal prosthesis were used for hernia repair. In 1894, silver wire coils were placed in the inguinal canal to induce fibrosis and strengthen the hernia repair. A few years later these wires were woven and the first “mesh”

was introduced. Silver and metal however lacked pliability, caused pain, was not inert, and fatigue of the material led to disintegration and subsequent sinus tract formation and infections. After the invention of nylon by the Wallace brothers, one of the most important milestones in hernia surgery was introduced: the mesh prosthesis. Meshes are prosthetic materials that can be used as reinforcement for the abdominal wall when repairing abdominal wall hernia. One of the first synthetic polymer (plastics) meshes used was Marlex (4). This was a poly propylene compound which revolutionized hernia repair. In 1965 Rives developed a hernia repair placing mesh in the pre-peritoneal space. He felt that all patients did not need this type of repair and consequently was very selective about using it. In 1984 Stoppa used a large Dacron prosthesis to reinforce the transversalis fascia for complex hernias in patients who were deemed at high risk for recurrences. Before the introduction of meshes recurrence rates of hernia repair were incredibly high, up to 60%. After the introduction of meshes recurrence rates after hernia repair dropped dramatically (5). Meshes can also be used to prevent patients from developing incisional hernia, especially in high risk patients (6). On the other hand the introduction of meshes has also led to mesh related complications, such as infection, adhesions, erosion, shrinkage and bulging (7, 8). Although the industry puts a lot of effort into research and development the ideal mesh has not been invented (yet) and over 200 different prostheses are commercially available nowadays.

One of these new meshes, a Parietex mesh with self-gripping polylactic acid microhooks was successfully introduced in inguinal hernia repair (9-11). In **Chapter 2** we investigated if the characteristics of this mesh are valuable in incisional hernia repair. The mesh was placed on the retromuscular plane in the Rives-Stoppa technique or modified component separation technique with mesh.

Next to the search for the best mesh prosthesis, surgical techniques are getting optimized and new or modified surgical techniques got introduced. In **Chapter 3** the relevance of watchful waiting in incisional hernia was evaluated.However, operative treatment of patients with minimally symptomatic abdominal wall hernia is frequently been questioned (12, 13). Patients who were treated for an abdominal wall hernia who preoperatively had no or minimal symptoms suffered postoperatively from clinically relevant pain after short- and long term follow-up. The question is whether conservative treatment or watchful waiting is safe. The various symptoms and regarding abdominal wall hernia and its natural course are mentioned in literature (14-16). Nevertheless, published data accurately describing these symptoms and the indications for surgery with postoperative outcomes is truly relevant (17). In inguinal hernia, cost effectiveness and safety have already led to implementation of the watchful waiting strategy (18, 19).

In **Part 2** of the thesis we looked into three complex patient categories with abdominal wall hernia: premature infants, kidney recipients and patients with an abdominal aortic aneurysm. When operating on patients it is important to be aware of risk factors to develop postoperative complications. Some patients appear to be more prone to develop postoperative complications, such as an (recurrent) incisional hernia. Therefore, indications and the preferred technique for repair of abdominal wall hernia are multifactorial and should be tailor-made to the individual patient. The objective was to collect evidence for the optimal management of abdominal wall hernia repair in complex patients by comparing the outcomes of procedures and by identifying the risk factors for the development of complications.

In **Chapter 4 and 5** a retrospective cohort of premature infants with inguinal hernia has been investigated in search for new potential risk factors for incarceration. Furthermore we looked in detail to direct medical costs of inguinal hernia repair in premature infants and compared patients who had to undergo emergency repair with those who underwent elective repair. Inguinal hernia repair is the most frequently performed surgical procedure in neonates, especially in preterm born children. Almost 10% of children born preterm will undergo inguinal hernia repair before the age of seven years, more than half in the first year of life (20, 21). The most important factor that contributes to the increased risk for inguinal hernia in premature infants is a persistent processes vaginalis. The optimal timing of inguinal hernia repair in premature infants is not clear (22). Common surgical knowledge is that repair should be postponed until a certain weight or age is reached because of technical challenges, particularly the very preterm born with a very low birth weight, comorbidities, and potential risk for anaesthetic and surgical complications (23, 24).

In **Chapter 6** we evaluated the incidence and treatment of incisional hernia after kidney transplantation and tried to identify independent potential risk factors for the development of incisional hernia. Kidney transplant recipients may have an increased risk to develop incisional hernia due to the use of postoperative immunosuppressive therapy resulting in postoperative wound infections. This impaired wound healing could hypothetically lead to the development of incisional hernia (25, 26). Use of a permanent prosthetic material is now the gold standard for the treatment of incisional hernia. Even with the placement of a permanent prosthesis (from now on referred to as “mesh”), recurrence rates are still very high at up to 32%, and the use of mesh predisposes patients to mesh-related complications, such as seroma, hematoma, mesh infection, and enterocutaneous fistula. In addition, mesh placement after kidney transplantations makes the iliac fossa less accessible for future transplant removal or kidney retransplantation in the ipsilateral iliac fossa.

Several studies demonstrated that collagen metabolism disorders such as Marfan and Ehlers-Danlos are strongly associated with development of hernia and with high recurrence rates, making it plausible that hernia is a disease of the extracellular matrix. The extracellular matrix exists mainly out of collagen which is responsible for most of its tensile strength (27). Moreover, AAA is associated with pre-existent collagen deficiencies and systemic fibre degeneration (28). An imbalance between collagen type 1 and type 3 result in aneurysm of the abdominal aorta (29, 30). Hypothetically these deficiencies may affect the whole human body, resulting in weakness of the linea alba or even the whole abdominal wall, causing widening of the linea alba. Hypothetically, this could result in the development of abdominal wall hernia. Patients with an aneurysm are especially known to have a significant risk to develop incisional hernia postoperatively, with literature stating percentages of over 30% in 2.5 - 3 years (31, 32). In **Chapter 7** the anatomical differences of the linea alba were investigated using pre-operative computed tomography-scans of patients with AAA and a control group. Risk factors for development of incisional hernia in correlation with the linea alba were searched and other independent contributing variables associated with the width of the linea alba were analysed.

References

1. Papavramidou NS, Christopoulou-Aletras H. Treatment of "hernia" in the writings of Celsus (first century AD). World J Surg. 2005 Oct;29:1343-7.
2. Doganay E. Sir Astley Paston Cooper (1768-1841): The man and his personality. J Med Biogr. 2015 Nov;23:209-16.
3. Marcy HO. The Cure of Hernia. The Boston Medical and Surgical Journal. 1897;136:381-3.
4. Usher FC, Ochsner J, Tuttle LL, Jr. Use of marlex mesh in the repair of incisional hernias. Am Surg. 1958 Dec;24:969-74.
5. Luijendijk RW, Hop WC, van den Tol MP, et al. A comparison of suture repair with mesh repair for incisional hernia. N Engl J Med. 2000 Aug 10;343:392-8.
6. Timmermans L, Eker HH, Steyerberg EW, et al. Short-term results of a randomized controlled trial comparing primary suture with primary glued mesh augmentation to prevent incisional hernia. Ann Surg. 2015 Feb;261:276-81.
7. Eriksson A, Rosenberg J, Bisgaard T. Surgical treatment for giant incisional hernia: a qualitative systematic review. Hernia. 2014 Feb;18:31-8.
8. Rosen MJ. Polyester-based mesh for ventral hernia repair: is it safe? Am J Surg. 2009 Mar;197:353-9.
9. Ronka K, Vironen J, Kossi J, et al. Randomized Multicenter Trial Comparing Glue Fixation, Self-gripping Mesh, and Suture Fixation of Mesh in Lichtenstein Hernia Repair (FinnMesh Study). Ann Surg. 2015 Nov;262:714-20.
10. Sanders DL, Nienhuijs S, Ziprin P, et al. Randomized clinical trial comparing self-gripping mesh with suture fixation of lightweight polypropylene mesh in open inguinal hernia repair. Br J Surg. 2014 Oct;101:1373-82; discussion 82.
11. Jorgensen LN, Sommer T, Assaadzadeh S, et al. Randomized clinical trial of self-gripping mesh versus sutured mesh for Lichtenstein hernia repair. Br J Surg. 2013 Mar;100:474-81.
12. Lauscher JC, Leonhardt M, Martus P, et al. [Watchful waiting vs surgical repair of oligosymptomatic incisional hernias: Current status of the AWARE study)
13. Bellows CF, Robinson C, Fitzgibbons RJ, et al. Watchful waiting for ventral hernias: a longitudinal study. Am Surg. 2014 Mar;80:245-52.
14. Nieuwenhuizen J, Halm JA, Jeekel J, Lange JF. Natural course of incisional hernia and indications for repair. Scand J Surg. 2007;96:293-6.
15. Nieuwenhuizen J, Kleinrensink GJ, Hop WC, et al. Indications for incisional hernia repair: an international questionnaire among hernia surgeons. Hernia. 2008 Jun;12:223-5.
16. Lauscher JC, Rieck S, Loh JC, et al. Oligosymptomatic vs. symptomatic incisional hernias--who benefits from open repair? Langenbecks Arch Surg. 2011 Feb;396:179-85.
17. Lauscher JC, Loh JC, Rieck S, et al. Long-term follow-up after incisional hernia repair: are there only benefits for symptomatic patients? Hernia. 2013 Apr;17:203-9.
18. Fitzgibbons RJ, Jr., Giobbie-Hurder A, Gibbs JO, et al. Watchful waiting vs repair of inguinal hernia in minimally symptomatic men: a randomized clinical trial. JAMA. 2006 Jan 18;295:285-92.
19. O'Dwyer PJ, Norrie J, Alani A, et al. Observation or operation for patients with an asymptomatic inguinal hernia: a randomized clinical trial. Ann Surg. 2006 Aug;244:167-73.
20. Pan ML, Chang WP, Lee HC, et al. A longitudinal cohort study of incidence rates of inguinal hernia repair in 0- to 6-year-old children. J Pediatr Surg. 2013 Nov;48:2327-31.
21. Lautz TB, Raval MV, Reynolds M. Does timing matter? A national perspective on the risk of incarceration in premature neonates with inguinal hernia. J Pediatr. 2011 Apr;158:573-7.
22. Baird R, Gholoum S, Laberge JM, Puligandla P. Prematurity, not age at operation or incarceration, impacts complication rates of inguinal hernia repair. J Pediatr Surg. 2011 May;46:908-11.

23. Gollin G, Bell C, Dubose R, et al. Predictors of postoperative respiratory complications in premature infants after inguinal herniorrhaphy. J Pediatr Surg. 1993 Feb;28:244-7.
24. Coren ME, Madden NP, Haddad M, Lissauer TJ. Incarcerated inguinal hernia in premature babies--a report of two cases. Acta Paediatr. 2001 Apr;90:453-4.
25. de Goede B, Eker HH, Klitsie PJ, et al. Incisional hernia after liver transplantation: risk factors and health-related quality of life. Clin Transplant. 2014 Jul;28:829-36.
26. Knight RJ, Villa M, Laskey R, et al. Risk factors for impaired wound healing in sirolimus-treated renal transplant recipients. Clin Transplant. 2007 Jul-Aug;21:460-5.
27. Antoniou SA, Antoniou GA, Granderath FA, Simopoulos C. The role of matrix metalloproteinases in the pathogenesis of abdominal wall hernias. Eur J Clin Invest. 2009 Nov;39:953-9.
28. Henriksen NA, Yadete DH, Sorensen LT, et al. Connective tissue alteration in abdominal wall hernia. Br J Surg. 2011 Feb;98:210-9.
29. Powell JT, Adamson J, MacSweeney ST, et al. Genetic variants of collagen III and abdominal aortic aneurysm. Eur J Vasc Surg. 1991 Apr;5:145-8.
30. Powell JT, Adamson J, MacSweeney ST, et al. Influence of type III collagen genotype on aortic diameter and disease. Br J Surg. 1993 Oct;80:1246-8.
31. Bevis PM, Windhaber RA, Lear PA, et al. Randomized clinical trial of mesh versus sutured wound closure after open abdominal aortic aneurysm surgery. Br J Surg. 2010 Oct;97:1497-502.
32. Henriksen NA, Helgstrand F, Vogt KC, et al. Risk factors for incisional hernia repair after aortic reconstructive surgery in a nationwide study. Journal of Vascular Surgery. 2013;57:1524-30.e3.

1

Part 1

Chapter 2

Open incisional hernia repair with a self-gripping retromuscular Parietex mesh: A retrospective cohort study

J. Verhelst [a], B. de Goede [a], G.J. Kleinrensink [b], J. Jeekel [b], J.F. Lange [a, c], K.H.A. van Eeghem [c]

[a] Erasmus University Medical Center Rotterdam, Department of Surgery, The Netherlands
[b] Erasmus University Medical Center Rotterdam, Department of Neuroscience, The Netherlands
[c] Havenziekenhuis Rotterdam, Department of Surgery, The Netherlands

Int J Surg. 2015 Jan;13:184-8. doi: 10.1016/j.ijsu.2014.11.043. Epub 2014 Dec 10.

Abstract

Introduction: The Rives-Stoppa and component separation technique are considered to be favorable techniques in the treatment of complex incisional hernias. However, mesh-related complications like chronic pain are still a common problem after mesh repair. As a result, a new self-gripping mesh to omit suture fixation has been developed. This study aimed to evaluate the safety and feasibility of the Parietex™ Progrip self-gripping mesh in retromuscular position for the treatment of incisional hernias.

Methods: Patients with incisional hernia who underwent repair between June 2012 and June 2014, using a self-gripping mesh in retromuscular position, were included in the study. All patients visited the outpatient clinic to identify postoperative complications and early recurrence.

Results: A total of 28 consecutive patients with a median age of 48 years were included in the study. Twenty-two patients (79%) were diagnosed with an incisional hernia, of whom nine (32%) had a recurrence. Six patients (21%) had an incisional hernia combined with another abdominal wall hernia. The median follow-up was 12 weeks (IQR: 8e20 weeks). Twenty-three patients (82%) did not report any pain at their final outpatient clinic visit; two patients (7%) reported mild abdominal pain, and three patients (11%) had moderate abdominal pain. None of the 28 patients developed a recurrence during follow-up.

Conclusion: This is the first study concerning the use of a Parietex™ Progrip mesh placed in retromuscular position. The study shows that it is a safe and feasible prosthesis in incisional hernias repair, as short-term recurrence did not occur and adverse events were limited.

Introduction

Incisional hernia repair is one of the most common operations in general surgery. Annually, approximately 350,000 incisional hernia repairs are performed in the United States alone (1). Repair of large incisional hernias is challenging because it is associated with high morbidity and recurrence rates up to 17% [2-5). The current treatment of choice is mesh repair. Recurrent incisional hernia and comorbidities such as obesity, diabetes mellitus, and chronic obstructive pulmonary disease are associated with even higher morbidity and recurrence rates up to 34% (3-6). The Rives-Stoppa technique or the component separation technique with mesh placement (modified Ramirez) are widely accepted techniques for hernia repair of complicated and large incisional hernias and appear to be advantageous compared to other surgical techniques concerning complications and recurrence rates (7-9).

The use of meshes in the retromuscular position for incisional hernia repair reduces the recurrence rates to 0%-15% (9-13) However, it may also result in mesh-related complications, such as infections, seroma, fistulas and chronic pain (7,9,14). It is hypothesized that chronic pain is associated with suture-related nerve entrapment or suture-induced nerve irritation due to fixation of the mesh by sutures.

In an attempt to reduce these mesh-related complications induced by sutures, a new self-gripping mesh (Parietex™ Progrip, Sofradim, Trevoux, France) has been developed, making the use of sutures for mesh repair redundant. This mesh may reduce acute and chronic postoperative pain, as previous studies have suggested a relation between these complaints and the use of sutures (15). This Parietex™ Progrip mesh combines the properties of a Parietex lightweight mesh with a surface coverage of absorbable, polylactic acid (PLA) micro hooks for mesh fixation to the tissue. Human studies of this mesh in inguinal hernia repair have shown promising results with regard to infection, chronic pain and recurrence rates (16-19). Currently, no literature is available regarding the use of a self-gripping mesh in incisional hernia repair. Therefore, the objective of the study was to evaluate the safety and feasibility of the Parietex™ Progrip self-gripping mesh in a retromuscular position for the treatment of incisional hernias.

Material and methods

Patients and data collection

Between June 2012 and June 2014, a retrospective single center cohort study was performed. All patients who underwent incisional hernia repair at the 'Havenziekenhuis', a satellite

hospital of the Erasmus University Medical Center with high expertise in the field of very complex hernia repair, were included and followed at the outpatient clinic. All hernias were diagnosed based on clinical examination at the outpatient clinic. If the examination was inconclusive, ultrasonography or computed tomography was used to confirm the diagnosis. All patients in the study were planned for elective surgical repair. During the study the self-gripping Parietex™ Progrip mesh was the treatment of choice in incisional hernia repair in our hospital.

The following data were collected using the electronic hospital data system and medical charts: age, sex, Body Mass Index (BMI), smoking, Diabetes Mellitus (DM), other comorbidities, American Society of Anesthesiologists score (ASA), indication of repair, surgical technique (Rives-Stoppa or component separation), defect size (cm), mesh size (cm*cm), duration of hospital admission, postoperative pain and adverse events, indication and duration of re-admissions, number of visits at the outpatient clinic, and duration of follow-up. Pain was defined as following: mild (i.e., no use of analgesics), moderate (i.e., daily use of non-steroid anti-inflammatory drugs or weak opioids), or severe (i.e., daily opioid use). All hernias were scored using criteria for definition of complex abdominal wall hernia (20). Missing values are reported as unknown.

Surgical procedure

In all procedures a Rives-Stoppa and/or component separation technique (modified Ramirez technique) was used (8, 21). The previous scar was excised and the hernia sac was identified and opened. In case of multiple defects, all individual defects were connected to create one defect. After adhesiolysis of the omentum and viscera, the rectus sheet was opened. The plane between the posterior fascia and the rectus muscle was dissected to create space for the mesh. The posterior fascia and peritoneum were closed using a slowly absorbable suture. The Parietex™ Progrip mesh was placed over the closed posterior fascia but underneath the abdominal rectus- and oblique muscles. The polylactic acid selfgripping surface of the mesh was placed on the fascia (Fig. 1). No additional sutures or tackers were used to fixate the mesh. In order to reduce tension for tension free closure of the midline, the abdominal rectus muscle was mobilised through an incision in the aponeurosis of the external oblique muscle (component separation technique or modified Ramirez technique). The anterior fascia was closed using a slowly absorbable suture. Additional subcutaneous drains were placed if indicated. All patients were invited to the outpatient clinic at a minimum follow-up of two months to diagnose early recurrence.

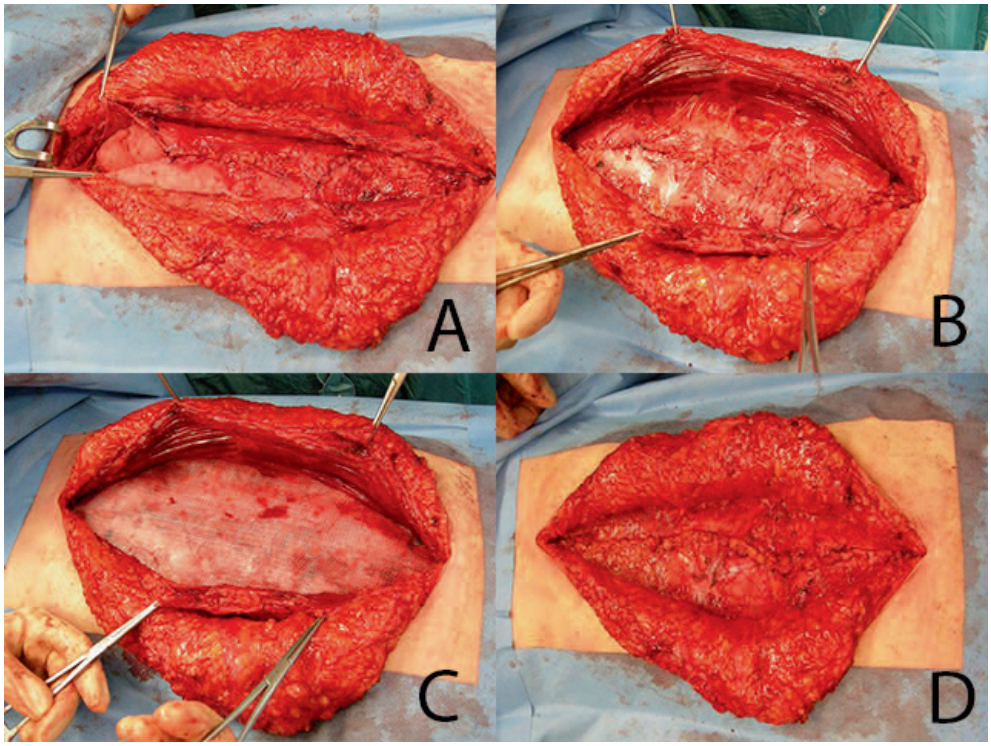


Fig. 1. The Rives-Stoppa technique using the self-gripping mesh. A. Closing the posterior fascia with a running suture. B The retromuscular plane. C. Placement of the mesh on the posterior fascia. D. Closed anterior fascia.

Statistical analyses

Statistical analyses were performed with the SPSS statistical software package (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Categorical variables are presented as numbers with percentage between brackets; continuous variables are presented as medians with Inter Quartile Range (IQR) between brackets. Missing values are reported as unknown.

Results

Patient characteristics

A total of 28 consecutive patients, 18 males and 10 females, with a median age of 48 years (IQR: 40-64 years) were included in the study. The median BMI was 26.8 kg/m2 (IQR: 24.8-29.3 kg/m2). At the time of repair 11 patients (39%) reported smoking and four patients (14%) had DM in their medical history. Five patients (18%) were ASA class I, 22 (79%) were class II and one (4%) was class III.

Hernia characteristics

The hernia characteristics are outlined in Table 1. Twenty-eight patients were diagnosed with an incisional hernia, of whom six (21%) had an incisional hernia combined with another abdominal hernia (parastomal, umbilical or inguinal), and nine (32%) had a recurrence after previous hernia repair. All hernias were complex abdominal wall hernias referring to the criteria of a complex hernia stated by Slater et al. two patients (7%) scored minor severity score, twenty-three (82%) had moderate severity score and three (11%) had a major severe complex abdominal wall hernia.

Table 1. Hernia and procedure characteristics.

	N¼28
Hernia type	
Incisional only	22 (79%)
Combination	6 (21%)
Multiple defects	11 (39%)
Recurrence after previous hernia repair	9 (32%)
Complex hernia severity class	
Minor	2 (7%)
Moderate	23 (82%)
Major	3 (11%)
Defect size	
0-4.99 cm	8 (29%)
5-9.99 cm	6 (21%)
≥ 10 cm	13 (46%)
Unknown	1 (3%)
Mesh size	
20*15 cm	10 (36%)
30*15 cm	18 (64%)
Drains used	26 (93%)

All data are presented as number (percentage).

Twenty-three patients (82%) were planned for repair because of a symptomatic hernia and two (7%) patients because of hernia growth. One patient (4%) required a surgical revision because of a mesh infection after primary hernia repair elsewhere, one patient (4%) had sanitary problems due to a parastomal hernia, and one patient (4%) had signs of incarceration. All patients were operated in an elective setting with an open technique under general anesthesia.

Surgical procedure and hospital stay

In 18 patients (64%) a Rives-Stoppa procedure was performed, in seven patients (25%) a bilateral component separation technique and in three patients (11%) a unilateral component separation technique. In three patients the mesh of previous repair needed to

be removed. Two patients needed a small bowel resection due to multiple serosa injuries during adhesiolysis, and one patient had an additional repair of his inguinal hernia in the same setting. In 18 procedures the size of the mesh was 30*15 cm. In the other ten cases a smaller mesh of 20*15 cm was placed in order to gain a minimum overlap of 5 cm. Acute postoperative pain was controlled with an epidural catheter. The median hospital stay was five days (IQR: 4-7 days).

Follow-up and adverse events

The median follow-up was 12 weeks (IQR: 8-20 weeks) in which the median number of outpatient clinic visits was four (IQR: 3-6). None of the 28 patients had a recurrence during follow-up.

Three patients had adverse events during primary hospital admission. One patient had an extended hospital stay of 17 days because of postoperative ileus, treated conservatively; one suffered from postoperative angina pectoris, another patient had postoperative pneumonia, successfully treated with antibiotics. Five patients were diagnosed with a postoperative seroma; one was treated with an ultrasound-guided punction and four patients were treated conservatively.

Seven patients had an adverse event during outpatient follow-up. Four patients were readmitted to the hospital for various reasons. One was readmitted for 5 days because of administering intravenous antibiotics for the treatment of wound and a mesh infection. The other two patients were admitted for diagnostic imaging of late abdominal complaints and ileus, which could not be explained by the surgical intervention. None of the patients died during follow-up.

At the final visit at the outpatient clinic 23 patients (82%) were without pain. Two patients (7%) had mild abdominal pain without use of analgesics; three patients (11%) used daily analgesics for moderate abdominal pain. None of the patients suffered from severe pain.

Discussion

This retrospective cohort of 28 consecutive patients is the first study that shows promising results in the use of a self-gripping Parietex™ Progrip mesh in incisional hernia repair, as none of the patients in this study had a recurrence after a median follow-up of three months. Previous studies have demonstrated a wide variation of recurrence rates 0-30% for incisional hernia repair using mesh in retro-muscular position (9-13). In the current study incisional hernias were all complex hernias regarding to the criteria. These hernias are expected to increase the perioperative risks, complications and recurrence rates (20). Hence, the use of the Parietex™ Progrip mesh has shown to be feasible even in these complex patients.

The use of a self-gripping Parietex™ Progrip mesh has also proven to be a safe procedure, as five patients in this study had a mesh related adverse event. Post-operative seroma was the most frequent complication in our study group (18%). This is slightly higher compared to previously reported rates (4%-16%) for seroma in open incisional hernia repair (9, 14, 22-24). However, the complexity of the hernia and the fact that seroma only once required an intervention make this rate acceptable. Current literature on the 30 days readmission rates varies up to 13.3% for incisional hernia repair which corresponds with data in this study (23, 25).

Self-gripping meshes in open and laparoscopic inguinal hernia repair have already shown promising results, including lower infection rates, less chronic pain and lower recurrence rates (16-19). Recently published data show a significant reduction in pain after inguinal hernia repair in the first week postoperatively (17). In this study postoperative pain levels were adequately low; only few patients had complaints of mild to moderate abdominal pain.

Besides the retrospective nature of the study, a limitation of this study is the relatively small sample size. However, the results of this very first report correspond with earlier reported data of open incisional hernia repair. Furthermore, the follow-up in the current study was relatively short compared to other studies with a longer follow-up (21-52 months) describing open incisional hernia repair using the Rives-Stoppa or component separation technique (7). This study collected data with a median follow-up of 12 weeks, as it is believed that most adverse events in this group of complex patients as postoperative complications and recurrences due to the use of the self-gripping mesh will occur during the first three months. During the study the self-gripping Parietex™ Progrip mesh was the treatment of choice in incisional hernia repair in our hospital. Hence, there was no patient selection. To give an adequate impression of post-operative pain the use of analgesic drugs in time of OPC visit was analysed. This was the only quantified measurement that could be collected from retrospective data. The direct post-operative pain was mostly treated with an epidural catheter. Therefore, the direct postoperative pain scales were unreliable. All patients were discharged from follow-up without a clinical recurrence. Furthermore none of the patients returned to the hospital with a late recurrence. Because the studies on the use of a selfgripping mesh in inguinal hernia repair show a reduction in duration of the surgical procedure, it is expected that the use of this self-gripping mesh in open incisional hernia repair may also reduce the operating time. However, these data could not be collected in the current study.

Although this study is a retrospective single center cohort study with a limited number of patients, it is the first study cohort that describes the use of a self-gripping mesh in incisional hernia repair. To determine the added value of the suture-less repair with this self-gripping mesh further randomised prospective studies with long-term follow-up need to be conducted.

Keeping these limitations in mind, this study promisingly shows that the Parietex™ Progrip mesh placed in a retromuscular position appears to be safe and feasible for open incisional hernia repair with minimal postoperative sequela and no recurrences within in the short term follow-up.

References

1. B.K. Poulose, J. Shelton, S. Phillips, D. Moore, W. Nealon, D. Penson, W. Beck, M.D. Holzman, Epidemiology and cost of ventral hernia repair: making the case for hernia research, Hernia 16 (2012) 179-183.
2. U.A. Dietz, M.S. Winkler, R.W. Hartel, A. Fleischhacker, A. Wiegering, C. Isbert, C. Jurowich, P. Heuschmann, C.T. Germer, Importance of recurrence rating, morphology, hernial gap size, and risk factors in ventral and incisional hernia classification, Hernia 1 (2014) 19-30.
3. R.W. Luijendijk, W.C. Hop, M.P. van den Tol, D.C. de Lange, M.M. Braaksma, J.N. IJ, R.U. Boelhouwer, B.C. de Vries, M.K. Salu, J.C. Wereldsma, C.M. Bruijninckx, J. Jeekel, A comparison of suture repair with mesh repair for incisional hernia, N. Engl. J. Med. 343 (2000) 392-398.
4. F.P. Albino, K.M. Patel, M.Y. Nahabedian, M. Sosin, C.E. Attinger, P. Bhanot, Does mesh location matter in abdominal wall reconstruction? A systematic review of the literature and a summary of recommendations, Plast. Reconstr. Surg. 132 (2013) 1295-1304.
5. T.S. de VriesReilingh, H. van Goor, C. Rosman, M.H. Bemelmans, D. de Jong, E.J. van Nieuwenhoven, M.I. van Engeland, R.P. Bleichrodt, "Components separation technique" for the repair of large abdominal wall hernias, J. Am. Coll. Surg 196 (2003) 32-37.
6. D.M. Krpata, J.A. Blatnik, Y.W. Novitsky, M.J. Rosen, Evaluation of high-risk, comorbid patients undergoing open ventral hernia repair with synthetic mesh, Surgery 153 (2013) 120-125.
7. A. Eriksson, J. Rosenberg, T. Bisgaard, Surgical treatment for giant incisional hernia: a qualitative systematic review, Hernia 1 (2013) 31-38.
8. E.M. Pauli, M.J. Rosen, Open ventral hernia repair with component separation, Surg. Clin. North Am. 93 (2013) 1111-1133.
9. T.S. de VriesReilingh, H. van Goor, J.A. Charbon, C. Rosman, E.J. Hesselink, G.J. van der Wilt, R.P. Bleichrodt, Repair of giant midline abdominal wall hernias: "components separation technique" versus prosthetic repair: interim analysis of a randomized controlled trial, World J. Surg. 31 (2007) 756-763.
10. O.M. Ramirez, E. Ruas, A.L. Dellon, "Components separation" method for closure of abdominal-wall defects: an anatomic and clinical study, Plast. Reconstr. Surg. 86 (1990) 519-526.
11. J.N. DiBello Jr., J.H. Moore Jr., Sliding myofascial flap of the rectus abdominus muscles for the closure of recurrent ventral hernias, Plast. Reconstr. Surg. 98 (1996) 464-469.
12. J.A. Girotto, M.J. Ko, R. Redett, T. Muehlberger, M. Talamini, B. Chang, Closure of chronic abdominal wall defects: a long-term evaluation of the components separation method, Ann. Plast. Surg. 42 (1999) 385-394 discussion 394-385.
13. K.C. Shestak, H.J. Edington, R.R. Johnson, 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. 105 (2000) 731-738 quiz 739.
14. M.J. Rosen, Polyester-based mesh for ventral hernia repair: is it safe? Am. J. Surg. 197 (2009) 353-359.
15. H. Paajanen, Do absorbable mesh sutures cause less chronic pain than nonabsorbable sutures after Lichtenstein inguinal herniorraphy? Hernia 6 (2002) 26-28.
16. P. Chastan, Tension-free open hernia repair using an innovative self-gripping semi-resorbable mesh, Hernia 13 (2009) 137-142.
17. A. Kingsnorth, M. Gingell-Littlejohn, S. Nienhuijs, S. Schule, P. Appel, P. Ziprin, A. Eklund, M. Miserez, S. Smeds, Randomized controlled multicenter international clinical trial of self-gripping ParietexProGrip polyester mesh versus lightweight polypropylene mesh in open inguinal hernia repair: interim results at 3 months, Hernia 16 (2012) 287-294.
18. N. Pedano, C. Pastor, J. Arredondo, I. Poveda, J. Ruiz, S. Monton, M. Molina, J.L. Hernandez-Lizoain, Open tension-free hernioplasty using a novel lightweight self-gripping mesh: medium-term experience from two institutions, Langenbecks Arch. Surg. 397 (2012) 291-295.

19. D. Birk, S. Hess, C. Garcia-Pardo, Low recurrence rate and low chronic pain associated with inguinal hernia repair by laparoscopic placement of ParietexProGrip mesh: clinical outcomes of 220 hernias with mean follow-up at 23 months, Hernia 17 (2013) 313-320.
20. N.J. Slater, A. Montgomery, F. Berrevoet, A.M. Carbonell, A. Chang, M. Franklin, K.W. Kercher, B.J. Lammers, E. Parra-Davilla, S. Roll, S. Towfigh, E. van Geffen, J. Conze, H. van Goor, Criteria for definition of a complex abdominal wall hernia, Hernia 18 (2014) 7-17.
21. J.J. Bauer, M.T. Harris, S.R. Gorfine, I. Kreel, Rives-Stoppa procedure for repair of large incisional hernias: experience with 57 patients, Hernia 6 (2002) 120-123.
22. R.F. Williams, D.F. Martin, M.T. Mulrooney, G.R. Voeller, Intraperitoneal modification of the Rives-Stoppa repair for large incisional hernias, Hernia 12 (2008) 141-145.
23. C.W. Iqbal, T.H. Pham, A. Joseph, J. Mai, G.B. Thompson, M.G. Sarr, Long-term outcome of 254 complex incisional hernia repairs using the modified RivesStoppa technique, World J. Surg. 31 (2007) 2398-2404.
24. H.M. Kaafarani, K. Hur, A. Hirter, L.T. Kim, A. Thomas, D.H. Berger, D. Reda, K.M. Itani, Seroma in ventral incisional herniorrhaphy: incidence, predictors and outcome, Am. J. Surg. 198 (2009) 639-644.
25. F. Helgstrand, J. Rosenberg, H. Kehlet, L.N. Jorgensen, T. Bisgaard, Nationwide prospective study of outcomes after elective incisional hernia repair, J. Am. Coll. Surg. 216 (2013) 217-228.

Chapter 3

Watchful waiting in incisional hernia: Is it safe?

J. Verhelst, MD, [a] L. Timmermans, MD, PhD, [a] M. van de Velde, MSc, [a] A. Jairam, MD, [a]
K.A. Vakalopoulos, MD, [a] J. Jeekel, MD, PhD and J.F. Lange, MD, PhD, [a]

[a] Departments of Surgery Erasmus University Medical Center, Rotterdam, The Netherlands
[b] Departments of Neuroscience Erasmus University Medical Center, Rotterdam, The Netherlands

Surgery. 2015 Feb;157(2):297-303. doi: 10.1016/j.surg.2014.09.017.

Abstract

Background: Incisional hernia (IH) is among the most common postoperative complications after abdominal surgery. Operative treatment (OT) using mesh is the treatment of choice. A strategy of watchful waiting (WW) might be a considered in some patients. This retrospective study compares the outcomes of WW and OT.

Methods: All patients presenting with IH in an academic surgery department between January 2004 and December 2009 were analyzed according to whether they were treated by WW or OT. Crossovers between both groups were also analyzed. Patient characteristics, information about the initial abdominal operative procedure, symptoms at presentation, and characteristics of the hernia were collected retrospectively. In case of OT, postoperative complications were analyzed.

Result: In total, 255 patients were included; 151 (59%) in the OT group and 104 (41%) in WW group. The median follow-up was 68 months (interquartile range [IQR], 52–93). The reasons for WW were the absence of symptoms in 34 patients (33%), comorbidities in 24 (23%), and obesity in 23 (22%). During follow-up, 34 patients (33%) crossed over from WW to OT. Eight of the crossovers (24%) were emergency repairs owing to incarceration at a median of 1 month (IQR, 1–5 months) after the start of WW. The incidence of unexpected intraoperative intestinal perforation was greater in the crossover group (13%) compared with the OT group (2%; P = 0.002). Postoperative fistulas were seen in 7% of patients who crossed over from WW to OT versus 0% in primary OT (P = 0.002). Postoperatively, 3 patients died, 2 of whom were treated operatively after belonging initially to the WW group.

Conclusion: WW for IH leads to high crossover rates with significantly greater incidence of intraoperative perforations, fistulas, and mortality, than in the OT group, particularly in patients who require emergency repair of IH owing to incarceration.

Introduction

Incisional hernia (IH) is among the most common complications after abdominal surgery. Incidences of IH range from 11 to 20% and are even greater in high-risk groups (1-3). In the United States alone, about 100,000 IH are treated each year (4). After many years of research, the treatment of choice is mesh repair (5). However, recurrence rates after mesh repair are still unacceptable high, with a 10-year cumulative incidence rate of <32% (6). The use of mesh facilitates the possibility of mesh-related complications, such as wound infection (6–10%), mesh infection (1–4%), and formation of seroma (30%), hematoma (7.5%), and fistulas (0.5–3.5%) resulting in need potentially for mesh explantation (5.1%) and/or complex abdominal wall wounds (6-13). Recently, operative treatment (OT) of patients with minimally symptomatic IH has been questioned (14). Patients who were treated for IH who preoperatively had no or minimal symptoms suffered postoperatively from clinically relevant pain after short- and long-term follow-up. The question is whether conservative treatment or watchful waiting (WW) is an option in IH patients. WW for IH as an option has never been investigated properly, and outcomes are unknown. Various symptoms and indications regarding IH repair and its natural course are mentioned in literature. Nevertheless, published data describing accurately these symptoms, indications, and outcomes of WW in IH is lacking (15). In inguinal hernia, cost effectiveness and safety have already led to implementation of WW (16-18). Despite the high incidence of minimally symptomatic inguinal hernia undergoing surgical repair in the following 10 years (19). Because of this controversy, we conducted a retrospective study to evaluate the value of WW in IH, incentives for OT or WW, outcome of these approaches, and potential crossovers between the groups. The aim of the study was to compare the outcomes of WW and OT in patients with IH.

Methods

A single-center, retrospective study was performed. All patients who presented with IH between January 2004 and December 2009 at the Erasmus University Medical Center Rotterdam were included. The study cohort was retrieved via review of the medical records involving both the electronic hospital data systems and patient records. All patients were identified by searching the electronic hospital database for DBC Codes (Diagnose Behandel Combinatie; Diagnosis Related Groups (DRGs)) and followed until a minimum follow-up of 3 years was reached. The median follow-up of the entire group was 68 months (interquartile range (IQR), 52–93).

According to the primary management of the hernia patients were divided into 2 groups: Patients who were managed with WW and a group of patients who were planned for elective OT. Some of the patients in the initial WW group, however, underwent surgical repair during follow-up. In addition, for some of the patients in the OT group, either the patient or the surgeon decided to cancel the operation and switch to WW. These crossovers between both groups were analyzed individually. Patients who presented with incarcerated IH and required an emergency operation were excluded because WW had never been an option.

The following data were collected retrospectively through patient records review: Patient characteristics (sex, age at diagnosis, body mass index, smoking, and medical history). Information about the initial abdominal operative procedure was collected and analyzed for type of operation (gastrointestinal, gynecologic, vascular, urologic, trauma, and others), admission to intensive care unit, and postoperative complications.

The symptoms at presentation were divided into categories (pain, signs of incarceration, nausea, aesthetic complaints, difficulties with defecation, inconvenience during daily activities, and absence of symptoms). If the patient had >1 symptom at presentation, all symptoms were scored. The hernia size was collected if an objective measurement was available in the medical records.

Patients with IH who underwent OT, postoperative complications (surgical site infection, other infections, abscess, postoperative ileus, perforation, and fistula) were scored. For patients undergoing WW, the reasons for WW were divided into categories (absence of symptoms, comorbidity, obesity, large hernia size, and patient preference). If there were more reasons for WW, all potential reasons were scored separately.

Statistical analyses were performed with the SPSS statistical software package (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY). Levene's test for equality of variances was used to assess normality of continuous data. Continuous variables are presented either as medians with IQRs and or as means with standard deviations (SD) depending on the normality of data distribution. Categorical variables are presented as numbers with percentages (%). Differences between the 2 groups were compared using a Mann– Whitney U test (continuous data) or a Chi-square test (categorical data). Time to crossover was calculated using life-table methods. $P < 0.05$ was considered significant.

Results

A total of 255 eligible patients with IH were identified in the hospital database. Seven patients (3%) were excluded from analysis because they presented with incarcerated IH and needed emergency OT. At presentation with IH, 151 patients (59%) were planned for elective OT. In 104 patients (41%), WW was chosen. In the WW group, 34 patients (33%) eventually underwent OT during follow-up; 8 of these patient crossovers (24%) required emergency operation owing to incarceration. Furthermore, 11 patients (7%) withdrew from OT and switched to the WW group (Fig 1).

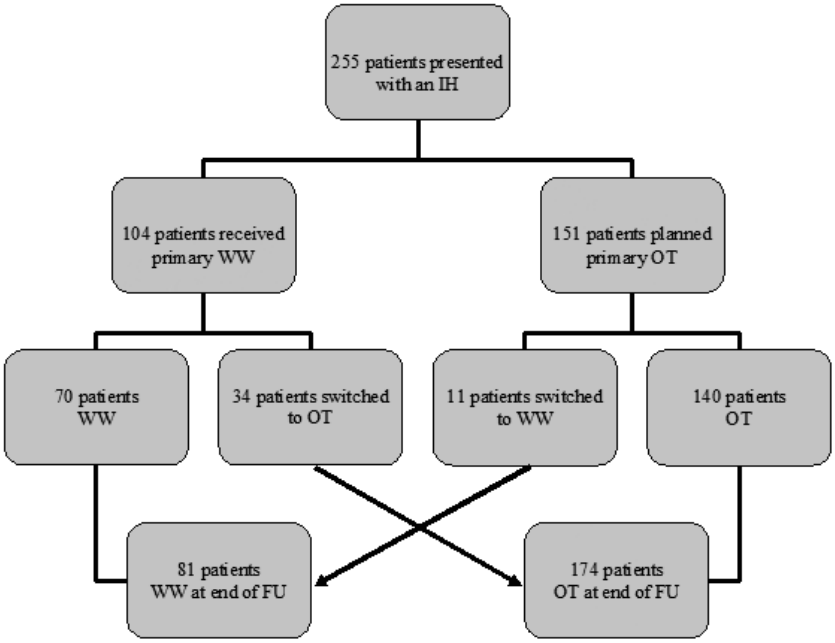


Fig 1. Flow diagram depicting patient acquisition. FU, Follow-up; IH, incisional hernia; OT, operative treatment; WW, watchful waiting

Patient characteristics. Baseline demographic characteristics of the initial WW and OT groups are given in Table 1. At the time of diagnosis, the mean age was 58 years (SD 13) in the WW group and 53 years (SD 13) in the OT group (P = 0.003). At the time of presentation, 20% of the patients in the WW group and 34% in the OT group reported smoking (P = 0.020). Gastrointestinal surgery was the initial type of operation leading to IH in 64% in the WW group versus 51% in the OT group (P = 0.035). There were no other differences in baseline characteristics, medical history, and types of operations, comorbidities, or complications after the initial operation leading to IH.

Table 1. Patient characteristics

Characteristic	Watchful waiting (n = 104)	Operative treatment (n = 151)	P value
Age (SD)	58 (13.0)	53 (13.2)	.009
Female (%)	53 (51)	72 (47.7)	.607
BMI (SD)	28.5 (6.5)	27.7 (5.6)	.424
Smoking (%)	17 (19.8)	51 (34)	.02
Initial type of operation (%)			
Gastrointestinal	66 (64.1)	77 (51.0)	.034
Urology	12 (11.7)	24 (15.9)	.268
Vascular	6 (11.7)	16 (10.6)	.13
Gynecology	9 (8.7)	18 (11.9)	.213
Trauma	1 (1.0)	1 (0.7)	.65
Other	9 (8.7)	15 (9.9)	.454
Medical history (%)			
COPD	17 (17.5)	20 (13.3)	.367
Malignancy	33 (34.4)	44 (29.5)	.425
AAA	6 (6.2)	11 (7.4)	.718
Corticosteroid use	19 (19.8)	29 (19.3)	.929
Stoma	14 (14.1)	13 (8.7)	.18
Initial admission data			
ICU admission	19 (20.7)	37 (26.6)	.3
SSI	19 (20.7)	21 (15.1)	.276
Postoperative fistula	0 (0)	3 (2.2)	.156
Abscess	8 (8.7)	13 (9.4)	.524
Ileus	4 (4.3)	5 (3.6)	.773
Pneumonia	2 (2.2)	11 (8.0)	.062
Anastomotic leakage	6 (6.5)	6 (4.3)	.46

AAA, Abdominal aortic aneurysm; BMI, Body mass index; COPD, chronic pulmonary obstructive disease; ICU, intensive care unit; SSI, surgical site infection.

Hernia characteristics. The operation characteristics of the hernias are outlined in Table 2. The median time between initial abdominal operation and the presentation with IH was 15 months (IQR, 7–39). The mean hernia size was 7.0 cm (SD 5.7) in the WW group and 6.4 cm (SD 4.7) in the OT group (P = 0.625). Patients who presented with asymptomatic IH were more often assigned to the WW group (23% vs 2%; P = 0.001).

WW group. In total, 104 patients were assigned to the WW group. In 39 patients (38%), the absence of symptoms was the reason to choose for WW. Obesity and comorbidities were reasons for WW strategy in 24 (23%) and 23 (22%) patients, respectively. Eleven patients (11%) refused OT and in 4 patients (4%) the large size of the hernia was the decisive factor leading to WW.

Table 2. Hernia characteristics

Characteristics	WW	OT	P value
Size in cm (SD)	7.0 (5.7)	6.4 (4.7)	.652
Symptoms at presentation (%)			
No symptoms	23 (23.2)	2 (1.4)	.000
Pain	38 (38.4)	73 (49.3)	.09
Signs of incarceration	2 (2.0)	3 (2.0)	.997
Nausea	1 (1.0)	4 (2.7)	.355
Aesthetic considerations	14 (14.1)	28 (18.9)	.327
Defecation difficulties	23 (23.2)	40 (27.0)	.503
Limitations daily activity	5 (5.1)	8 (5.4)	.573

WW, watchful waiting. OT, Operative treatment.

During follow-up, 34 patients (33%) crossed over to the OT group. The median time to crossover from the WW group to the OT group was 21 weeks (IQR, 2–53). The majority of the patients (94%) crossed-over from WW to OT in the first 24 months after diagnosis (Fig 2). Eight patients (24%) were operated in an emergency setting with incarceration of the hernia at a median follow-up of 1 months (IQR, 1–5) and 13 patients (38%) crossed to OT, because they developed increased abdominal pain without signs of incarceration at a median of 7 months (IQR, 1–18) of WW. Six patients (18%) were not satisfied with WW, 3 (9%) lost weight preoperatively, and 4 (12%) had an increase of hernia size or aesthetic complaints.

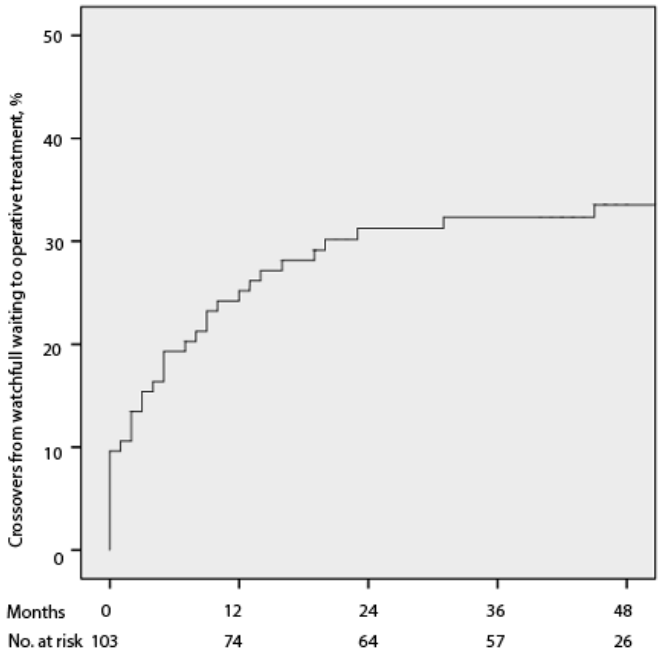


Fig 2. Probability to crossover from watchful waiting to operative treatment.

Asymptomatic patients in WW group. Thirty-nine patients (38%) were assigned to the WW group because of an asymptomatic hernia. Twelve patients (31%) crossed over from the WW to the OT group at a median of 7 months (IQR, 2–10) of WW. One patient (of 39) needed emergency OT because of an incarceration. Seven patients became symptomatic or developed abdominal pain during follow-up, 3 patients had progression of the size of the hernia or had aesthetic complaints, and one was not satisfied with WW.

OT group. In total, 151 patients were planned for elective OT of whom 140 patients underwent the surgical procedure after a median of 14 weeks (IQR, 8–22). The remaining 11 patients (7%) crossed over to WW; 6 patients (55%) crossed over to WW, because their IH became of less importance with regard to their comorbidities, 4 (36%) decided to not undergo OT, and 1 was cancelled because of increased operation risk owing to obesity.

Morbidity and mortality. The complications are summarized in Table 3. Between diagnosis and follow-up, 43 patients died, 24 (23%) in the WW group and 19 (13%) in the OT group. The incidence of intraoperative intestinal perforations (operative trauma, ischemic bowel, etc.) was 13% in the crossover group compared versus 2% in the OT group (P = 0.002). The incidence of postoperative fistulas was 7% in patients who crossed over from WW to OT versus 0% in the OT group (P = 0.003). During follow-up, 19 patients (13%) died in the OT group and 24 (23%) in the WW group (P = 0.003). Three patients died postoperatively; 2 patients were initially treated by WW but required emergency surgical repair owing to incarceration of the hernia and 1 patient died after elective OT (P = 0.035). The death of the other 40 patients during follow-up was not related to IH.

Table 3. Morbidity and mortality after incisional hernia (IH) repair

Characteristic	WW-> OT	OT	P value
Overall morbidity (%)	9 (29)	22 (17)	.141
SSI (%)	0 (0)	7 (5)	.192
Fistula (%)	2 (6.5)	0 (0)	.003
Abscess (%)	0 (0)	4 (3)	.328
Intraoperative perforation (%)	4 (13)	2 (2)	.002
Postoperative ileus (%)	0 (0)	3 (2)	.397
Infection (%)	2 (6)	4 (3)	.358
IH-related mortality (%)	2 (6.1)	1 (0.7)	.035

OT, Operative treatment; SSI, surgical site infection; WW, watchful waiting.

Discussion

This is the first study that offers a closer look into the conservative treatment of IH---the WW approach. The study describes the incentives to choose between OT and the natural history of WW. In our study, we found a high rate of crossover from WW to OT, and greater morbidity and mortality. Eight patients (8%) in the WW group eventually required emergency treatment, usually within the first 2 years after the start of WW.

The decision for OT or WW was made by individual surgeons in the hospital; no standard protocols were used for decision making. According to the medical charts, the decisions whether to operate or not were based on the patient's medical history, characteristic of the hernia, and the presence or absence of symptoms at presentation. A questionnaire sent among renowned surgeons in IH repair demonstrated that pain and limitations during daily activities were considered the most important indications for repair; aesthetic complaints were considered least important (20). In our study, the absence of symptoms was greater, as expected in the WW group. Patients with episodes of pain tend to be scheduled more frequently for elective OT, although this difference was not significant in our study.

During the study, 43 patients died between diagnosis and follow-up. We presume that the greater number of patients in the WW group that died during the follow-up period is a reflection of a worse general health status of these patients. The greater age of the patients in the WW group also likely contributed to the greater mortality in the WW group.

In our study, 33% of the WW patients switched to OT after a median of 21 weeks of WW (IQR, 2–53). Eight of these patients initially treated by WW required an emergency operation that led to significantly more postoperative complications (i.e., bowel perforations and postoperative fistulas). Two of the 8 patients in the crossover group died during their hospital admission after an emergency operation. Although the absolute numbers are small, the risks for poor early outcomes after emergency operative intervention, such as postoperative mortality, recurrence, and readmissions, have been described previously (21-23). In contrast, 70 patients (67%) in the WW group never needed operative repair during a median follow-up of 66 months of WW (IQR, 46–86) and therefore have not been at risk for any postoperative complication. The asymptomatic patients in the WW group nearly have the same crossover rates as the whole WW group, 31% versus 33%, respectively; in contrast, the emergency repair rates appear to be less; 8% in the OT group versus 24% in the WW group. A large, nationwide, prospective cohort comparing emergency and elective incisional hernia repair showed a 30-day mortality of 6.4% (21). An explanation for the greater 30-day mortality in our group may be that a number of these patients were assigned to WW owing to comorbidity

(23%) and obesity (22%). Furthermore, patients who presented with incarcerated IH were excluded from our study. In case of emergency repair, it is likely that these crossover patients have a greater risk of morbidity and mortality than relatively healthy patients. Therefore, controlled elective treatment of complex and compromised patients should be considered to prevent emergency repair. Although smoking is an independent risk factor for readmission and complications after IH repair, there were significantly more patients who smoked in the initial OT group (24). This factor indicates that smoking does not contribute to the decision whether or not to operate. The majority of patients who switched from WW to OT did so during the first 24 months after diagnosis of IH.

Our study has limitations, most of which are attributable to its retrospective design. It may be that patients in the WW group underwent OT elsewhere. This possibility might contribute to a selection bias and lead to an underestimation of crossovers and hernia-related morbidity and mortality. This study does not provide data regarding quality of life or long-term follow-up. A recent study showed no deterioration in quality of life in a cohort of patients assigned to WW (25). Standard follow-up, which includes long-term follow-up of both groups and more data about quality of life, might strengthen the results of further studies and might provide more insight into safety and cost effectiveness of WW in IH. We have to be careful to draw general conclusions from the patient's characteristics because of the heterogeneity of the selected patient groups and the absence of decision-making tools (guidelines or protocols for the treatment of IH). There is a need for valid guidelines on the management of asymptomatic IH. Therefore, international collaboration and prospective, randomized trials are necessary. A current, randomized, prospective trial comparing OT with WW in minimally and asymptomatic IH should be awaited before drawing general conclusions (26). Patients who are treated conservatively should be informed and aware of potential risks of need for emergency repair resulting in greater morbidity and mortality.

In conclusion, WW strategy in IH leads to one third crossover rates with a greater risk of postoperative sequelae, especially in those patients who require emergency repair of IH. Controlled elective treatment of IH can be considered to prevent emergency repair.

References

1. Bevis PM, Windhaber RA, Lear PA, Poskitt KR, Earnshaw JJ, Mitchell DC. Randomized clinical trial of mesh versus sutured wound closure after open abdominal aortic aneurysm surgery. Br J Surg 2010;97:1497-502.
2. van 't Riet M, Steyerberg EW, Nellensteyn J, Bonjer HJ, Jeekel J. Meta-analysis of techniques for closure of midline abdominal incisions. Br J Surg 2002;89:1350-6.
3. Wissing J, van Vroonhoven TJ, Schattenkerk ME, Veen HF, Ponsen RJ, Jeekel J. Fascia closure after midline laparotomy: results of a randomized trial. Br J Surg 1987;74:738-41.
4. Sanders DL, Kingsnorth AN. The modern management of incisional hernias. BMJ 2012;344:e2843.
5. Luijendijk RW, Hop WC, van den Tol MP, de Lange DC, Braaksma MM, IJzermans JN, et al. A comparison of suture repair with mesh repair for incisional hernia. N Engl J Med 2000;343:392-8.
6. Burger JW, Luijendijk RW, Hop WC, Halm JA, Verdaasdonk EG, Jeekel J. Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia. Ann Surg 2004;240:578-83.
7. Abdollahi A, Maddah GH, Mehrabi BM, Jangjoo A, Forghani MN, Sharbaf N. Prosthetic incisional hernioplasty: clinical experience with 354 cases. Hernia 2010;14:569-73.
8. Canziani M, Frattini F, Cavalli M, Agrusti S, Somalvico F, Campanelli G. Sutureless mesh fibrin glue incisional hernia repair. Hernia 2009;13:625-9.
9. Hawn MT, Gray SH, Snyder CW, Graham LA, Finan KR, Vick CC. Predictors of mesh explantation after incisional hernia repair. Am J Surg 2011;202:28-33.
10. Klinge U, Conze J, Krones CJ, Schumpelick V. Incisional hernia: open techniques. World J Surg 2005; 29:1066-72.
11. Leber GE, Garb JL, Alexander AI, Reed WP. Long-term complications associated with prosthetic repair of incisional hernias. Arch Surg 1998;133:378-82.
12. Sanchez VM, Abi-Haidar YE, Itani KM. Mesh infection in ventral incisional hernia repair: incidence, contributing factors, and treatment. Surg Infect (Larchmt) 2011;12:205-10.
13. den Hartog D, Dur AH, Tuinebreijer WE, Kreis RW. Open surgical procedures for incisional hernias. Cochrane Database Syst Rev 2008:CD006438.
14. Lauscher JC, Loh JC, Rieck S, Buhr HJ, Ritz JP. Long-term follow-up after incisional hernia repair: are there only benefits for symptomatic patients? Hernia 2013;17:203-9.
15. Nieuwenhuizen J, Halm JA, Jeekel J, Lange JF. Natural course of incisional hernia and indications for repair. Scand J Surg 2007;96:293-6.
16. Collaboration IT. Operation compared with watchful waiting in elderly male inguinal hernia patients: a review and data analysis. J Am Coll Surg 2011;212:251-259.e1-4.
17. Fitzgibbons RJ Jr, Giobbie-Hurder A, Gibbs JO, Dunlop DD, Reda DJ, McCarthy M Jr, et al. Watchful waiting vs repair of inguinal hernia in minimally symptomatic men: a randomized clinical trial. JAMA 2006;295:285-92.
18. Stroupe KT, Manheim LM, Luo P, Giobbie-Hurder A, Hynes DM, Jonasson O, et al. Tension-free repair versus watchful waiting for men with asymptomatic or minimally symptomatic inguinal hernias: a cost-effectiveness analysis. J Am Coll Surg 2006;203:458-68.
19. Fitzgibbons RJ Jr, Ramanan B, Arya S, Turner SA, Li X, Gibbs JO, et al. Long-term results of a randomized controlled trial of a nonoperative strategy (watchful waiting) for men with minimally symptomatic inguinal hernias. Ann Surg 2013;258:508-15.
20. Nieuwenhuizen J, Kleinrensink GJ, Hop WC, Jeekel J, Lange JF. Indications for incisional hernia repair: an international questionnaire among hernia surgeons. Hernia 2008;12:223-5.

21. Helgstrand F, Rosenberg J, Kehlet H, Bisgaard T. Outcomes after emergency versus elective ventral hernia repair: a prospective nationwide study. World J Surg 2013;37:2273-9.

22. Martinez-Serrano MA, Pereira JA, Sancho JJ, Lopez-Cano M, Bombuy E, Hidalgo J, et al. Risk of death after emergency repair of abdominal wall hernias. Still waiting for improvement. Langenbecks Arch Surg 2010;395:551-6.

23. Derici H, Unalp HR, Bozdag AD, Nazli O, Tansug T, Kamer E. Factors affecting morbidity and mortality in incarcerated abdominal wall hernias. Hernia 2007;11:341-6.

24. Lovecchio F, Farmer R, Souza J, Khavanin N, Dumanian GA, Kim JY. Risk factors for 30-day readmission in patients undergoing ventral hernia repair. Surgery 2014; 155:702-10.

25. Bellows CF, Robinson C, Fitzgibbons RJ, Webber LS, Berger DH. Watchful waiting for ventral hernias: a longitudinal study. Am Surg 2014;80:245-52.

26. Lauscher JC, Martus P, Stroux A, Neudecker J, Behrens U, Hammerich R, et al. Development of a clinical trial to determine whether watchful waiting is an acceptable alternative to surgical repair for patients with oligosymptomatic incisional hernia: study protocol for a randomized controlled trial. Trials 2012;13:14.

Part 2

Chapter 4

Very Low Birth Weight Is an Independent Risk Factor for Emergency Surgery in Premature Infants with Inguinal Hernia

J. Verhelst, MD[a], B. de Goede, MD[a], B.J. van Kempen, MD[b], M.G. Baartmans, MD, PhD[c], H.R. Langeveld, MD[d], J.A. Halm, MD, PhD[a], G. Kazemier, MD, PhD[e], J.F. Lange, MD, PhD[a], R.M.H. Wijnen, MD, PhD[d]

[a] Departments of Surgery Erasmus University Medical Center, Rotterdam
[b] Department of Epidemiology Erasmus University Medical Center, Rotterdam
[c] Department of Pediatrics, Maasstad Ziekenhuis, Rotterdam
[d] Department of Pediatric Surgery, Erasmus MC-Sophia Children's Hospital, Rotterdam
[e] Department of Surgery, VU University Medical Center, Amsterdam

J Am Coll Surg. 2015 Mar;220(3):347-52. doi: 10.1016/j.jamcollsurg.2014.11.023.
Epub 2014 Dec 3.

Abstract

Background: Common surgical knowledge is that inguinal hernia repair in premature infants should be postponed until they reach a certain weight or age. Optimal management, however, is still under debate. The objective of this study was to collect evidence for the optimal management of inguinal hernia repair in premature infants.

Methods: In the period between 2010 and 2013, data for all premature infants with inguinal hernia who underwent hernia correction within 3 months after birth in the Erasmus MC-Sophia Children's Hospital, Rotterdam were analyzed. Primary outcomes measures were the incidences of incarceration and subsequent emergency surgery. In a multivariate analysis, Cox proportional hazards model served to identify independent risk factors for incarceration requiring an emergency procedure.

Results: A total of 142 premature infants were included in the analysis. Median follow-up was 28 months (range 15 to 39 months). Seventy-nine premature infants (55.6%) presented with a symptomatic inguinal hernia; emergency surgery was performed in 55.7%. Complications occurred in 27.3% of emergency operations vs 10.2% after elective repair; recurrences occurred in 13.6% vs 2.0%, respectively. Very low birth weight (1,500 g) was an independent risk factor for emergency surgery, with a hazard ratio of 2.7 in the Cox proportional hazards model.

Conclusions: More than half of premature infants with an inguinal hernia have incarceration. Those with very low birth weight have a 3-fold greater risk of requiring an emergency procedure than heavier premature infants. Emergency repair results in higher recurrence rates and more complications. Elective hernia repair is recommended, particularly in very low birth weight premature infants.

Introduction

Inguinal hernia repair is the most frequently performed surgical procedure in neonates, especially in children born preterm. Up to 9.0% of children born preterm will undergo inguinal hernia repair before the age of 7 years, more than half in the first year of life (1, 2). Factors that contribute to the increased risk for inguinal hernia in premature infants include a persistent processus vaginalis, male sex, gestational age, low birth weight, and prolonged mechanical ventilation (2, 3).

The optimal timing of inguinal hernia repair in premature infants is not clear. Common surgical knowledge is that it should be postponed until a certain weight or age is reached because of technical challenges (particularly in very low birth weight [VLBW] premature infants), comorbidities, and potential anesthetic and surgical complications (4-7). Conservative treatment, however, can be complicated by incarceration, followed by ischemia of the bowel and ovarian or testicular atrophy necessitating emergency repair in these fragile newborns, who are probably at even greater risk of complications in an emergency setting compared with an elective repair. In addition, delaying repair could increase the difficulty of the procedure because repeated herniation and reduction might result in a thickened hernia sac and fibrous adhesions between the hernia sac and the spermatic cord (2, 8).

The objective of this study was to collect evidence for the optimal management of inguinal hernia repair in premature infants by comparing the outcomes of emergency procedures with the outcomes of elective repair, and by identifying the risk factors for inguinal hernia in premature infants who become acutely symptomatic.

Methods

A retrospective cohort study was performed at the Erasmus MC-Sophia Children's Hospital, a tertiary academic pediatric hospital in Rotterdam, the Netherlands. The Sophia Children's hospital is 1 of 6 referral hospitals for premature infants (i.e., gestational age less than 37 weeks) in the Netherlands. Each referral hospital has its own unique region; Erasmus MC-Sophia Children's Hospital covers a population of >4.5 million inhabitants.

All premature infants operated on for an inguinal hernia within 3 months after birth between January 2010 and December 2013 were included. They were identified from the electronic hospital data systems and medical charts using Centraal Orgaan Tarieven Gezondheidszorg codes (unilateral inguinal hernia repair, CTG335700; bilateral inguinal hernia repair,

CTG335701; incarcerated inguinal hernia repair without bowel resection, CTG335702; incarcerated inguinal hernia repair with bowel resection, CTG334639; recurrent inguinal hernia repair, CTG335710).

According to the hernia management chosen, two groups were distinguished: premature infants who underwent elective inguinal hernia repair and premature infants who needed an emergency procedure because of incarceration of contents in the hernia sac.

Premature infants that presented with a symptomatic inguinal hernia at our emergency department and could not be manually reduced were operated on within 24 hours, and were defined as cases of incarcerated hernia with subsequent emergency surgery. A pediatric surgeon examined all premature infants at time of first presentation. In our hospital, an open technique was used for all primary inguinal hernia repairs; in case of a recurrence, hernia repair was performed using a laparoscopic approach. Time at risk was calculated from the date of first presentation at our hospital until the date of either elective repair or emergency procedure. Prolonged mechanical ventilation was defined as mechanical ventilation that was continued after the initial procedure was completed. Patient characteristics and clinical data were collected retrospectively in the search for potential risk factors. They included:

1. Patient demographics (i.e., sex, gestational age, and weight at birth)
2. Preoperative comorbidities associated with the pulmonary system (i.e., history of apnea, infant respiratory distress syndrome [IRDS], bronchopulmonary dysplasia, and preoperative mechanical ventilation); cardiovascular system (i.e., history of bradycardia, cardiac anomalies [atrial septal defect, ventricular septal defect, valve abnormalities, and Tetralogy of Fallot], or intraventricular hemorrhage); and digestive system (i.e., GERD and necrotizing enterocolitis)
3. Factors associated with the inguinal hernia (i.e., palpable testis, hydrocele, incarceration, emergency procedure, other concurrent hernia such as umbilical hernia); hernia characteristics (i.e., type of hernia, such as uni-/bilateral; hernia side, i.e., right, left, or bilateral); and presence of a contralateral hernia or orchidopexy during procedure
4. Perioperative data (i.e., gestational age at repair; weight at repair; type of procedure, i.e., open or laparoscopic; duration of procedure; type of anesthesia; duration of anesthesia; type of ventilation; duration of ventilation; and reintubation)
5. Postoperative data (i.e., major complications, such as bowel resection, recurrence, testicular atrophy, spermatic cord injury; minor complications such as hematoma, hydrocele, wound infection, high testicle; length of postoperative hospital stay; length of postoperative neonatal ICU stay; and prolonged mechanical ventilation)

Statistical Analysis

SPSS software, version 21.0 (IBM Corp) was used for all statistical analyses. Chi-square and Mann-Whitney U tests were used to compare risk factors for emergency repair and elective repair in premature infants. Univariate regression analyses were performed to determine the relationship of incident cases of incarceration requiring emergency surgery with risk factors by analyzing each potential risk factor separately. Multivariate regression analyses were performed using a Cox proportional hazards model to control for effects of multiple potential risk factors. Potential risk factors that were related to cases of incarceration requiring an emergency procedure or that were known in literature (i.e., male sex, gestational age, weight of birth, pulmonary comorbidities, and mechanical ventilation) were included in the Cox proportional hazards model. A p value <0.05 was considered statistically significant.

Results

Between 2010 and 2013, one hundred and forty-two premature infants underwent inguinal hernia repair within 3 months after birth. One hundred and twenty-two (83.6%) were male, mean gestational age was 33 weeks þ 4 days (SD 20 days), mean birth weight was 1,859 g (SD 589 g), and median time to follow-up was 28 months (interquartile range 15 to 39 months). Preoperatively, 43 (29.5%) patients had a history of apnea of prematurity, 29 (19.9%) had IRDS, 53 (36.3%) required mechanical ventilation, and 12 (8.2%) had bronchopulmonary dysplasia. Nineteen (13%) patients had a cardiac anomaly and 21 (14.4%) had a history of bradycardia. Of all premature infants, 11 (7.5%) had GERD, necrotizing enterocolitis developed in 4 (2.7%), 8 (5.5%) had intraventricular hemorrhage, and 22 (15.1%) patients presented with a concurrent umbilical hernia. Mean duration of herniotomy was 29 minutes (SD 15 minutes), mean duration of anesthesia was 82 minutes (SD 32 minutes), and 13 (9.2%) premature infants were operated on after the initial procedure for an inguinal hernia on the contralateral side. During follow-up, two premature infants died after 13 and 14 months, respectively. None of the deaths were related to the procedure for inguinal hernia repair.

Emergency Repair

A total of 79 (55.6%) premature infants presented with a symptomatic inguinal hernia at our emergency room, 35 (43.3%) of the hernias could be reduced manually and 44 (55.7%) could not be reduced and required an emergency procedure. Mean time between first presentation at our hospital and emergency surgery was 2.5 days (SD 5.7 days) compared with 18.2 days (SD 11.0 days) for elective repair. Potential risk factors for emergency surgery and elective repair after univariate analysis are presented in Table 1.

Table 1. Patient- and hernia characteristics and comorbidities

	Emergency procedure (n = 44)	*Elective Repair* (n = 98)	*p-value*
Patient characteristics			
Birth weight, grams (SD)	1638 (584)	1977 (561)	0.003*
Gestational age at birth, weeks (SD)	32.3 (3.5)	34.2 (2.3)	0.005*
Male sex	41 (93.2%)	81 (82.7%)	0.120
Comorbidities			
Cardiac anomalies	8 (19.5%)	11 (12.1%)	0.290
Bradycardia	11 (26.8%)	10 (11.0%)	0.037*
IVH	4 (9.8%)	4 (4.4%)	0.254
IRDS	14 (34.1%)	15 (16.5%)	0.039*
BPD	9 (22.0%)	3 (3.3%)	0.001*
Apneas	19 (46.3%)	24 (26.4%)	0.028*
Preoperative MV	14 (56.1%)	11 (33.0%)	0.004*
NEC	2 (4.9%)	2 (2.2%)	0.588
GERD	5 (12.2%)	6 (6.6%)	0.316
Umbilical hernia	6 (14.3%)	16 (17.0%)	0.804
Hernia characteristics			
Left side	12 (27.3%)	35 (35.7%)	0.600
Right side	21 (47.7%)	40 (40.8%)	
Bilateral	11 (25.0%)	23 (23.5%)	
Palpable Testes	27 (61.4%)	67 (68.4%)	0.447
Hydrocele	10 (22.7%)	15 (15.3%)	0.342

*****Statistically significant.
P-values are 2-sided. For dichotomous variables chi-square test was performed and for continuous variables Mann-Whitney. IVH, intraventricular haemorrhage; IRDS, infant respiratory distress syndrome; BPD, bronchopulmonary dysplasia; MV, mechanical ventilation; NEC, necrotising enterocolitis; GERD, gastroesophageal reflux disease.

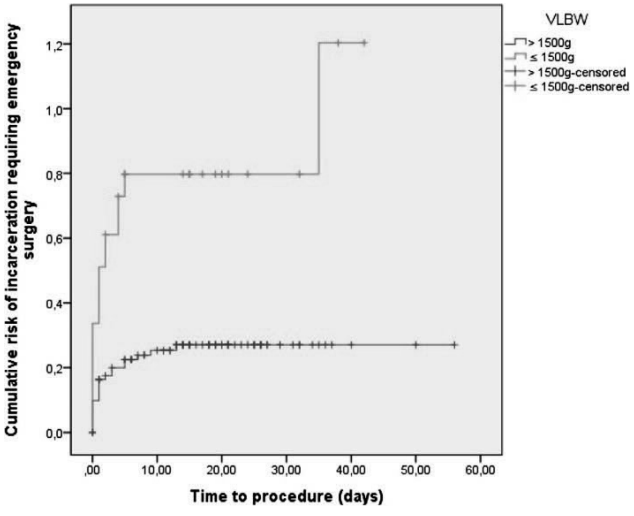
The postoperative complications rate for emergency surgery was 27.3% vs only 10.2% for elective repair (p = 0.013), and recurrence rates of inguinal hernia were significantly higher after emergency surgery (13.6% vs 2.0%; p = 0.011). Data on postoperative complications are presented in Table 2. Univariate regression analysis showed that gestational age (hazard ratio [HR] = 0.98; p = 0.003), IRDS (HR = 2.1; p = 0.027), and preoperative mechanical ventilation (HR = 2.5; p = 0.006) were associated with an emergency procedure. Premature infants with VLBW (<1,500 g) had a 3-fold greater risk of incarceration with a subsequent emergency procedure (HR = 3.0; 95% CI, 1.7-5.5; p < 0.001). The risk was 70.0% in the VLBW group compared with 23.7% in the group premature infants >1,500 g (Fig. 1). When we controlled for possible confounding variables in the multivariate regression analysis (male sex, gestational age, birth weight, IRDS, and preoperative mechanical ventilation), VLBW remained an independent risk factor for incarceration requiring an emergency procedure (HR = 2.7; 95% CI, 1.1-6.4; p = 0.027). None of the other variables included in the multivariate regression analysis were found to be statistically significant.

Table 2. Peri- /postoperative data and complications.

	Emergency procedure (n = 44)	*Elective repair* (n = 98)	*p-value*
Peri-/postoperative data			
Gestational age at repair, weeks (SD)	39.6 (4.0)	43.8 (2.9)	< 0.001*
Weight at repair, grams (SD)	3021 (883)	3889 (862)	< 0.001*
NICU stay, days (SD)	4.7 (9.0)	2.2 (4.8)	0.085
Hospital stay, days (SD)	6.8 (16.3)	3.5 (6.7)	0.210
Prolonged MV	11 (25.0%)	2 (2.0%)	< 0.001*
Reintubation	5 (11.4%)	2 (2.0%)	0.030*
Orchidopexy during initial repair	5 (11.4%)	6 (6.1%)	0.316
Contralateral repair after initial repair	8 (18.2%)	5 (5.1%)	0.023*
Duration of anaesthesia, min (SD)	95 (35)	76 (28)	0.001*
Time of herniotomy, min (SD)	34 (16)	26 (14)	0.005*
Major complications	**8 (18.2%)**	**4 (4.1%)**	**0.009***
Bowel resection	2 (4.5%)	-	0.094
Recurrence repair	6 (13.6%)	2 (2.0%)	0.011*
Testicular atrophy	2 (4.5%)	2 (2.0%)	0.588
Spermatic cord injury	-	2 (2.0%)	1.000
Minor complications	**8 (18.2%)**	**8 (8.2%)**	**0.092**
Haematoma	2 (4.5%)	4 (4.1%)	1.000
Hydrocele	6 (13.6%)	4 (4.1%)	0.070
Wound infection	-	-	-
High testicle	2 (4.5%)	2 (2.0%)	0.588
Total complications	**12 (27.3%)**	**10 (10.2%)**	**0.013***

***Statistically significant.
P-values are 2-sided. For dichotomous variables chi-square test was performed. NICU, neonatal intensive care unit; Complications (Total, major, and minor) are presented in **bold** and defined as # of premature infants with one or more complications.

Figure 1. Hazard function. Risk of incarceration requiring emergency surgery by weight of birth (1,500 g or >1,500 g) among premature infants. VLBW, very low birth weight.



Discussion

The current study reports that elective inguinal hernia repair is safe and successful in most premature infants and is associated with fewer complications. It also reports that postponing inguinal hernia repair in premature infants results in an incarceration requiring emergency correction in one third of patients, and that emergency surgery in those premature infants is associated with a significantly higher incidence of postoperative complications as compared with elective repair. This appears to be particularly true for VLBW premature infants, as they were found to have a 3-fold greater risk of incarceration.

These are relevant results in light of the fact that conflicting published data have made it hard to draw definite conclusions on the optimal management of inguinal hernia in premature infants. Although the levels of prematurity and dysmaturity are associated with high incidence of inguinal hernia, it is the technical challenges and risk of perioperative complications in these fragile newborns that make us reluctant to perform early elective repair (9, 10). Many pediatric surgeons prefer to perform herniotomy when infants born prematurely reach a certain weight or age. Although this more conservative approach can minimize the risk of surgical and anesthetic complications, it might also increase the risk for incarceration, forcing an emergency procedure with potentially more negative sequelae compared with early elective repair (2, 11, 12). Earlier research on this issue resulted in contradictory outcomes (2, 4-6, 9, 10, 12). However, none of the earlier studies performed a multivariate regression analysis to identify independent risk factors. In 2011, Lautz et al (2) compared premature neonates who presented with an incarcerated and non-incarcerated inguinal hernia and they provided data on timing for inguinal hernia repair. In this retrospective study, they found a 2-fold greater risk of incarceration when repair is delayed beyond 40 weeks of gestational age. This result, however, was not corrected for multiple factors and, therefore, gestational age beyond 40 weeks cannot be considered as an independent risk factor for incarceration.

The incarceration rate in the current study population is one of the highest described in the literature (2, 3, 10). This can be explained by the fact that the Erasmus MC Sophia Children's Hospital is a tertiary academic pediatric hospital. It covers a population of >4.5 million inhabitants and is the only hospital of its region that is allowed to perform inguinal hernia repair in premature infants both in the emergency setting and for the elective operation. More than half of all premature infants that presented with a symptomatic inguinal hernia could not be manually reduced and required emergency surgery within 24 hours, resulting in a complication rate of 27.3%, which renders early elective repair more appealing.

The use of contralateral inguinal exploration in premature infants is another topic still under debate (13). In the literature, incidences of metachronous inguinal hernia vary up to 18.6% (14, 15). In our study, the incidence of contralateral hernia after initial repair was considerably higher after emergency surgery (18.2%) compared with elective repair (5.1%). Because in this study, both the elective and emergency repairs were performed with an open procedure, this difference could not be explained by a difference in techniques used, as they (emergency vs elective repair) bear the same risk of overlooking a metachronous hernia. However, meticulous clinical examination of the contralateral side and its registration are still mandatory.

The current study has several shortcomings, most of which are attributable to the retrospective design. Selection bias could have occurred, as no protocol on timing of repair is available in our hospital for premature infants. In addition, the premature infants could have been diagnosed with an inguinal hernia earlier in a different hospital, resulting in a delay between diagnosis and first presentation in our hospital. This makes it difficult to draw general conclusions on the actual timing of repair.

Conclusions

Keeping these limitations in mind, this retrospective cohort shows that more than half of premature infants with an inguinal hernia experience incarceration, and that VLBW infants have a 3-fold greater risk of requiring an emergency procedure than heavier premature infants. Because emergency repair results in higher recurrence rates and more complications, it can even be argued that this particular group of premature infants should be operated on during their birth hospitalization. A multicenter, randomized controlled trial comparing direct and delayed inguinal hernia repair in premature infants should be conducted, stratifying for weight at birth (1,500 g or >1,500 g), to provide more evidence on optimal timing in this fragile group of patients. Until then, elective hernia repair, particularly in VLBW premature infants, is recommended.

References

1. Pan ML, Chang WP, Lee HC, et al. A longitudinal cohort study of incidence rates of inguinal hernia repair in 0- to 6- year-old children. J Pediatr Surg 2013;48:2327-2331.
2. Lautz TB, Raval MV, Reynolds M. Does timing matter? A national perspective on the risk of incarceration in premature neonates with inguinal hernia. J Pediatr 2011;158:573-577.
3. Baird R, Gholoum S, Laberge JM, Puligandla P. Prematurity, not age at operation or incarceration, impacts complication rates of inguinal hernia repair. J Pediatr Surg 2011;46: 908-911.
4. Davies BW, Fraser N, Najmaldin AS, et al. A prospective study of neonatal inguinal herniotomy: the problem of the postoperative hydrocele. Pediatr Surg Int 2003;19: 68-70.
5. Gollin G, Bell C, Dubose R, et al. Predictors of postoperative respiratory complications in premature infants after inguinal herniorrhaphy. J Pediatr Surg 1993;28:244-247.
6. Coren ME, Madden NP, Haddad M, Lissauer TJ. Incarcerated inguinal hernia in premature babies a report of two cases. Acta Paediatrica Int J Paediatr 2001;90:453-454.
7. Toki A, Watanabe Y, Sasaki K, et al. Adopt a wait-and-see attitude for patent processus vaginalis in neonates. J Pediatr Surg 2003;38:1371-1373.
8. Uemura S, Woodward AA, Amerena R, Drew J. Early repair of inguinal hernia in premature babies. Pediatr Surg Int 1999;15: 36-39.
9. Gonzalez Santacruz M, Mira Navarro J, Encinas Goenechea A, et al. Low prevalence of complications of delayed herniotomy in the extremely premature infant. Acta Paediatr Int J Paediatr 2004;93:94-98.
10. Lee SL, Gleason JM, Sydorak RM. A critical review of premature infants with inguinal hernias: optimal timing of repair, incarceration risk, and postoperative apnea. J Pediatr Surg 2011;46:217-220.
11. Misra D. Inguinal hernias in premature babies: wait or operate? Acta Paediatr Int J Paediatr 2001;90:370-371.
12. Vaos G, Gardikis S, Kambouri K, et al. Optimal timing for repair of an inguinal hernia in premature infants. Pediatr Surg Int 2010;26:379-385.
13. Antonoff MB, Kreykes NS, Saltzman DA, Acton RD. American Academy of Pediatrics Section on Surgery Hernia survey revisited. J Pediatr Surg 2005;40:1009-1014.
14. Marulaiah M, Atkinson J, Kukkady A, et al. Is contralateral exploration necessary in preterm infants with unilateral inguinal hernia? J Pediatr Surg 2006;41:2004-2007.
15. Steven M, Greene O, Nelson A, Brindley N. Contralateral inguinal exploration in premature neonates: is it necessary? Pediatr Surg Int 2010;26:703-706.

Chapter 5

Emergency repair of inguinal hernia in the premature infant is associated with high direct medical costs

J. Verhelst[a] B. de Goede[a] B.J.H. van Kempen[b] H.R. Langeveld[c] M. J. Poley[c,d] G. Kazemier[e] J. Jeekel[f] R.M.H. Wijnen[c] J.F. Lange[a]

[a] Department of Surgery, Erasmus University Medical Center Rotterdam, The Netherlands
[b] Department of Epidemiology and Radiology, Erasmus University Medical Center, Rotterdam, The Netherlands
[c] Department of Paediatric Surgery, Erasmus University Sophia Children's Hospital, Rotterdam, The Netherlands
[d] Institute for Medical Technology Assessment (iMTA), Erasmus University Rotterdam, Rotterdam, The Netherlands
[e] Department of Surgery, VU University Medical Center, Amsterdam, The Netherlands
[f] Department of Neuroscience, Erasmus University Rotterdam, Rotterdam, The Netherlands

Hernia. 2015 Dec 14. [Epub].

Abstract

Purpose: Inguinal hernia repair is frequently performed in premature infants. Evidence on optimal management and timing of repair, as well as related medical costs is still lacking. The objective of this study was to determine the direct medical costs of inguinal hernia, distinguishing between premature infants who had to undergo an emergency procedure and those who underwent elective inguinal hernia repair.

Methods: This cohort study based on medical records concerned premature infants with inguinal hernia who underwent surgical repair within 3 months after birth in a tertiary academic children's hospital between January 2010 and December 2013. Two groups were distinguished: patients with incarcerated inguinal hernia requiring emergency repair and patients who underwent elective repair. Real medical costs were calculated by multiplying the volumes of healthcare use with corresponding unit prices. Nonparametric bootstrap techniques were used to derive a 95 % confidence interval (CI) for the difference in mean costs.

Results: A total of 132 premature infants were included in the analysis. Emergency surgery was performed in 29 %. Costs of hospitalization comprised 65 % of all costs. The total direct medical costs amounted to €7418 per premature infant in the emergency repair group versus €4693 in the elective repair group. Multivariate analysis showed a difference in costs of €1183 (95 % CI-1196; 3044) in favor of elective repair after correction for potential risk factors.

Conclusion: Emergency repair of inguinal hernia in premature infants is more expensive than elective repair, even after correction for multiple confounders. This deserves to be taken into account in the debate on timing of inguinal hernia repair in premature infants.

Introduction

Inguinal hernia repair is the most frequently performed procedure in pediatric surgery. The cumulative incidence of inguinal hernia is up to 9.0 % in prematurely born children. More than half these patients will undergo hernia repair in the first year of life (1, 2).

Eventually all premature infants with an inguinal hernia have to undergo surgical repair (3–5). However, evidence on the optimal management and timing of inguinal hernia repair in these neonates is lacking. Delayed repair seems appealing as premature infants often have concomitant comorbidities and are vulnerable for perioperative complications (2). On the other hand, delaying elective repair can be complicated by incarceration, in which case emergency surgery is needed. In a previous study we showed that more than 50 % of premature infants with an inguinal hernia present with a symptomatic inguinal hernia, and emergency repair was needed in more than half of these cases due to incarceration (6). Emergency repair is associated with a higher risk of surgical and anesthetic complications and has been found to result in a longer duration of hospitalization, more readmissions, and even reoperations (2, 6).

To prevent possible emergency repair in premature infants, some surgeons prefer to perform surgery during the birth hospitalization, before discharge from the neonatal intensive care unit (NICU). Although this intervention prolongs initial hospitalization, it avoids readmission for elective repair (7). Delayed elective repair may also result in repeated herniation and reduction at the emergency department (ED), multiple visits to the outpatient clinic (OPC), and perhaps a longer perioperative admission on the pediatric ward or NICU, which is likely to raise direct medical costs (8, 9).

The timing of surgery is mostly based on expert opinion and the surgeon's personal preference. In the current era of tightening budgets, economic aspects have captured the interest of healthcare policy makers (10, 11). Except for a mid-1980s study that compared treatment costs in premature infants operated on prior to discharge from the NICU and in full-term infants operated on as outpatients, there are no data on costs of inguinal hernia repair in premature infants in relation to timing of repair (7). Bearing in mind that surgery in premature patients is very costly, insight into the actual costs of different strategies in inguinal hernia repair would be relevant for planning and organization of care, for supporting clinical decisions, and for efficient allocation of health care resources.

The objective of this study was to compare the medical costs of inguinal hernia repair in premature infants between patients who had to undergo emergency repair and those who underwent elective repair.

Methods

Setting and patients

A cohort study on medical records was performed at a tertiary academic children's hospital in the Netherlands. All premature infants (defined as gestational age <37 weeks) who presented at the ED or at the OPC and operated on for inguinal hernia within 3 months after birth between January 2010 and December 2013 were included. They were identified from the electronic hospital data systems and medical charts using the so-called ''Centraal Orgaan Tarieven Gezondheidszorg'' (COTG) codes (unilateral inguinal hernia repair: CTG335700; bilateral inguinal hernia repair: CTG335701; incarcerated inguinal hernia repair without bowel resection: CTG335702; incarcerated inguinal hernia repair with bowel resection: CTG334639; recurrent inguinal hernia repair: CTG335710).

Study groups and patient exclusion criteria

Two groups of premature infants were distinguished: (1) those who underwent elective inguinal hernia repair and (2) those who had to undergo an emergency procedure because of incarceration of contents in the hernia sac. Emergency surgery was defined as inguinal hernia repair performed within 24 h after incarceration and not scheduled on the surgeon's elective procedure list. Patient characteristics and clinical data were collected from medical records and have been published already (6). Premature infants who were initially admitted for conditions other than inguinal hernia, who were still hospitalized since birth, or who were admitted more than 72 h before surgery, were excluded because it was not possible to separate costs associated with inguinal hernia from costs associated with treatment for other conditions. All patients were operated on after discharge from their birth hospitalization; in all prematures general anesthesia were used, whether or not combined with a caudal block or loco-regional anesthesia. Premature born infants operated on with a gestational age of 40 weeks or younger, were postoperatively admitted to the NICU. Patients with a gestational age of 40–45 weeks had to stay in the recovery room for 2 h after which they were admitted to the ward. This institutional policy is based on national guidelines from the Dutch Society of Anesthesia. Prolonged mechanical ventilation was only performed if clinically indicated, mostly due to pulmonary comorbidities.

Cost calculation

Direct medical costs were considered to be all costs within the hospital sector directly related to the studied treatment, including the hospital's outpatient setting. Per patient, we took into account (1) costs of hospitalization (NICU or high care or medium care unit, and readmissions); (2) costs of outpatient care (i.e., visits to OPC, visits to ED, and telephone consultations); (3) costs of diagnostic procedures and perioperative care (i.e., ultrasound and anesthesiologist

consultations); and (4) costs of surgical procedures (i.e., operating rooms (OR), OR during after hours, reoperations and costs of anesthesiologists and surgeons). Table 1 provides an overview of the cost categories and the unit prices used in the cost calculations.

Table 1. Cost categories and data used in cost calculation based on real costs.

	Parameter	Cost price (€)
Hospitalization		
NICU	Day	1540
High care unit	Night	859
Normal care unit	Night	447
Outpatient clinic visits		
First visit to OPC	Visit	226
Follow up at OPC	Visit	175
Emergency department	Visit	243
Telephonic consultation	Call	135
Perioperative consultation		
Ultrasound	Number	81
Preoperative consultation ANA	Visit	125
Surgical procedure		
Use of OR	/10 min	74
Use of OR afterhours	/10 min	223
Anaesthetist's fee	/10 min	22
Surgeon's fee	/10 min	22
Anaesthetist's fee afterhours	/10 min	22
Surgeon's fee afterhours	/10 min	22

All cost prices are based on real costs rather than charges. Costs in Euro for the first of January 2014, when 1 Euro (€) equalled approximately 1.38 U.S. Dollar. Abbreviations: NICU, neonatal intensive care unit; OPC, outpatient clinic; ANA, anaesthesiology, OR; operating room. Parameters: Day; cost price calculated for each calendar day a patient is hospitalised; Night, cost price calculated for every overnight stay per patient.

Real medical costs were calculated by multiplying the volumes of healthcare use with the corresponding unit prices. Unit prices were determined with the micro-costing method, which implies a detailed inventory and measurement of all resources used (12, 13). For hospital days, the cost price included costs for nursing staff, buildings, and equipment (specialists' fees not included). The unit price for the NICU was calculated for each calendar day an individual was hospitalized; the unit price for a stay on the medium- or high-care was calculated per overnight stay. Regarding the costs of the surgical procedure, the cost price included fees of the surgeons and anesthesiologists, costs of the OR, including costs of OR assistants, anesthesiology nurses, equipment, buildings, etc. For visits to the ED and OPC, preoperative consultation, and ultrasounds, the cost price included the fees of the surgeons, anesthesiologists, and radiologists. All admissions due to a reoperation or admissions that were inguinal hernia related, or related to the first admission, were interpret

to be readmissions. We reported costs in Euro for the first of January 2014, when 1 Euro (€) equaled approximately 1.38 US Dollar.

Data analysis

SPSS 21.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Fisher exact tests and Mann–Whitney U tests were used to compare costs of emergency- and elective repair. Since cost data per patient are typically highly skewed, we used nonparametric simple bootstrap techniques with a 1000 samples. To derive a 95 % confidence interval for the differences in distributions of the direct medical costs, we used the percentile bootstrap method. We used a linear regression model to control for confounders. Potential risk factors with a p value \0.05 were included in the model (i.e., birth weight, age at repair, history of bradycardia, and mechanical ventilation). A p value of\0.05 was considered statistically significant.

Results

Between January 2010 and December 2013, 142 premature infants underwent inguinal repair within 3 months after birth. Ten patients were excluded because they were admitted more than 72 h before surgery. The mean gestational age at birth was 34 weeks (SD 17 days). Mean birth weight was 1916 g (SD 543 g), mean follow-up was 27 weeks (SD 15 weeks), and mean time from diagnosis to surgery was 13 days (SD 12 days).

Seventy-two of the 132 included infants (55 %) presented with a symptomatic inguinal hernia, of whom 38 (29 %) needed subsequent emergency repair due to incarceration within 24 h. In the other 34 infants (26 %), the symptomatic hernias could be reduced manually and delayed elective surgery was performed. Nine patients had no incarceration at first presentation, but returned to the ED with an incarcerated hernia and had to undergo emergency surgery. Table 2 presents characteristics of the two groups. Mean birth weight of patients who needed emergency repair was significantly lower than that of patients who underwent elective repair (1738 vs. 2001 g). Mean post conception age at the time of repair was 41 weeks (SD 3.2 weeks) in the emergency group and 44 weeks (SD 2.8 weeks) in the elective repair group (p\0.001). Mean age at diagnosis was 53 days (SD 18 days) versus 53 days (SD 14 days; p = 0.805), respectively. Mean time between first presentation and repair was 18.0 days (SD 10.7 days) for elective repair and 1.8 days (SD 2.9 days) for emergency 3912 g (SD 865 g) for elective repair and 3206 (SD 769 g) for the emergency repair (p <0.001).

Table 2. Baseline characteristics.

	Elective Repair (N=94)	Emergency Repair (N=38)	p-value
Male gender (%)	78 (83)	35 (92)	0.273
Birth weight, gram (SD)	2001 (552)	1738 (483)	0.022**
Gestational age at repair, weeks (SD)	44 (2.8)	41 (3.2)	<0.001**
Cardiac anomalies (%)	7(8)	4 (11)	0.727
Bradycardia of prematurity (%)	7(8)	8 (23)	0.034*
Apnoea of prematurity (%)	20(23)	14 (40)	0.075
IRDS (%)	13 (15)	10(29)	0.123
BPD (%)	2(4)	4(11)	0.056
History of mechanical ventilation (%)	26 (30)	18 (51)	0.036*
GERD (%)	5 (6)	4 (11)	0.276
NEC (%)	2 (2)	2 (6)	0.578

***Statistically significant (Fisher exact test). ****Statistically significant (Mann Whitney U test).
All values presented as percentages or means (standard deviations), p-values are 2-sided.
Abbreviations: IRDS, infant respiratory distress syndrome; BPD, bronchopulmonary dysplasia; GERD, gastroesophageal reflux disease; NEC, necrotising enterocolitis.

After elective surgery 48 out of 94 (51 %) patients were admitted to the NICU and after emergency repair 37 out of 38 (97 %; p\0.001). Seven (18 %) patients needed prolonged mechanical ventilation at the NICU after emergency repair versus two (2 %) after elective repair (p = 0.002). The median duration of prolonged mechanical ventilation was 123 min (range 31; 2379 min). The recurrence rate after an emergency procedure was significantly higher than that after elective repair (13 vs. 2 %; p = 0.021).

Cost analysis

Based on the cost prices outlined in Table 1, the mean total costs per patient amounted to €5477 (SD €3280). Contributions of four different cost components to the total costs are outlined in Fig. 1. At mean €3573 (SD €3280), cost of hospitalizations made up two thirds of the total costs. The mean costs of the surgical procedures were €1385 (SD €1181), of perioperative consultation €107 (SD €92), and of OPC and/or ED visits €412 (SD €302).

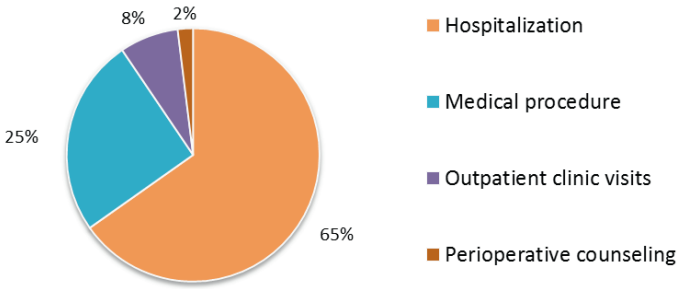


Figure 1. Costs divided into four subcategories presented with percentages.

Emergency repair resulted in 1.58 times higher total costs compared with elective repair: €7418 (SD €4484) versus €4693 (SD €3465; p=0.001), respectively. These are further detailed in Table 3. Except for the costs of perioperative consultations, costs for all categories were higher on average in the case of emergency repair. The difference in costs of hospitalizations (€1501) accounted for more than half of the difference in total costs between the two patient groups (€2725).

When we controlled for possible confounding variables in the linear regression analysis (i.e., birth weight, age at repair, history of bradycardia, mechanical ventilation and emergency repair), the difference in total costs between emergency and elective repair remained €1183 (95 % CI-1196; 3044) in favor of elective repair. None of the variables included in the linear regression analysis were found to be contributing significantly to the total costs.

Table 3. Difference in costs per patient between emergency and elective repair.

	Elective Repair (N=94)	**Emergency Repair (N=38)**	**Difference Bootstrap (CI 95%)**
Pre-op high care- and medium care, € (SD)	164 (459)	271 (405)	107 (-52; 268)
NICU, € (SD)	2491 (1154)	3608 (1400)	1117 (643; 1651)
Post-op high- and medium care, € (SD)	328 (2415)	27 (167)	-301 (-872; 37)
Readmissions ward, € (SD)	91 (408)	452 (2339)	361 (-108; 1307)
Readmissions NICU, € (SD)	66 (447)	284 (1004)	218(-62; 591)
Hospitalization	**3141 (2986)**	**4642 (3746)**	**1501(283; 3050)**
Emergency department, € (SD)	136 (217)	274 (233)	138 (53; 222)
OPC first visits, € (SD)	180 (103)	113 (137)	-67 (-114;-18)
OPC follow up visits, € (SD)	52 (135)	69 (155)	17 (-37;77)
Telephonic consultation, € (SD)	19 (61)	28 (64)	10 (14;34)
Outpatient clinic visits	**388 (264)**	**485 (369)**	**66 (-35; 228)**
Ultrasound, € (SD)	8 (34)	28 (47)	20 (3; 38)
Preop. consultation anesthetist, € (SD)	114 (63)	43 (73)	-72 (-97;-47)
Perioperative consultation	**122 (84)**	**71 (100)**	**-52 (-85; -15)**
Operating room, € (SD)	562 (211)	686 (270)	124 (32; 230)
Operating room afterhours, € (SD)	-	746 (1037)	746 (435; 1071)
Reoperation, € (SD)	143 (727)	231 (589)	87 (-153; 336)
Surgeon,€ (SD)	170 (64)	207 (82)	37 (10; 69)
Surgeon afterhours, € (SD)	-	75 (104)	75 (44; 109)
Anesthetist, € (SD)	170 (64)	207 (82)	37 (10; 69)
Anesthetist afterhours, € (SD)	-	75 (104)	75 (44; 109)
Surgical procedures	**1045 (886)**	**2227 (1423)**	**1182 (754; 1660)**
Total costs, € (SD)	**4695 (3463)**	**7424 (4480)**	**2729 (1291; 4166)**

Costs in Euro for the first of January 2014, when 1 Euro (€) equalled approximately 1.38 U.S. Dollar. All costs are rounded to whole Euro's. Non-parametric bootstrap techniques to derive a 95% confidence interval were used CI is presented with lower and upper values between brackets. Abbreviations: SD, Standard deviation; NICU, neonatal intensive care unit; OPC, outpatient clinic; CI, confidence interval.

Discussion

Insight into the actual costs of different strategies in inguinal hernia repair would be relevant for planning and organization of care around premature infants with inguinal hernia. The present study is the first study that provides information about the true medical costs of inguinal hernia repair in premature infants, comparing elective and emergency repair. Emergency repair appeared to be associated with significantly higher direct medical costs. Hospitalization was accountable for approximately two thirds of the total costs. Therefore, reducing length of stay on the ward and NICU could be an important target for cost reduction. The mean costs of hospitalization after elective repair were lower compared to costs after emergency repair. Almost all premature infants who had to undergo emergency repair were postoperatively admitted to the NICU and immediately discharged after overnight observation without admission to the high- or medium care unit. The question arises whether all patients should be admitted to the NICU postoperatively after an emergency procedure, or whether it would be possible to select only those who really need close observation. Very-low-birth weight premature infants with severe comorbidities are more likely to develop postoperative respiratory and cardiac incidents; obviously, a close observation or intervention on the NICU is advised for those (14–16). The incarceration rate in our study population is relatively high compared to literature (2, 4, 17). This can be explained by the fact that our hospital is the only tertiary academic pediatric hospital in the region and covers 4.5 million inhabitants. Our hospital is the only hospital in its region that is allowed to perform surgery in premature infants. Additionally, it also explains the relatively high recurrence rate because all patients with recurrences hernia will always return to our institution.

There were significant differences between the two study groups in pulmonary comorbidities, birth weight, weight at repair, age at repair, age at diagnosis and prolonged mechanical ventilation, which could be explained by the longer hospitalization and NICU stays in patients after emergency surgery. Still, preventing these patients from emergency repair could result in a reduction of costs.

Only one other study made a cost analysis of inguinal hernia in premature infants (7). This study compared premature infants with full-term born infants, however, these groups are hardly comparable in terms of comorbidity, risk factors, and complications. In this study all premature patients underwent surgery with the use of general anesthesia. However, the use of spinal anesthesia alone can be advocated in patients with pre-existing diseases and incarceration undergoing inguinal hernia repair (18). The costs of preoperative consultation of anesthesiologist were significantly higher in the elective repair group. If patients were scheduled for elective repair, it was common practice in our hospital to consult an anesthesiologist; in case of emergency surgery this was omitted.

The health- and peri-operative care around premature born infants have dramatically changed over the last three decades and new technical advances in neonatal surgery have driven up health care costs (10). The policy to perform surgery during birth hospitalization before discharge from the NICU is still relevant, as this could prevent these neonates from readmissions and incarceration resulting in emergency surgery. Early herniotomy has already shown to improve postoperative outcomes without increasing postoperative bradycardia, apnea and other events (5). Nevertheless, repair of inguinal hernia before discharge from the NICU is associated with a prolonged hospital stay (4). Sufficient capacity, resources and a decision-making tool enabling surgery at least 1 week before planned discharge could solve this problem. Early surgery, on the other hand, is associated with a higher risk of surgical and anesthetic complications in view of the infant's lower body weight. The present study has limitations. Selection bias could have occurred due to the absence of a protocol on timing of inguinal hernia repair in premature infants. Furthermore, a financial analysis is dependent on the local financing process, and local institutional policies (e.g., in our institution, specialists' fees are similar during day and night shifts and admission to the NICU postoperative for patients under the gestational age of 40 weeks).

Keeping this limitation in mind, we provide solid evidence on the direct medical costs of emergency repair in premature infants. It appeared that emergency repair is almost 60 % more expensive than elective repair. Therefore, it can be argued that preventing premature infants from incarceration, for which often emergency repair is needed, will reduce aggregate direct medical costs. Further evidence on actual costs of different strategies in inguinal hernia repair in premature infants would be welcome as a basis for the development of decision-making tools. For instance, it would be worth knowing the additional costs of performing surgery during the birth hospitalization compared to the costs of elective surgery when delayed. Outcomes of new prospective randomized trials, including cost-effectiveness, will help allocate health care resources even more efficiently.

References

1. Pan ML, Chang WP, Lee HC, Tsai HL, Liu CS, Liou DM, SungYJ, Chin TW (2013) A longitudinal cohort study of incidence rates of inguinal hernia repair in 0- to 6-year-old children. J Pediatr Surg 48:2327–2331
2. Lautz TB, Raval MV, Reynolds M (2011) Does timing matter? Premature neonates with inguinal hernia. J Pediatr 158:573–577
3. Lau ST, Lee YH, Caty MG (2007) Current management of hernias and hydroceles. Semin Pediatr Surg 16:50–57
4. Lee SL, Gleason JM, Sydorak RM (2011) A critical review ofpremature infants with inguinal hernias: optimal timing of repair, incarceration risk, and postoperative apnea. J Pediatr Surg 46:217–220
5. Vaos G, Gardikis S, Kambouri K, Sigalas I, Kourakis G,Petoussis G (2010) Optimal timing for repair of an inguinal hernia in premature infants. Pediatr Surg Int 26:379–385
6. de Goede B, Verhelst J, van Kempen BJ, Baartmans MG, Langeveld HR, Halm JA, Kazemier G, Lange JF, Wijnen RM (2015) Very low birth weight is an independent risk factor for emergency surgery in premature infants with inguinal hernia. J Am Coll Surg 220:347–352
7. Groff DB, Nagaraj HS, Pietsch JB (1985) Inguinal hernias inpremature infants operated on before discharge from the neonatal intensive care unit. Arch Surg 120:962–963
8. Melone JH, Schwartz MZ, Tyson KRT, Marr CC, Greenholz SK,Taub JE, Hough VJ (1992) Outpatient inguinal herniorrhaphy in premature infants: is it safe? J Pediatr Surg 27:203–208
9. Peutrell JM, Hughes DG (1992) Ex-premature infants can safelyhave outpatient inguinal herniotomies. J Pediatr Surg 27:1487–1488
10. Poley MJ, Brouwer WB, Busschbach JJ, Hazebroek FW, TibboelD, Rutten FF, Molenaar JC (2008) Cost-effectiveness of neonatal surgery: first greeted with scepticism, now increasingly accepted. Pediatr Surg Int 24:119–127
11. Stolk EA, Post HA, Rutten FF, Molenaar JC, Busschbach JJ(2000) Cost-effectiveness of neonatal surgery: a review. J Pediatr Surg 35:588–592
12. Drummond MF, O'Brien BJ, Stoddart GL, Torrance GW (1997) Torrance Methods for the economic evaluation of health care programmes. Oxford University Press, Oxford
13. Gold M, Siegel JE, Russel LB, Weinstein MC (1996) Cost-effectiveness in health and medicine. Oxford University Press, New York
14. Kinouchi K (2004) Anaesthetic considerations for the management of very low and extremely low birth weight infants. Best Pract Res Clin Anaesthesiol 18:273–290
15. Holzman RS (1994) Morbidity and mortality in pediatric anesthesia. Pediatr Clin N Am 41:239–256
16. Rappaport B, Mellon RD, Simone A, Woodcock J (2011) Defining safe use of anesthesia in children. N Engl J Med 364:1387–1390
17. Baird R, Gholoum S, Laberge JM, Puligandla P (2011) Prematurity, not age at operation or incarceration, impacts complication rates of inguinal hernia repair. J Pediatr Surg 46:908–911
18. Lambertz A, Schalte G, Winter J, Roth A, Busch D, Ulmer TF,Steinau G, Neumann UP, Klink CD (2014) Spinal anesthesia for inguinal hernia repair in infants: a feasible and safe method even in emergency cases. Pediatr Surg Int 30:1069–1073

Chapter 6

Incidence, risk factors, and treatment of incisional hernia after kidney transplantation: An analysis of 1,564 consecutive patients

J. Verhelst, MD,[a] L.S. Ooms, MD,[a] J. Jeekel, MD, PhD,[b] J.N. Ijzermans, MD, PhD,[a] J.F. Lange, MD, PhD,[a] and T. Terkivatan, MD, PhD,[a]

[a]Department of Surgery, Erasmus University Medical Center Rotterdam, The Netherlands
[b]Department of Neuroscience, Erasmus University, Rotterdam, the Netherlands

Surgery. 2016 Jan 7. pii: S0039-6060(15)00964-2. doi: 10.1016/j.surg.2015.11.017.

Abstract

Background: The objective was to evaluate the incidence and treatment of incisional hernia after kidney transplantation and to identify potential risk factors.

Methods: A retrospective cohort study was performed. All kidney transplant recipients between 2002 and 2012 were included. Two groups were identified: patients with and without incisional hernia. An analysis of risk factors for the development of incisional hernia was performed.

Results: A total of 1,564 kidney recipients were included. Fifty patients (3.2%) developed incisional hernia. On univariate analysis, female sex (54 vs 35%), body mass index (BMI) >30 kg/m2 (38 vs 17%), concurrent abdominal wall hernia (30 vs 16%), multiple explorations of the ipsilateral iliac fossa (38 vs 19%), left iliac fossa implantation (36 vs 24%), history of smoking (72 vs 57%), and duration of the kidney transplantation procedure (210 vs 188 minutes) were associated with the development of incisional hernia ($P < .05$ each). In multivariate analyses, female sex (hazard ratio [HR] 2.6), history of smoking (HR 2.2), obesity (BMI >30; HR 2.9), multiple explorations of the ipsilateral iliac fossa (HR 2.0), duration of operation (HR 1.007), and concurrent abdominal wall hernia (HR 2.3) were independent risk factors. Twenty-six of 50 patients (52%) underwent operative repair, of whom 9 (35%) required emergency repair.

Conclusion: The incidence of incisional hernia after kidney transplantation with a median follow-up of 59 months is 3.2%. Obesity (BMI >30), female sex, concurrent abdominal wall hernias, history of smoking, duration of surgery, and multiple explorations were independent risk factors for the development of incisional hernia after kidney transplantation. Attempts at preventing incisional hernias based on these risk factors should be explored.

Introduction

Incisional hernia is one of the most frequent postoperative complications after abdominal operations. The incidence varies between 8 and 20% in general population and may be even greater in risk subgroups (1-4). Incisional hernias have substantial impact on health-related quality of life and body image (4, 5). Known risk factors for the development of incisional hernias are obesity, abdominal aortic aneurysm, immunosuppressive therapy, and postoperative wound infection (1,4-7) Hence, transplant recipients may have an increased risk to develop incisional hernia due to the use of postoperative immunosuppressive therapy resulting in impaired wound healing (5,7). The incidence of incisional hernia after kidney transplantation in the literature, however, is reported to be remark ably low and varies between 1 and 7% (6, 8-14).

Use of a permanent prosthetic material is now the gold standard for the treatment of incisional hernia. Even with the placement of a permanent prosthesis (from now on referred to as "mesh"), recurrence rates are still very high at up to 32%, and the use of mesh predisposes the patient to mesh-related complications, such as seroma, hematoma, mesh infection, and enterocutaneous fistula (2) In addition, mesh placement after kidney transplantations makes the iliac fossa less accessible for future transplant removal or kidney retransplantation in the ipsilateral iliac fossa. In contrast, a conservative, nonoperative treatment of these incisional hernias leads to secondarily high crossover rates to the operative repair of the hernia with increased postoperative morbidity and mortality, particularly in patients who need emergency operative intervention as the result of incarceration of the hernia contents (15).

We conducted this retrospective case-control study to evaluate the incidence and treatment of incisional hernia after kidney transplantation and to identify independent potential risk factors for the development of incisional hernia.

Methods

A retrospective cohort study was performed at the Department of Transplant Surgery of the Erasmus University Medical Center, Rotterdam, The Netherlands. All patients who underwent kidney transplantation between January 2002 and December 2012 were identified from the electronic hospital data systems. Electronic hospital data systems and medical charts of all kidney transplantation recipients were reviewed manually, and patients diagnosed with incisional hernia were identified. Second transplantations in the contralateral fossa were considered to be new cases; in contrast, a second transplantation in the ipsilateral fossa was defined as an operative reintervention.

Our cohort was divided in 2 groups, one group of kidney transplant recipients that developed incisional hernia and one that did not develop an incisional hernia during follow-up. The following patient characteristics and clinical data were registered in search for potential risk factors: patient demographics (i.e., sex, body mass index [BMI], age), preoperative comorbidities associated with impaired wound healing or incisional hernia (i.e., diabetes mellitus, preoperative immunosuppressive therapy, smoking, "pre-emptive" transplantation in patients who had never been on hemo- or peritoneal dialysis, other concurrent hernia), perioperative data (i.e., deceased/living donor, implantation side, duration of the kidney transplantation procedure, kidney transplantation performed during after hours, and multiple explorations of the ipsilateral fossa and hernia characteristics (i.e., time to diagnose, treatment, emergency repair, use of mesh, and recurrence). After hours were defined as operations starting between 5 PM and 8 AM. Operations in the ipsilateral iliac fossa included retransplantations, transplant removal, or operations to treat complications (i.e., urologic complications, bleeding). All patients had a semilunar supra inguinal incision to gain access to retroperitoneal space. Standard immunosuppressive therapy consisted of tacrolimus, mycophenolate mofetil, and prednisolone. Prednisone was tapered gradually and eventually stopped at 4 months. On indication, conversions to cyclosporine, azathioprine, sirolimus, or prednisone were adopted in individual patients.

Incisional hernias were diagnosed at the outpatient clinic or emergency department. The follow-up of kidney transplant recipients was performed by the nephrologists in our center. When the nephrologist believed that an incisional hernia was present, the patient was referred to the surgery outpatient clinic. Incisional hernias were diagnosed by physical examination by surgeons. When there was doubt after physical examination, additional radiologic imaging was performed. In case of incisional hernia repair, defects were corrected either primarily with a suture repair or with mesh in intraperitoneal, preperitoneal, sublay, or onlay fashion. If possible, a tension-free, non-bridging technique was preferred over a bridging technique to close the defect.

Data analysis. SPSS 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. IBM Corp, Armonk, NY) was used for all statistical analyses. Continuous variables were presented as means with standard deviations or as medians with interquartile range (IQR). Categorical variables were presented as numbers with percentages (%). Independent t test, Mann Whitney U, and chi-square tests were used to compare risk factors for incisional hernia after kidney transplantation. Univariate regression analyses were performed for the development of incisional hernia with risk factors by analyzing each potential risk factor separately. Potential risk factors that were related to incisional hernia in the univariate regression analysis (i.e., BMI >30 kg/m2, sex, concurrent abdominal wall hernia, history of

smoking, multiple explorations of the ipsilateral fossa, duration of the kidney transplantation procedure, and implantation side) were included in our multivariate regression analyses. The multivariate regression analyses were performed with a Cox proportional hazards model to control for effects of multiple potential risk factors.

Results

Baseline demographics. Between 2002 and 2012, a total of 1,564 kidney transplantations were performed; 1,004 (64%) were male recipients, and mean age at transplantation was 51 ± 14 years. Mean BMI was 25.7 ± 4.7. Median follow-up was 59 months (IQR 34–95 months), and 274 (17.5%) patients died during follow-up. Preoperatively, 349 (23%) patients were smokers at time of transplantation, 532 (35%) had smoked in the past, and 659 (42%) never smoked. One thousand and twenty-two (65%) transplantations were living-related transplantations, whereas 542 (35%) grafts were from deceased donors. Before transplantation, 370 (24%) patients did not receive hemo- or peritoneal dialysis. Preoperatively, in total 222 (14%) patients already used immunosuppressive drugs, of whom 3 patients (6%) developed incisional hernia and 219 patients (15%) did not (P = 0.089). A total of 1,187 (76%) kidneys were placed in the right and 377 (24%) in the left iliac fossa. Mean duration of the kidney transplantation procedure was 188 ± 44 minutes, and 294 (19%) transplantations took place during after-hours (between 5 PM and 8 AM). Three hundred one (19%) patients needed a repeat operation conducted through the same iliac fossa after initial transplantation because of bleeding, urologic complications, or removal of the transplanted kidney.

Incisional hernia. A total of 50 (3.2%) patients developed incisional hernia over the median follow-up of 59 months. Median time between transplantation and the development of incisional hernia was 68 weeks (IQR 24–149 weeks). The time to the development of an incisional hernia after kidney transplantation is presented in Fig 1. The cumulative incidence of development of incisional hernia was 1.6% at 12 months after transplantation, 3.7% at 60 months, and 4.4% at 120 months postoperatively. Potential risk factors for incisional hernia after univariate analyses were conducted are presented in Table 1.

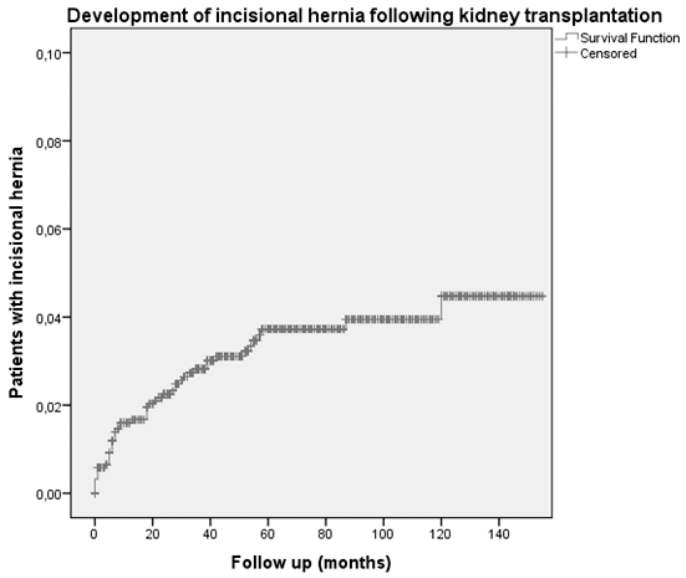


Figure 1.

Table 1. Univariate analyses

	With IH (n=50)	Without IH (n=1514)	p value
Female gender (%)	27 (54)	533 (35)	0.006*
BMI, kg/m^2 (mean) (SD)	28.7 (5.6)	25.6 (4.6)	<0.001*
BMI > 30 kg/m^2 (%)	19 (38)	260 (17)	<0.001*
Age (mean) (SD)	51.4 (12.1)	51.4 (14.5)	0.968
Diabetes mellitus (%)	12 (24)	300 (20)	0.466
Pre-emptive transplantation (%)	16 (32)	354 (23)	0.158
Pre-operative immunosuppression	3 (6)	219 (15)	0.089
Current smoking (%)	11 (22)	338 (23)	0.909
History of smoking** (%)	36 (72)	845 (57)	0.032*
Concurrent abdominal wall hernia (%)	15 (30)	238 (16)	0.007*
Living donor (%)	31 (62)	991 (66)	0.613
Left side implantation (%)	18 (36)	359 (24)	0.046*
Duration surgery, min (mean) (SD)	210 (64)	188 (43)	0.020*
Surgery during after-hours (%)	12 (24)	282 (19)	0.340
Multiple explorations same fossa (%)	19 (38)	282 (19)	0.001*

*****Statistically significant.
** History of smoking includes all current and past smokers
P-values are 2-sided. For dichotomous variables chi-square test and for continuous variables Mann-Whitney U or t-test was performed.
IH, Incisional hernia; BMI, body mass index.

Operative repair of the incisional hernia was performed in 26 patients (52%), whereas 24 (48%) were treated by observation alone. Operative repair was performed with polypropylene mesh in 15 patients and polyester meshes in 4. In 1 patient, a polyglactin mesh (Vicryl; Ethicon, Inc, Somerville, NJ) was placed because of a contaminated environment, and 6 patients underwent hernia repair without mesh (of whom 5 were operated during an emergency repair). When used, the mesh was placed with a bridging technique in 11 patients and a non-bridging technique in 7. Details of the technique were not documented in 2. Nine patients (35%) required emergency repair because of small bowel incarceration. In 6 of these 26 (23%) operated patients, the incisional hernia recurred; 2 underwent initial surgical repair with polypropylene, 2 with polyester, 1 with polyglactin, and 1 via primary tissue repair.

Risk factor analyses. Univariate regression analysis showed that a concurrent abdominal wall hernia (hazard ratio [HR] 2.4; P = 0.005), female sex (HR 2.1; P = 0.011), history of smoking (HR 1.9; P = 0.035), obesity (HR 3.0; P < 0.001), multiple explorations in the ipsilateral fossa (HR 2.7; P = 0.001), duration of the kidney transplantation procedure (HR 1.009; P < 0.001), and left-sided implantation (HR 1.8 P = 0.046) were associated with the development of an incisional hernia. When we corrected for possible confounding variables in the multivariate regression analysis, all aforementioned risk factors except for the implantation side remained as independent risk factors for the development of incisional hernia after transplantation. HRs with 95% confidence intervals are presented in Table 2.

Table 2. Multivariable risk factor analyses

	HR	95% CI	p value
BMI >30 kg/m2	2.9	1.6-5.2	<0.001*
Female gender	2.6	1.4-4.7	0.002*
Concurrent abdominal wall hernia	2.3	1.2-4.3	0.009*
History of smoking	2.2	1.1-4.1	0.019*
Multiple explorations	2.0	1.1-3.7	0.026*
Left sided implantation	1.6	0.9-2.8	0.132
Duration of surgery, min	1.007	1.001-1.012	0.014*

* Statistically significant.
2-sided chi-square tests were performed
HR, hazard ratio; CI, confidence interval; BMI, body mass index.

Discussion

In this retrospective analysis we found an incidence of incisional hernia after kidney transplantation of 3.2% at a median follow-up of 59 months. Presumably, this incidence is less compared with other abdominal wall incisions because of the anatomical location of

the iliac incision in kidney transplantation and some believe because of the transfascial and muscular approach perpendicular to the tension lines of the abdomen. This incidence of incisional hernia corresponds with the incidence described in the literature (6, 12-14). Beside the known risk factors of smoking and obesity, we found female sex, duration of the kidney transplantation surgery, the presence of other abdominal wall hernias, and multiple operations in the ipsilateral iliac fossa also to be independent risk factors for the development of incisional hernia after kidney transplantation. Operative repair of the incisional hernia was performed in 26 (52%) patients, 9 of whom (35%) required emergency repair.

This study describes new independent risk factors for the development of incisional hernia after transplantation and gives information about the treatment of incisional hernia in a well-defined population. A recent publication provided an overview of incisional hernia formation after abdominal organ transplantation, including 2,247 kidney transplantations. The authors reported an incidence of 7% after 10 years' follow-up. The only independent risk factors for development of incisional hernia in their cohort were the nonuse of mycophenolate mofetil and surgical-site infection (6). In our study, we identified other predisposing independent risk factors, such as female sex, duration of the transplantation procedure, obesity, other abdominal wall hernia, multiple operations in to the ipsilateral iliac fossa, and smoking. These preoperative and perioperative risk factors should be taken into account by surgeons when closing the fascia.

According to the guidelines of the European Hernia Society on abdominal wall closure, small-bite sutures are suggested for fascia closure after midline incisions to prevent incisional hernia (16, 17). Furthermore, a running suture length–to-wound length ratio of at least 4 to 1 is advised (16, 18). Research is necessary to prove the effect of small-bite sutures in iliac fossa incisions. In our opinion, the placement of prophylactic mesh in kidney transplant recipients with non-modifiable preoperative risk factors is not preferable, because this would make future explorations of the iliac fossa more difficult, and the use of immunosuppressive drugs postoperatively could predispose patients to mesh infection Preoperative weight reduction in obese patients should not only be advised to benefit graft survival, prevent diabetes, and decrease hospital stay but might also to prevent postoperative complications, such as wound infection and incisional hernia (19). Another publication reported an incidence of 2.6% for incisional hernia after kidney transplantation, of whom 71% needed surgical repair. These authors reported a recurrence rate of 20%, which corresponds with our recurrence rate of 23% and recurrence rates after other abdominal incisional hernia (2, 13).

Synthetic polypropylene was the mesh used most frequently in our cohort, which is also mentioned in the literature for the repair of incisional hernia after kidney transplantation (10-14). Nevertheless, it is conceivable that biologic prosthesis (i.e., porcine dermis collagen) could be useful in patients who are prone to develop wound infection (20).

A prolonged duration of the transplantation procedure in the group that developed incisional hernia can be explained by the complexity of the procedure. Also, the relationship between obesity and prolonged duration of the transplantation procedure has been described previously (19).

The present study has limitations, most of which are attributable to the retrospective design. A few potential risk factors, for instance, the number of wound infections that are known to be a potential risk factor for the development of incisional hernia, could not be analyzed thoroughly in our hospital data systems (6, 21). Because the diagnosis of incisional hernia is made clinically and radiography is not a standard procedure, the number of incisional hernias could be underestimated. Nevertheless, our patients have meticulous follow-up with physical examination postoperatively in our outpatient clinic. Moreover, patients who developed incisional hernia who present in another hospital are always referred back to the surgery department in our center.

In conclusion, we found that the incidence of incisional hernia after kidney transplantation is 3.2% at a median follow-up of 59 months in our 1,564 patients. The emergency operative repair for an incarcerated incisional hernia was 35%. Recurrences occurred in 23%. Beside the known risk factors obesity (BMI >30) and smoking, female sex, concurrent abdominal wall hernias, duration of the transplantation procedure, and multiple operations in the ipsilateral iliac fossa appear to be new independent risk factors for the development of incisional hernia after kidney transplantation. Possible future research should be devoted to addressing those preoperative risk factors able to be modified.

References

1. Bevis PM, Windhaber RA, Lear PA, et al. Randomized clinical trial of mesh versus sutured wound closure after open abdominal aortic aneurysm surgery. Br J Surg 2010;97: 1497-502.
2. Burger JW, Luijendijk RW, Hop WC, et al. Long-term followup of a randomized controlled trial of suture versus mesh repair of incisional hernia. Ann Surg 2004;240:578-83; discussion 83–5.
3. van 't Riet M, Steyerberg EW, Nellensteyn J, et al. Meta-analysis of techniques for closure of midline abdominal incisions. Br J Surg 2002;89:1350-6.
4. van Ramshorst GH, Eker HH, Hop WC, et al. Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study. Am J Surg 2012;204:144-50.
5. de Goede B, Eker HH, Klitsie PJ, et al. Incisional hernia after liver transplantation: risk factors and health-related quality of life. Clin Transplant 2014;28:829-36.
6. Smith CT, Katz MG, Foley D, et al. Incidence and risk factors of incisional hernia formation following abdominal organ transplantation. Surg Endosc 2015;29:398-404.
7. Knight RJ, Villa M, Laskey R, et al. Risk factors for impaired wound healing in sirolimus-treated renal transplant recipients. Clin Transplant 2007;21:460-5.
8. Massarweh NN, Clayton JL, Mangum CA, et al. High body mass index and short- and long-term renal allograft survival in adults. Transplantation 2005;80:1430-4.
9. Singh D, Lawen J, Alkhudair W. Does pretransplant obesity affect the outcome in kidney transplant recipients? Transplant Proc 2005;37:717-20.
10. Birolini C, Mazzucchi E, Utiyama EM, et al. Prosthetic repair of incisional hernia in kidney transplant patients. A technique with onlay polypropylene mesh. Hernia 2001;5:31-5.
11. Li EN, Silverman RP, Goldberg NH. Incisional hernia repair in renal transplantation patients. Hernia 2005;9:231-7.
12. Mahdavi R, Mehrabi M. Incisional hernia after renal transplantation and its repair with propylene mesh. Urol J 2004;1:259-62.
13. Mazzucchi E, Nahas WC, Antonopoulos I, et al. Incisional hernia and its repair with polypropylene mesh in renal transplant recipients. J Urol 2001;166:816-9.
14. Varga M, Matia I, Kucera M, et al. Polypropylene mesh repair of incisional hernia after kidney transplantation: single-center experience and review of the literature. Ann Transplant 2011;16:121-5.
15. Verhelst J, Timmermans L, van de Velde M, et al. Watchful waiting in incisional hernia: is it safe? Surgery 2015;157: 297-303.
16. Millbourn D, Cengiz Y, Israelsson LA. Effect of stitch length on wound complications after closure of midline incisions: a randomized controlled trial. Arch Surg 2009;144:1056-9.
17. Muysoms FE, Antoniou SA, Bury K, et al. European Hernia Society guidelines on the closure of abdominal wall incisions. Hernia 2015;19:1-24.
18. Israelsson LA, Jonsson T, Knutsson A. Suture technique and wound healing in midline laparotomy incisions. Eur J Surg 1996;162:605-9.
19. Lafranca JA, Hagen SM, Dols LF, et al. Systematic review and meta-analysis of the relation between body mass index and short-term donor outcome of laparoscopic donor nephrectomy. Kidney Int 2013;83:931-9.
20. L Santangelo M, Carlomagno N, Spiezia S, et al. Use of biological prostheses in transplant patients with incisional hernias. Preliminary experience. Ann Ital Chir 2013;84:471-5.
21. Humar A, Ramcharan T, Denny R, et al. Are wound complications after a kidney transplant more common with modern immunosuppression? Transplantation 2001;72:1920-3.

Chapter 7

The myth of the width: the linea alba in patients with abdominal aortic aneurysm: A comparative analysis

J. Verhelst, MD[a]*, J. Nieuwenhuizen, MD[b], T. Vijfvinkel MSc[a], J. Jeekel, MD, PhD[c], G.J. Kleinrensink, PhD[c,] H.J.M. Verhagen, MD, PhD[d], J.F. Lange, MD, PhD[a]

[a]Erasmus University Medical Center, Rotterdam, Department of Surgery, The Netherlands
[b] Leiden University Medical Center, Rotterdam, Department of Surgery, The Netherlands
[c] Erasmus University, Rotterdam, Department of Neuroscience, The Netherlands
[d] Erasmus University, Rotterdam, Department of Vascular Surgery, The Netherlands

Submitted

Abstract

Background: Incisional hernia is a frequent phenomenon after abdominal surgery, causing decreased quality of life, morbidity and mortality. Patients with abdominal aortic aneurysm (AAA) are more at risk to develop incisional hernia. The objective of this study was to determine if anatomical differences of the linea alba exist between patients with AAA and a control group.

Methods: A retrospective study was performed. Males, with virgin linea alba, who were to undergo elective open repair of AAA were compared with patients undergoing surgery for colorectal cancer. Baseline characteristics were collected and preoperative CT-scans were analysed. The width was measured at six standard levels between xiphoid and pubic bone. The surface of the linea alba was reconstructed and multivariable analysis was performed.

Results: Eighty AAA patients were included and compared to 98 patients in the control group. There was no significant difference in width of the linea alba between groups. Mean reconstructed surface in patients with AAA was 58.7 cm^2 (SD 24.4 cm^2) and 58.4 cm^2 (SD 33.0 cm^2) in the control group, p=0.951. Multivariable analysis showed that higher BMI was associated with a wider linea alba and higher age was associated with a wider linea alba below the umbilicus. Postoperatively, Thirteen patients (16%) in the AAA group and 23 (24%) in the control group developed an incisional hernia, p=0.264.

Conclusion: The present study shows no difference in width and surface of the linea alba between patients with AAA and colorectal cancer. A higher BMI is associated with a wider linea alba and higher age is also associated with a wider linea alba below the umbilicus. These, however, were no risk factors for incisional hernia. In this cohort there was no evidence that a wider linea alba results in the development of postoperative incisional hernia.

Introduction

Incisional hernia is a frequent phenomenon after abdominal surgery, resulting in decreased quality of life, poor body image, morbidity, and even mortality in patients after median laparotomies (1-4). Despite studies on optimal closing techniques, the risk for incisional hernia after midline incision is still 5-20 % (5-7). Risk factors for incisional hernia after laparotomy are obesity, steroid use, and smoking and connective tissue disorders. These risk factors can even increase the incidence of incisional hernia formation up to 35% (8-13). Patients with an abdominal aortic aneurysm (AAA) are especially known to have a significant risk to develop incisional hernia postoperatively, with literature stating percentages of over 30% in 2.5 - 3 years (14, 15).

A correlation between AAA and the incidence of inguinal hernia has already been described (15-17). Moreover, AAA is associated with pre-existent collagen deficiencies and systemic fibre degeneration. These deficiencies may affect the whole human body, resulting in weakness of the linea alba or even the whole abdominal wall, causing widening of the linea alba, hypothetically resulting in development of abdominal wall hernia. Nevertheless, available publications about width or surface of the linea alba in patients with AAA compared with control groups, are contradictory and the methodology is often poorly described (18-21). Furthermore, there are indications that the width of the linea alba is associated with the development of incisional hernia, however, clear evidence is lacking. A clear correlation between the width of the linea alba and development of incisional hernia might be helpful as decision making tool for primary mesh augmentation in order to prevent incisional hernia (22, 23).

The objective of this retrospective analysis was to determine the anatomical differences of the linea alba using pre-operative computed tomography-scans of patients with AAA and a control group. Risk factors for development of incisional hernia in correlation with the linea alba were investigated and other independent contributing variables associated with the width of the linea alba were analysed.

Methods

A retrospective cohort study was performed at Erasmus University Medical Center, Rotterdam, a large tertiary referral hospital in the Netherlands. Only male patients who underwent elective open repair of AAA between September 2003 and July 2014 were included. The control group consisted of male patients with colorectal cancer who underwent surgery

through a midline incision between July 2008 and July 2013. This control group was chosen, because all colorectal cancer patients in our hospital had preoperative CT-scans for staging of the colorectal cancer disease, and therefore their scans could be compared with the preoperative scans of patients with AAA, Moreover the baseline characteristics of patients with a colorectal carcinoma were expected to approximate the baseline characteristics of patients with AAA.

Only patients with a virgin linea alba (e.g. no prior abdominal surgery through midline incision) with a preoperative available CT-scan were included. Female patients were excluded because of possible post pregnancy diastasis of the rectus muscles and to make the two groups uniform. Patients who suffered from both colorectal carcinoma as well as AAA were also excluded from analysis. Data were collected from electronic hospital databases and medical records. Patient characteristics and clinical data were collected retrospectively. Potential risk factors for a widened linea alba and the development of incisional hernia were recorded (i.e., age, weight, length, body mass index (BMI), history of smoking, diabetes mellitus (DM), concomitant inguinal hernia, maximum diameter of AAA or, in case of the control group, the maximum diameter of the aorta at the level of the renal artery branches).

Besides radiological measurements of linea alba, preoperative and postoperative data about incisional hernia formation were collected through medical chart review of the postoperative visits to the surgical outpatient clinic. If an incisional hernia was not described in the medical charts we assumed that these did not occur. By reviewing all post-operative radiological diagnostic images were checked for occult incisional hernia. Because multiple incisions in the linea alba are a risk factor for development of incisional hernia we also looked at the incidence in the interval between the first and second midline laparotomy.

Radiological Measurements

Philips, iSite Enterprise DICOM viewer inbuilt tools were used to measure the width of the linea alba. The first observer (J.V.) assessed the linea alba at fixed measuring levels (Figure 1). First a reference length between the xiphoid bone and symphysis pubis was determined by multiplying the number of slides by the thickness of the slides. The thickness of the slides of the CT-scans was varying between 1 mm and 6 mm. To measure the width of the linea alba, the inter rectus muscle distance was taken. For each patient the measurements were taken at 1/3 and 2/3 of the reference length (A, B), level of the umbilicus (C), 30 mm above and below the umbilicus (D, E), and maximum width of the linea alba (F).

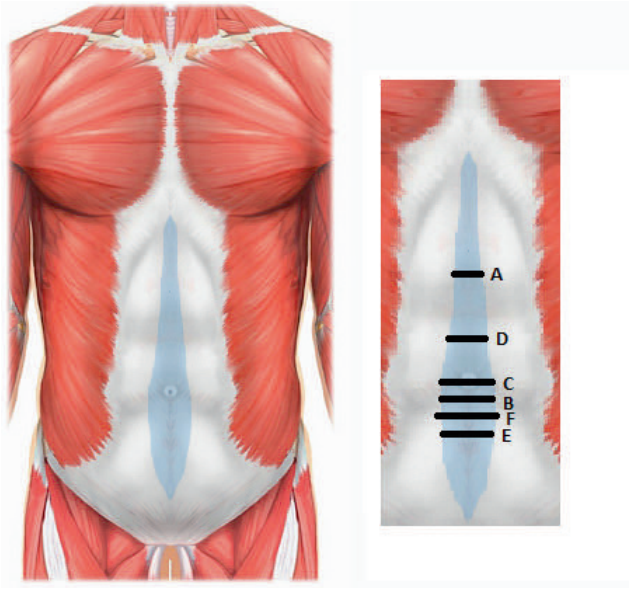


Figure 1. Anatomical presentation of the linea alba with the measuring heights of the inter rectus distance.
The width of the linea alba. Measurements were taken at A) 1/3 of the reference length, B) 2/3 of the reference length, C) level of the umbilicus, D) 30 mm above the umbilicus, E) below the umbilicus, F) maximum width of the linea alba.

In order to verify the first observer measurements, a second observer (T.V.) measured the length and interrectus distance independently to control for agreement on the measurements and check the reliability of the data. Bland-Altman statistical methods and plots were used to assess the agreement between the two independent observers (24). Data are presented as mean difference with confidence interval (CI). GraphPad Prism (version 6.00 for Windows, GraphPad Software, La Jolla California USA) was used for analysis.

Data analysis

SPSS 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. Armonk, NY: IBM Corp.) was used for statistical analyses. Continuous variables were presented as means with standard deviations (SD) or medians with inter quartile range (IQR). Categorical variables were presented as numbers with percentages (%). Independent T-test, and Fisher exact test were used for baseline characteristics and to analyse the inter rectus distance. A linear regression model was used to control for other potential confounding factors for the width of the linea alba at all levels of measurements. Contributing factors that are known from literature were included in the model (i.e. BMI, history of smoking, AAA, age at CT-scan, DM). Data are presented as beta unstandardized coefficients (β) with p-values. A p-value less than 0.05 was considered statistically significant.

MATLAB commercial software package (MATLAB R2013b, The MathWorks Inc., Natick, MA) was used to reconstruct the surface of the linea alba. Using the width of the linea alba at the defined measuring heights, the surface area of the linea alba could be constructed. All the measurements were converted to coordinates that describe the outline of the linea alba. The approximated circumference of the linea alba was created by interpolating the coordinates the piecewise cubic hermite interpolating polynomial (PCHIP) algorithm. This algorithm is suited to obtain a realistic representation of the linea alba, because it yields a smooth circumference. The surface area within the closed circumference was then calculated by numerical integration.

Results

Between September 2003 and July 2014, 80 male patients with virgin linea alba underwent open repair of AAA and were included. Ninety-eight male patients who underwent open colorectal surgery were included in the control group. The mean time between preoperative CT-scan and surgery was 100 days (SD 112 days) and 68 days (SD 56 days) in the AAA group and control group respectively. Mean follow-up was 29.1 months (SD 28.7 months) in the AAA group and 29.4 months (SD 21.1 months in the control group), p=0.929. Data on baseline characteristics are presented in Table 1. Preoperatively 17 patients (21%) with AAA were diagnosed or operated for an inguinal hernia compared to 22 patients (22%) in the control group (p=1.000).

Table 1. Baseline characteristics

		AAA group (N=80)	Control group (N=98)	p-value
Age at surgery, *year (SD)*		67 (7.8)	63 (11.0)	0.012*
Length, *cm (SD)*		178 (7.4)	178 (7.0)	0.743
Weight, *kg (SD)*		84 (14)	83 (14)	0.522
Body Mass Index, *kg/m^2 (SD)*		26.4 (3.7)	25.9 (4.0)	0.394
History of smoking *(%)*		73 (91)	63 (65)	<0.001*
Diabetes Mellitus *(%)*		10 (13)	17 (17)	0.408
Diameter aorta, *mm (SD)*		66 (12)	22 (3)	<0.001*
History of inguinal hernia *(%)*		17 (21)	22 (22)	1.000
ASA Class	I *(%)*	1 (2)	31 (34)	<0.001*
	II *(%)*	24 (37)	43 (47)	
	III *(%)*	38 (59)	17 (19)	
	IV *(%)*	2 (3)	0 (0)	
Death during follow up *(%)*		27 (34)	20 (20)	0.060*

*****Statistically significant. P-values are 2-sided. T-test (continuous variables) and Fisher exact test (categorical variables) were performed.
Abbreviations: AAA, Abdominal Aorta Aneurysm; ASA, American Society of Anaesthesiologists

Reference length between xiphoid bone and symphysis pubis and the distance between the rectus muscles i.e. the width of the linea alba, are presented in Table 2. In the multivariable analysis, BMI, history of smoking, AAA, age at CT-scan, and DM were included. Only BMI was an independent contributing factor for the width of the linea alba to all 6 different levels of measurements (A, β=1.673, p<0.001; B, β=1.116, p<0.001; C, β=1.075, p<0.001; D, β=1.100, p<0.001; E, β=0.482, p<0.001; F, β=1.765, p<0.001). When BMI was increased by 1.0 kg/m^2, the width of the linea alba increases with β in mm. Age appeared to be an independent contributing factor on levels below the umbilicus, B and E respectively (B, β=0.241, p=0.001; E, β=0.104, p=0.042). None of the other variables included in the linear regression analysis were found to be statistically significant.

Table 2. Measurements of the linea alba

		AAA group (N= 80)	Control group (N=98)	p-value
Reference length (Xyphoid-Pubic bone)*, mm (SD)*		351 (28)	357 (32)	0.179
Width, *mm (SD)*	A. (1/3 length)	28 (12)	27(18)	0.729
	B. (2/3 length)	14 (10)	13(11)	0.425
	C. (umbilicus)	28(8)	28(11)	0.772
	D. (30mm. above umbilicus)	28(10)	27(12)	0.543
	E. (30mm. below umbilicus)	15(7)	14(6)	0.136
	F. (maximum)	36(12)	36(17)	0.960

P-values are 2-sided. T-test (continuous variables) was performed.
Abbreviations: AAA, Abdominal Aorta Aneurysm.

Bland-Altman statistical methods and plot was built to assess the agreement between the two independent observers. All individual measurements were merged and used in the analysis. The results are plotted in Figure 2. The calculated mean difference between the observers was 2.98 mm. (95% CI-6.3 mm; 12.2 mm), p=0.270. This implies that the first observers (J.V.) measurements were almost 3 mm. wider than the second observers' measurements.

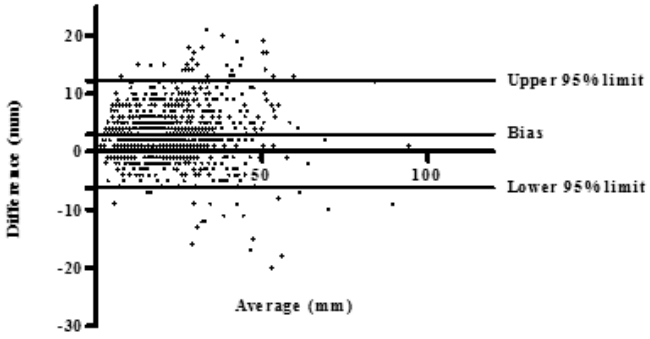


Figure 2. Bland-Altman plot of the inter observer agreement

The interpolated circumferences of the linea alba are presented in Figure 3. The surface was calculated for each individual reconstruction. The mean surface area of the linea alba in patients with AAA was 58.7 cm^2 (SD 24.4 cm^2) and 58.4 cm^2 (SD 33.0 cm^2) in the control group: p=0.951.

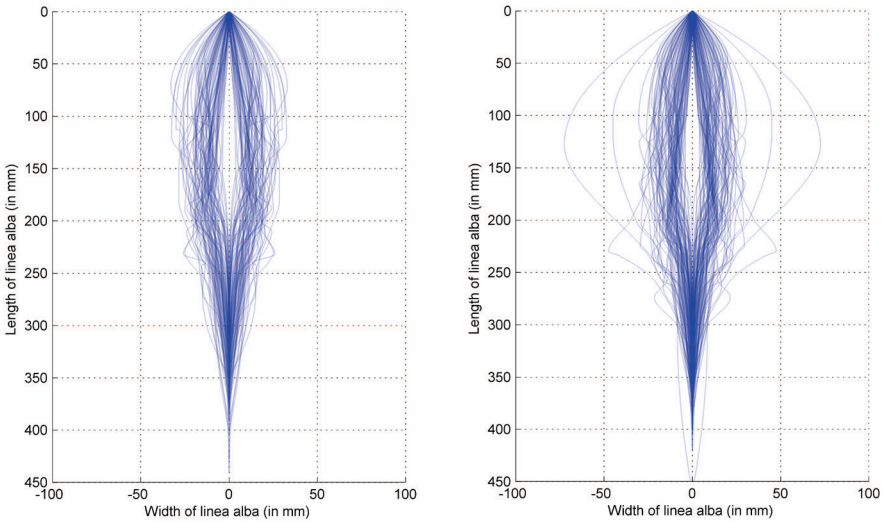


Figure 3. Reconstruction of the surface of the linea alba in patients with AAA and the control group
Reconstruction of the linea alba using an interpolation
Left: Patients with AAA, right control group (patients with colorectal carcinoma)

During follow-up, 36 patients developed incisional hernia. Thirteen patients (16%) in the AAA group and 23 (24%) in the control group: p=0.264. During follow up multiple patients underwent a second or even third laparotomy. There was no significant difference in preoperative width of the linea alba between patients who developed incisional hernia and patients who did not develop incisional hernia during follow-up. Twelve patients (17%) with AAA underwent a relaparotomy. One of the patients who underwent a relaparotomy after AAA surgery developed an incisional hernia (8%). In the control group 58 patients (59%) underwent a relaparotomy. Twelve patients developed an incisional hernia after the relaparotomy (21%).

Discussion

The present study showed no difference in width and surface of the linea alba between patients with AAA and the control group as measured in the preoperative setting. It also showed no evidence that a wider linea alba is an independent risk factor for the development

of incisional hernia. However, a higher BMI was associated with a wider linea alba from xiphoidal bone to symphysis pubis, and higher age was also associated with a wider linea alba, beneath the level of the umbilicus. These are relevant results, as the available literature is contradictory and methodology in other studies was poorly described (18, 20, 21).

A study published in 2009 showed a significant higher incidence of diastasis recti in patients with AAA compared with patients with peripheral arterial occlusive disease (PAOD). These results were only based on physical examination done by a single observer. Also the number of patients, (18 vs. 24 patients) included in this study was relatively small (21). Another study published in 2009 compared 75 male patients with AAA to matched controls. A single observer measured the maximum width of the linea alba above and below the umbilicus and found no differences. In this study the baseline characteristics between both groups (except from age) were not described. Moreover, the lack of fixed levels for the measurements and using the measurements of one single observer make the results of this study possibly less reliable (20). Another, published in 2010, also found an increased width of the inter rectus muscle distance in patients with AAA. In this study the male-female ratio was different between the groups (56% in the control group and 89% in the AAA group). The comparison may have been confounded by anatomical differences caused simply by gender or previous childbirth. Furthermore the clinical assessment of fifty patients showed a wider linea alba in patients with AAA (18). However, the higher BMI and age of the patients with AAA in the assessment, compared to the control group, could also explain the difference between the groups, since BMI and age are independent factors that are associated with a wider linea alba in our present study.

None of the aforementioned studies on the linea alba looked at postoperative incisional hernia. These data provides more insight in the clinical relevance of a wide linea alba. In the present study there was no association between the width of the linea alba and the incidence of incisional hernia. Therefore, the preoperative width of the linea cannot be used as a predictive tool for incisional hernia. The incidence of incisional hernia in the present study is similar to the incidence described in literature (6-9). However the patients with a colorectal carcinoma underwent more radiological imaging postoperatively. An occult incisional hernia therefore could be diagnosed more often in the control group.

Using fixed assessment levels to measure the width of the linea alba and using a second observer to control for agreement on the measurements make the data more reliable and consistent. This study provides a unique dataset on contributing factors for a wider linea alba. None of the previous studies performed a multivariable regression analysis in order to identify independent contributing factors. We found higher BMI and age to be new contributing factors for a wider linea alba. It is hypothesized that obesity results in higher

intraabdominal pressure. Repeated stress to the linea alba, as a result of this pressure could explain the wider linea alba in obese patients. Age is also associated with a wider linea alba. We hypostasize that ongoing degeneration of collagen as result of the aging process leads to a wider linea alba. AAA was not associated with a wider linea alba. A higher incidence of incisional hernia in patients with AAA, described in literature, can possibly be explained by poor healing of the laparotomy wound by pre-existent collagen deficiencies. Poor wound healing will result in the development of incisional hernia. A poor preoperative condition of the linea alba as a result of the collagen deficiencies could not be found.

The present study has several limitations of which most are attributable to the retrospective design. Selection bias could have occurred. Only the patients who underwent open elective repair of their AAA were included. In our hospital most patients had an endovascular aneurysm repair during the inclusion period, which makes our group a selected patient category. Furthermore, the control group consisted of patients with colorectal carcinoma referred to an academic hospital. Subsequently, this often resulted in midline laparotomies because of locally advanced or metastatic diseases. It could be possible that their poor clinical condition influenced the results found by the present study.

No significant difference has been found between the groups according to the incidence of incisional hernia. This could be due to different follow up schedules between the two groups; patients with a carcinoma had more postoperative radiological imaging and outpatient clinic visits. Therefore more incisional hernia could have been diagnosed, before causing possible symptoms. This is contrary to the patients with AAA, who only underwent radiological imaging when indicated. Therefore, the incidence of incisional hernia in the AAA group could have been underestimated.

The first observers (J.V.) measurements were almost 3 mm. wider than the second observers' measurements. However this difference is consequent in both groups and not significant. Therefore conclusions can be drawn about the differences between the patients with an AAA and the control group.

Keeping these limitations in mind, this retrospective cohort shows no difference in width and surface of the linea alba between patients with AAA and colorectal cancer. A higher BMI is associated with a wider linea alba and higher age is associated with a wider linea alba below the umbilicus. There is no evidence that a wider linea alba will result in the development of postoperative incisional hernia.

References

1. Anthony T, Bergen PC, Kim LT, Henderson M, Fahey T, Rege RV, et al. Factors affecting recurrence following incisional herniorrhaphy. World J Surg. 2000;24(1):95-100;discussion 1.
2. Manninen MJ, Lavonius M, Perhoniemi VJ. Results of incisional hernia repair. A retrospective study of 172 unselected hernioplasties. Eur J Surg. 1991;157(1):29-31.
3. 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(5):361-7.
4. Read RC, Yoder G. Recent trends in the management of incisional herniation. Arch Surg. 1989;124(4):485-8.
5. Deerenberg EB, Harlaar JJ, Steyerberg EW, Lont HE, van Doorn HC, Heisterkamp J, et al. Small bites versus large bites for closure of abdominal midline incisions (STITCH): a double-blind, multicentre, randomised controlled trial. Lancet. 2015.
6. van 't Riet M, Steyerberg EW, Nellensteyn J, Bonjer HJ, Jeekel J. Meta-analysis of techniques for closure of midline abdominal incisions. Br J Surg. 2002;89(11):1350-6.
7. Wissing J, van Vroonhoven TJ, Schattenkerk ME, Veen HF, Ponsen RJ, Jeekel J. Fascia closure after midline laparotomy: results of a randomized trial. Br J Surg. 1987;74(8):738-41.
8. Burger JW, Luijendijk RW, Hop WC, Halm JA, Verdaasdonk EG, Jeekel J. Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia. Ann Surg. 2004;240(4):578-83; discussion 83-5.
9. Fassiadis N, Roidl M, Hennig M, South LM, Andrews SM. Randomized clinical trial of vertical or transverse laparotomy for abdominal aortic aneurysm repair. Br J Surg. 2005;92(10):1208-11.
10. Langer C, Schaper A, Liersch T, Kulle B, Flosman M, Fuzesi L, et al. Prognosis factors in incisional hernia surgery: 25 years of experience. Hernia. 2005;9(1):16-21.
11. Sauerland S, Korenkov M, Kleinen T, Arndt M, Paul A. Obesity is a risk factor for recurrence after incisional hernia repair. Hernia. 2004;8(1):42-6.
12. Sorensen LT, Hemmingsen UB, Kirkeby LT, Kallehave F, Jorgensen LN. Smoking is a risk factor for incisional hernia. Arch Surg. 2005;140(2):119-23.
13. Sugerman HJ, Kellum JM, Jr., 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(1):80-4.
14. Bevis PM, Windhaber RA, Lear PA, Poskitt KR, Earnshaw JJ, Mitchell DC. Randomized clinical trial of mesh versus sutured wound closure after open abdominal aortic aneurysm surgery. Br J Surg. 2010;97(10):1497-502.
15. Henriksen NA, Helgstrand F, Vogt KC, Jorgensen LN, Bisgaard T. Risk factors for incisional hernia repair after aortic reconstructive surgery in a nationwide study. Journal of Vascular Surgery. 2013;57(6):1524-30.e3.
16. Olsson C, Eriksson P, Franco-Cereceda A. Association between thoracic aortic disease and inguinal hernia. Journal of the American Heart Association. 2014;3(4).
17. Antoniou GA, Georgiadis GS, Antoniou SA, Granderath FA, Giannoukas AD, Lazarides MK. Abdominal aortic aneurysm and abdominal wall hernia as manifestations of a connective tissue disorder. Journal of Vascular Surgery. 2011;54(4):1175-81.
18. De'Ath HD, Lovegrove RE, Javid M, Peter N, Magee TR, Galland RB. An assessment of between-recti distance and divarication in patients with and without abdominal aortic aneurysm. Ann R Coll Surg Engl. 2010;92(7):591-4.
19. McPhail I. Abdominal aortic aneurysm and diastasis recti. Angiology. 2008;59(6):736-9.
20. Moesbergen T, Law A, Roake J, Lewis DR. Diastasis recti and abdominal aortic aneurysm. Vascular. 2009;17(6):325-9.

21. McPhail I. Abdominal aortic aneurysm and diastasis recti. Angiology. 2009;59(6):736-9.
22. Timmermans L, Eker HH, Steyerberg ES, Jairam A, De Jong D, Pierik EGJM, et al. Short-term results of a randomized controlled trial comparing primary suture with primary glued mesh augmentation to prevent incisional hernia. Annals of Surgery. 2015;261(2):276-81.
23. Timmermans L, De Goede B, Eker HH, Van Kempen BJH, Jeekel J, Lange JF. Meta-analysis of primary mesh augmentation as prophylactic measure to prevent incisional hernia. Digestive Surgery. 2014;30(4-6):401-9.
24. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986;1(8476):307-10.

Chapter 8

Summary and conclusions

This thesis consists of two parts: **part 1** describes a new prosthesis for the treatment of large and complex incisional hernia. Furthermore the natural course and consequences of conservative treatment are described; **part 2** focusses on three complex groups of patients with abdominal wall hernia. The treatment and risk factors for complications in premature infants with an inguinal hernia, kidney transplant recipients with incisional hernia, and patients with an abdominal aneurysm of the aorta are described.

Part 1

In **Chapter 2** a new mesh prosthesis used for the treatment of large and complex incisional hernia is described. Mesh placement in retromuscular position is a widely accepted technique for the repair of large ventral hernia. A new Parietex mesh with self-gripping microhooks (velcro) was placed in the retromuscular position. After closing the posterior rectus fascia the mesh was placed with the microhooks on the posterior fascia without additional fixation of sutures. Twenty-eight consecutive patients were treated with this new mesh. During a short median follow up of twelve weeks, none of the patients developed a recurrence. Twenty-three patients (82%) did not report any pain at their final outpatient clinic visit. Seven percent of the patients reported mild abdominal pain and 11% had moderate abdominal pain. This study was the first cohort that describes the use of this self-gripping mesh in incisional hernia repair and promisingly shows that placement in retro-muscular position appears to be safe and feasible for open incisional hernia repair with minimal postoperative sequela and no recurrences within the short term follow-up.

In some patients, who developed incisional hernia, watchful waiting or conservative treatment can be considered. In **Chapter 3** the differences in outcome between watchful waiting and direct operative treatment after diagnosis were investigated. Data from 255 patients was collected retrospectively. Fifty-nine percent underwent surgical repair and in 41% a watchful waiting strategy was adapted. Reasons for watchful waiting were the absence of symptoms and comorbidities such as obesity. During follow-up 33% of the patients crossed over from watchful waiting to operative treatment, in some cases patients even underwent emergency repair due to incarceration. Crossover from watchful waiting to operative treatment led to significantly greater incidence of intraoperative perforations, fistulas and mortality than in patients who underwent elective repair direct after diagnosis, particularly in patients who required emergency repair due to incarceration. The majority of patients, who switched, did so during the first two years after diagnosis. Patients who are treated conservatively should be informed and aware of potential risks of need for emergency repair resulting in higher morbidity and mortality.

Part 2

In **Chapter 4** risk factors for incarceration of inguinal hernia in premature born infants were investigated. Common surgical knowledge is that inguinal hernia repair in premature infants should be postponed until they reach a certain weight or age. Optimal management, however, is still under debate. We tried to collect evidence for the optimal management and timing of inguinal hernia repair. Retrospective data of premature infants with inguinal hernia, who underwent hernia correction within 3 months after birth, were analysed. Hundred-forty-two premature infants were included in the analysis. More than half of the patients presented with a symptomatic inguinal hernia and more than for half of these symptomatic hernia emergency surgery was performed. The complication rate was 27% after emergency operations versus 10% after elective repair. Also the recurrence rate was significantly higher after emergency surgery: 14% versus 2% after elective repair. A multivariate analysis: Cox proportional hazards model was used to identify independent risk factors for incarceration requiring an emergency procedure. Premature infants with a birth weight below 1.500 grams appeared to have almost a threefold greater risk for emergency surgery than heavier premature infants with inguinal hernia. Emergency repair resulted in higher recurrence rates and more complications. Elective hernia repair is recommended, particularly in very low birth weight premature infants. It can even be argued that this particular group of premature infants should be operated on during their birth hospitalization.

In **Chapter 5** a detailed overview of the direct medical costs and healthcare consumption of premature born infants with inguinal hernia was provided. Again, we distinguished between premature infants, who had to undergo an emergency procedure and those, who underwent elective inguinal hernia repair. Real medical costs were calculated by multiplying the volumes of healthcare use with corresponding unit prices. Per patient costs of hospitalization, outpatient care, diagnostic procedures, perioperative care and the surgical procedures were taken into account. Hundred-thirty-two patients were included in the analysis. The mean costs per patient amounted to € 5477. Hospitalisations made up two thirds of the total costs (€ 3573). It appeared that emergency repair is almost 60 % more expensive than elective repair. Total costs of emergency repair compared with elective repair €7418 versus €4693, respectively. Therefore, it can be argued that preventing premature infants from incarceration, for which often emergency repair is needed, will reduce aggregate direct medical costs. Surgery in premature patients is very costly, insight into the actual costs of different strategies in inguinal hernia repair would be relevant for planning and organization of care, for supporting clinical decisions, and for efficient allocation of health care resources.

In **Chapter 6** we evaluated the incidence and treatment of incisional hernia after kidney transplantation and identified new potential risk factors. Transplant recipients may have an increased risk to develop incisional hernia due to the use of postoperative immunosuppressive therapy resulting in impaired wound healing, on the other hand the anatomical location of the iliac space in kidney transplantation and the transfascial and muscular approach perpendicular to the tension lines of the abdomen will lower the incidence of incisional hernia. In a retrospective cohort study all kidney transplant recipients (n=1564) between 2002 and 2012 were included with a median follow up of fifty-nine months. Fifty patients (3.2%) developed incisional hernia. Obesity (BMI >30), female sex, concurrent abdominal wall hernias, history of smoking, duration of surgery, and multiple explorations were independent risk factors for the development of incisional hernia after kidney transplantation. Thirty-five percent needed emergency operative repair for an incarcerated incisional hernia. Recurrences occurred in 23%. Possible future research should be devoted to addressing those preoperative risk factors to be modified, such as weight reduction.

The linea alba is a fibrous structure that runs down the midline of the abdomen in humans. It runs from the xiphoid process to the pubic symphysis and is composed mostly of collagen connective tissue. In **Chapter 7** anatomical differences of the linea alba between patients with an aneurysm of the abdominal aorta and a control group i.e. patients with colorectal cancer were looked for. Male patients, with virgin linea alba, who were to undergo elective open repair of aneurysm were compared with patients undergoing surgery for colorectal cancer. Preoperative CT-scans were analysed. The width was measured at six standard levels between xiphoid and pubic bone. The surface of the linea alba was reconstructed and analysed. Eighty patients with an abdominal aneurysm of the aorta were included and compared to ninety-eight patients in the control group with a mean follow-up of twenty-nine months. We measured the width of the linea alba through the inter rectus muscle distance. For each patient the measurements were taken at 1/3 and 2/3 of the reference length between the xyphoid bone and the pubic bone, at the level of the umbilicus, thirty millimeters above the umbilicus and thirty millimeters below the umbilicus and maximum width of the linea alba. No difference in width and surface of the linea alba between patients with aneurysms and the control group as measured in the preoperative setting was found. It also showed no evidence that a wider linea alba is an independent risk factor for the development of incisional hernia. Mean reconstructed surface in patients with an aneurysm was 58.7 cm^2 and 58.4 cm^2 in the control group. Multivariable analysis showed that higher BMI was associated with a wider linea alba and higher age was associated with a wider linea alba below the umbilicus. Postoperatively, 16% of the patients in the aneurysm group and 24% in the control group developed an incisional hernia. The study showed no difference in width and surface of the linea alba. In this cohort there was no evidence that a wider linea alba results in the development of incisional hernia.

Chapter 9

Nederlandse samenvatting en conclusies

Dit proefschrift bestaat uit twee delen: **deel 1** beschrijft een nieuw soort “mesh” toegepast voor de behandeling van grote en complexe littekenbreuken. Daarnaast wordt het natuurlijke beloop van onbehandelde littekenbreuken en de gevolgen van een conservatief beleid beschreven; **deel 2** is gericht op een drietal complexe patiënten populaties met buikwandbreuken. De behandeling en analyse van risicofactoren met betrekking tot het ontwikkelen van complicaties werd onderzocht. Bij premature patiënten met een liesbreuk zijn de incidentie, kosten en complicaties onderzocht. Bij de ontvangers van een niertransplantaat is gekeken naar de ontwikkeling van littekenbreuken en bij patiënten met een abdominaal aneurysma van de aorta is de relatie tussen de breedte van de linea alba en het ontstaan van littekenbreuken onderzocht.

Deel 1

In **Hoofdstuk 2** wordt een nieuw soort meshprothese beschreven, die onder andere wordt gebruikt voor de behandeling van grote en complexe littekenbreuken. Het plaatsen van een mesh in de retromusculaire positie is een alom bekende en veel toegepaste techniek voor de behandeling van grote ventrale buikwandbreuken. Deze nieuwe Parietex mesh met unieke, zelfklevende microhaakjes (velcro, klittenband) gemaakt van polymelkzuur werd geplaatst in de retro-musculaire positie. Na het sluiten van de posterieure rectusfascia werd de mesh geplaatst met de microhaakjes op de fascie en zonder extra fixatietechnieken. Achtentwintig patiënten werden achtereenvolgens behandeld met deze nieuwe mesh. Na een korte mediane follow up van twaalf weken werden patiënten terug gezien op de polikliniek. Geen van de patiënten ontwikkelde een recidief littekenbreuk. Drieëntwintig patiënten (82%) hadden geen pijnklachten bij het laatste bezoek op de polikliniek. De overige 18% van de patiënten, die met deze mesh behandeld werden, had milde tot middelmatig ernstige abdominale pijnklachten. Deze studie is het eerste cohort dat het gebruik van deze nieuwe mesh in de retromusculaire positie beschrijft. De resultaten zijn veelbelovend en laten zien dat het gebruik van deze mesh veilig en goed toepasbaar is gezien dat er weinig complicaties optraden en geen recidieven werden gezien.

Bij sommige patiënten, die een littekenbreuk ontwikkelen, kan een conservatieve behandeling worden overwogen. In **Hoofdstuk 3** werden de verschillen onderzocht tussen een conservatieve en operatieve behandeling van de littekenbreuk. Gegevens van 255 patiënten werden retrospectief verzameld en geanalyseerd. In 59% van de patiënten werd aanvankelijk operatief behandeld en in 41% werd een afwachtend conservatief beleid ingezet. Redenen om niet te opereren waren het afwezig zijn van symptomen of klachten en comorbiditeit zoals bijvoorbeeld obesitas. Gedurende de follow-up werd 33% van de patiënten met

een aanvankelijk conservatief beleid alsnog geopereerd. In een aantal gevallen betrof het zelfs een spoedoperatie in verband met beklemming van de littekenbreuk. Wanneer er in tweede instantie pas geopereerd werd, leidde dit tot meer postoperatieve complicaties zoals peroperatieve darmletsels, fistelvorming en zelfs mortaliteit. Voornamelijk de patiënten, die een spoedingreep moesten ondergaan als gevolg van een beklemming, hadden een grotere kans op het ontwikkelen van complicaties. Het merendeel van de operaties van patiënten, die alsnog werden geopereerd, vond plaats in de eerste twee jaar na diagnose. Bij patiënten, bij wie een expectatief beleid wordt ingezet, moet daarom goed worden uitgelegd wat de risico's zijn op een latere spoedoperatie en de daarbij horende morbiditeit en mortaliteit.

Deel 2

In **Hoofdstuk 4** werden de risicofactoren voor het krijgen van een beklemde liesbreuk bij prematuur geboren neonaten onderzocht. Over het algemeen wordt aangenomen dat het verstandig is om te wachten met opereren van prematuren tot ze een bepaald gewicht of leeftijd hebben. Echter zijn hier de boeken nog niet over gesloten. We hebben getracht het meest ideale moment te definiëren om deze kwetsbare patiënten te opereren. De retrospectieve gegevens van premature patiënten, die binnen drie maanden na de geboorte een liesbreukoperatie hebben ondergaan, werden verzameld en geanalyseerd. Honderdtweeënveertig patiënten werden geanalyseerd. Meer dan de helft van deze patiënten presenteerde zich met een symptomatische liesbreuk, de helft van deze symptomatische patiënten moesten daarop een spoedoperatie ondergaan. Het aantal complicaties na een spoedoperatie was 27% versus 10% na een geplande operatie. Daarnaast was het percentage recidief liesbreuken significant hoger na een spoedoperatie namelijk 14% versus 2% na electieve liesbreukcorrectie. Een multivariate analyse werd verricht om onafhankelijke risicofactoren voor het moeten ondergaan van een spoedingreep te onderzoeken. De prematuur geboren patiënten met een geboortegewicht lager dan 1,5 kilogram hadden een bijna drie keer zo hoog risico op een spoedoperatie in vergelijking met prematuren met een hoger geboortegewicht. Een spoedoperatie leidde tot hogere recidief percentages en meer complicaties. Electieve chirurgie bij een prematuur geboren patiënt verdient nog steeds de voorkeur, zeker bij de erg kwetsbare patiënten met zeer laag geboortegewicht. Daarom is het te overwegen om juist deze patiënten te opereren gedurende de opname na geboorte en niet af te wachten tot ze een zekere leeftijd of gewicht hebben bereikt.

In **Hoofdstuk 5** wordt een overzicht gegeven van de kosten, die gepaard gaan met de behandeling van prematuren met een liesbreuk. Wederom werd onderscheid gemaakt tussen een spoedoperatie en een geplande liesbreukcorrectie. De kosten werden berekend

door de volumina van de zorg (bijvoorbeeld een ligdag op de afdeling) te vermenigvuldigen met de daarbij behorende kostprijzen. Per patiënt werden de kosten van het verblijf in het ziekenhuis, de poliklinische zorg, perioperatieve zorg, diagnostiek en de kosten van de operatie zelf berekend. Honderdtweeëndertig patiënten werden geselecteerd voor analyse. De gemiddelde kosten per patiënt werden vastgesteld op €5,477. Twee-derde van de kosten bestonden uit de kosten voor het verblijf in het ziekenhuis te weten €3,573. Het bleek dat de gemiddelde kosten voor een spoedoperatie 60% hoger uitvielen dan voor een geplande operatie. De totale kosten waren € 7,418 en € 4,693 voor respectievelijk een spoedoperatie en een geplande operatie. Op het gebied van kosten verdient het daarom de aanbeveling om patiënten snel gepland te opereren, voordat ze in een spoedoperatie terecht komen. Het opereren van premature patiënten is relatief duur en daarom is het ook belangrijk dat de verschillende opties en timing van een operatie ook vanuit een kostenperspectief moeten worden belicht.

In **Hoofdstuk 6** werd de incidentie onderzocht van littekenbreuken bij patiënten, die een niertransplantatie hebben ondergaan. Daarnaast werd ook gekeken naar riscofactoren voor het krijgen van een littekenbreuk. De ontvangers van een donororgaan zouden theoretisch een verhoogd risico hebben op het ontwikkelen van littekenbreuk, omdat het gebruik van immunosuppressiva tot een vergroot risico op het ontwikkelen van wondinfecties en secundair daaraan een littekenbreuk leidt. Anderzijds zal de anatomische benadering van de fossa iliaca waar het transplantaat wordt geplaatst door middel van een incisie, evenwijdig aan de trekrichting van de buikwand, het risico op het ontstaan van een littekenbreuk verlagen. Alle patiënten, die tussen 2002 en 2012 een niertransplantatie ondergingen, werden geïncludeerd. Een totaal van 1,564 patiënten werd geëvalueerd op het ontwikkelen van een littekenbreuk na de transplantatie. De mediane follow up was 59 maanden. Slechts vijftig patiënten: 3.2%, ontwikkelde een littekenbreuk. Obesitas, het vrouwelijk geslacht, het hebben van simultane andere buikwandbreuken, roken, duur van de transplantatieprocedure en meerdere ingrepen in dezelfde fossa bleken onafhankelijke riscofactoren voor het ontwikkelen van een littekenbreuk. 50% van de patiënten werd aan de littekenbreuk geopereerd, waarvan 35% een spoedoperatie als gevolg van beklemming moest ondergaan. Daarnaast was het recidief percentage na een operatieve behandeling 23%. In de toekomst zal onderzoek moeten worden gedaan om te bezien hoe deze risicofactoren te beïnvloeden zijn.

De linea alba is de lijn, waar de twee rechte buikspieren samenkomen. Deze verloopt vanaf het xyphoid naar beneden tot aan de symfyse van het os pubis en bestaat voornamelijk uit collageen en bindweefsel. In **Hoofdstuk 7** werden de anatomische verschillen van de linea alba tussen twee verschillende patiëntpopulaties onderzocht. De eerste groep bestond uit

patiënten met een aneurysma van de abdominale aorta en de controle groep bestond uit patiënten met een colorectaal carcinoom. Mannelijke patiënten, die nooit eerder waren geopereerd door middel van een incisie door de linea alba, werden onderzocht. Aan de hand van preoperatieve CT-scans werd de linea alba opgemeten. De breedte van de linea alba werd bepaald op zes verschillende niveaus tussen het xyphoid en het os pubis, waarbij de oppervlakte gereconstrueerd en uitgerekend werd. In totaal werden 80 patiënten met een aneurysma uitgezet tegenover 98 in de controlegroep. De gemiddeld duur van follow up na de operatie door de linea alba was 29 maanden. De metingen werden verricht op 1/3 en 2/3 van de lengte. Daarnaast werd de breedte opgemeten ter hoogte van de navel, 30 mm boven de navel en 30 mm onder de navel, waarbij de maximale breedte bepaald werd. Er werd geen verschil gevonden tussen beide patiënten populaties op alle zes niveaus. Ook de gereconstrueerde oppervlakte van de linea alba was nagenoeg gelijk in respectievelijk de aneurysma groep en de controlegroep namelijk 58.7 cm^2 en 58.4 cm^2. Een multivariabele analyse toonde wel aan dat een hogere BMI tot een bredere linea alba op alle zes de niveaus leidt. Een hogere leeftijd leidt tot een bredere linea alba op het niveau onder de navel. Postoperatief ontwikkelde 16% van de patiënten in de aneurysma groep een littekenbreuk, in de controle groep lag dat percentage nog hoger op 24%. Er werd in dit cohort echter geen verband gevonden tussen de breedte van de linea alba en het ontwikkelen van een littekenbreuk.

Chapter 10

General discussion and future perspectives

List of publications

Dankwoord

Curriculum Vitae

PhD Portfolio

General discussion and future perspective

Abdominal wall surgery is emerging more and more as a separate specialism within the large field of surgery, however still touching all surgical specialities like gastro-intestinal, transplantation, vascular, paediatric and trauma surgery. As long as abdominal wall surgery is not a well-established subspecialism it should only be performed by dedicated surgeons within the aforementioned specialties. Moreover, if hernia surgery becomes a subspecialism, the next step would be the development of dedicated hernia centres, supported by scientific committees and government. Incidences of abdominal wall hernia are high and hernia repair is the most common operation performed worldwide. Approaching the abdominal wall from all different subspecialisms means that consensus is necessary on how to approach abdominal wall hernia and how to guarantee best practice. Much research is performed and it becomes more and more evident which techniques and mesh are preferable for each individual patient. Hernia surgery is still rapidly evolving and it is challenging for clinicians to remain up to date.

Mesh and techniques

Nowadays, in hernia surgery there is need for standardisation in research. The industry puts a lot of effort in research and development of new meshes, which has resulted in the introduction of many new types of meshes with different characteristics. The ideal mesh for all circumstances has not been invented (yet), but over 200 different mesh prostheses are commercially available nowadays (1). Beside the different materials, all these meshes have different features and characteristics. For a surgeon it remains difficult to select which is best for each patient category. Future research should become standardised and uniform to make a better, carefully weighted, comparisons between the different types of meshes. For example, to achieve this uniformity, international research groups should collaborate even more and come to an agreement about standard levels of evidence needed before the introduction of a new prosthesis. Not only there should be more cooperation between international research groups, but also the mesh industry should be involved in these collaborations.

Experimental (animal) models should be standardised in order to make a clear comparison between all the prosthetic meshes commercially available nowadays. Another way to achieve standardisation in research could be the development of reproducible, artificial models. A validated model of the human abdominal wall could help to compare different sutures and mesh materials. It could also give new insight on the common used surgical procedures, suture techniques, mesh placement and become a substantial alternative for clinical and animal studies.

Besides the search for the best mesh prosthesis, surgical techniques are getting optimized and new surgical techniques have been invented. Reconstruction of the abdominal wall can be achieved by either laparoscopic or open repair. There appears to be a shift towards favouring the laparoscopic repair of abdominal wall hernia in the last decades. On the other hand, the TREPP (Trans Rectus sheath Extra-Peritoneal Procedure) and TIPP (Trans Inguinal Pre-Peritoneal) are new introduced open hernia repair approaches, invented to reduce postoperative groin pain (2-5). The open repair of large abdominal wall defects using the (open) Rives-Stoppa technique or component separation technique is still preferred and not replaced by laparoscopic repair. Even hybrid techniques with a laparoscopic and an open phase are described (6). Existing surgical techniques could be enhanced by 3D-laparoscopy, robot-surgery, or even virtual reality (7-10). These new extensions could potentially benefit the outcomes of laparoscopic surgery and should be further investigated. Therefore, both, open and laparoscopic hernia repair, are expected to be further developed.

The applicability of currently available meshes for other indications and techniques should also be explored more often. In Chapter 2 we investigated a mesh that was only used for inguinal hernia repair at that time (11, 12). In our cohort, this relatively new mesh was used for the repair of incisional hernia and it was placed in well-known retro-muscular position. This mesh appeared to be feasible for different type of abdominal wall hernia. Exploring the possibilities of existing meshes used for other indications or techniques could also lead to new insights in search for the ideal mesh.

Patient selection and timing

After the diagnosis of a hernia, the choice of management depends on several aspects. The complaints of the patients however, should always be leading. Patients can suffer from pain, discomfort, or have cosmetic complaints. After many years of research, surgical repair is the treatment of choice for these symptomatic patients (13). However, a significant group of patients do not have any symptoms or complaints.

Operative treatment of patients with minimally symptomatic or asymptomatic hernia has frequently been questioned (14, 15). In inguinal hernia, cost effectiveness and safety have already led to implementation of watchfully waiting in daily practice (16, 17). Performing hernia surgery on asymptomatic patients facilitates the possibility of surgical and mesh-related complications. The most important question is which patients benefit from watchful waiting and which benefit from surgical repair. Patients with a symptomatic incisional hernia seem to profit from surgical repair in the long-term course. However, in minimal and asymptomatic patients, postoperative clinically relevant pain and recurrence cast doubt on whether these patients benefit from surgical repair. On the other hand, the risk to undergo

surgery in an emergency setting with worse postoperative outcome advocates early elective repair. In Chapter 3 we investigated the natural course of conservatively treated patient with incisional hernia.

The preferred technique and golden standard in premature infants is the open herniotomy. Conservative treatment is not an option because of high incarceration rates in these specific patients. The fact that inguinal hernia repair in premature infants should be postponed until they reach a certain weight or age is common surgical knowledge. Optimal management, however, is still under debate (18, 19). Despite the research that has been done, conflicting published data have made it hard to draw definite conclusions about the timing of repair. Although the level of prematurity and dysmaturity are associated with high incidence of inguinal hernia, the technical challenges and risks of perioperative complications make postponing surgical repair more appealing, instead of performing early elective repair (20, 21). Although this more conservative approach can minimize the risk of surgical and anaesthetic complications, it might also increase the risk of incarceration, forcing an emergency procedure with potentially more negative sequelae compared with early elective repair. A multicentre, randomized controlled trial comparing quick repair during birth hospitalisation and delayed inguinal hernia repair in premature infants should be conducted. According to this thesis stratifying for weight at birth (1,500 g or >1,500 g), to provide clear evidence on optimal timing in this fragile group of patients, is necessary.

When deciding on which treatment is best for which patient, cost have to play a role. More evidence on actual costs of different surgical strategies would be welcome as a basis for the development of new decision-making tools. Outcomes of new prospective randomized trials, including cost-effectiveness, will help allocate health care resources even more efficiently (22). The mean direct medical costs of emergency repair of inguinal hernia repair in premature infants were significantly higher than the costs of elective repair. Attempting to prevent these fragile new-borns from an emergency procedure is not only appealing from a medical point of view but also from an economic point of view.

Complications and risk factors

Trying to prevent patients from getting postoperative complications, it is important to understand the pathophysiology of these complications. Therefore, fundamental research remains important to predict more carefully in whom, and when, postoperative sequela do occur. We already know that patients react differently to implantation of mesh with regard to the foreign body reaction. The perfect mesh, i.e., one without mesh related complications such as adhesions, shrinkage, seroma, or infection, which is applicable in every situation, will probably never be developed. Therefore, a tailor-made approach should be explored,

with regard to characteristics and foreign body reaction of the individual patient, through a preoperative evaluation of each patient. To understand these characteristics, risk factor analyses are needed to choose the right treatment options, or even influence them. For example, tell people to lose weight before hernia surgery, in order to prevent them from postoperative complications. Possible future research should be devoted to addressing preoperative risk factors that can be modified.

Another important focus for abdominal wall research is prevention. Preventing patients from developing incisional hernia or developing hernia recurrences is a very interesting and promising new field of research in abdominal wall surgery. Searching for preoperative risk factors for these postoperative complications is also welcome tool in terms of prevention. If we better understand which group of patients has an increased risk for developing hernia, we only have to intervene in these certain group of patients. For example, to prevent patient from developing incisional hernia after a median laparotomy, different closing techniques have been investigated. A continues running slowly absorbable suture with a suture length to wound length ratio of 4:1 significantly decreases the incidences of incisional hernia (23-25). However, some patients still have an increased risk developing incisional hernia. Well-known risk factors are obesity and patients with abdominal aortic aneurysms. Prevention through mesh prophylaxis, or primary mesh augmentation does reduce the incidence of incisional hernia after a median laparotomy. However mesh prophylaxis also induces mesh related complications, such as; pain, seroma, and mesh infections. If we can even better predict which patients are prone to develop an incisional hernia, according to new independent risk factors, we can limit the placement of prophylactic meshes to those with the highest risk to develop an incisional hernia.

New developments

Mobile apps are developed for use by patients and surgeons, in order to predict the risk of developing postoperative complications. Independent risk factors investigated in Chapters 4 and 6 could be implemented in new apps to calculate the individual risk of developing complications. They can also give an estimate of the postoperative quality of life and, moreover, the costs can be calculated. These new innovations help us to inform patients about their treatment and even give patients responsibility in their own treatment and prevent them from postoperative complications. Patients can try to modify preoperative risk factors, such as quitting smoking or losing weight. Besides this evaluation of the treatment in terms of symptom relief, quality of life and patient satisfaction measured in PROMs (Patient Reported Outcome Measurements) are becoming more important. When combining these data with objective clinical outcomes, it can be very valuable as research tool. Moreover, PROMs could be used as a diagnostic tool to discover complications or recurrences during follow-up without a visit to the outpatient clinic.

In conclusion, abdominal wall surgery is rapidly evolving and challenging. In the future we should even more "bridge the gaps", the gaps between fundamental research and clinical practice, between mesh industry and clinicians, and between the individual subspecialisms performing abdominal wall surgery.

References

1. Klinge U, Park JK, Klosterhalfen B. 'The ideal mesh?'. Pathobiology. 2013;80(4):169-75.
2. Lange JF, Lange MM, Voropai DA, van Tilburg MW, Pierie JP, Ploeg RJ, et al. Trans rectus sheath extraperitoneal procedure (TREPP) for inguinal hernia: the first 1,000 patients. World J Surg. 2014;38(8):1922-8.
3. Koning GG, Koole D, de Jongh MA, de Schipper JP, Verhofstad MH, Oostvogel HJ, et al. The transinguinal preperitoneal hernia correction vs Lichtenstein's technique; is TIPP top? Hernia. 2011;15(1):19-22.
4. Chen DC, Amid PK. Chronic pain and quality of life after transinguinal preperitoneal (TIPP) inguinal hernia repair: a few tips on TIPP. Hernia. 2013;17(6):693-5.
5. Gillion JF, Chollet JM. Chronic pain and quality of life (QoL) after transinguinal preperitoneal (TIPP) inguinal hernia repair using a totally extraperitoneal, parietalized, Polysoft (R) memory ring patch: a series of 622 hernia repairs in 525 patients. Hernia. 2013;17(6):683-92.
6. Chelala E, Barake H, Estievenart J, Dessily M, Charara F, Alle JL. Long-term outcomes of 1326 laparoscopic incisional and ventral hernia repair with the routine suturing concept: a single institution experience. Hernia. 2016;20(1):101-10.
7. Abdalla RZ, Garcia RB, Costa RI, Luca CR, Abdalla BM. [Modified robot assisted Rives/Stoppa videosurgery for midline ventral hernia repair]. Arq Bras Cir Dig. 2012;25(2):129-32.
8. Allison N, Tieu K, Snyder B, Pigazzi A, Wilson E. Technical feasibility of robot-assisted ventral hernia repair. World J Surg. 2012;36(2):447-52.
9. Gonzalez AM, Romero RJ, Seetharamaiah R, Gallas M, Lamoureux J, Rabaza JR. Laparoscopic ventral hernia repair with primary closure versus no primary closure of the defect: potential benefits of the robotic technology. Int J Med Robot. 2015;11(2):120-5.
10. Shekhar R, Dandekar O, Bhat V, Philip M, Lei P, Godinez C, et al. Live augmented reality: a new visualization method for laparoscopic surgery using continuous volumetric computed tomography. Surg Endosc. 2010;24(8):1976-85.
11. Kohler G, Lechner M, Mayer F, Kockerling F, Schrittwieser R, Fortelny RH, et al. Self-Gripping Meshes for Lichtenstein Repair. Do We Need Additional Suture Fixation? World J Surg. 2016;40(2):298-308.
12. Sanders DL, Nienhuijs S, Ziprin P, Miserez M, Gingell-Littlejohn M, Smeds S. Randomized clinical trial comparing self-gripping mesh with suture fixation of lightweight polypropylene mesh in open inguinal hernia repair. Br J Surg. 2014;101(11):1373-82; discussion 82.
13. Nieuwenhuizen J, Kleinrensink GJ, Hop WC, Jeekel J, Lange JF. Indications for incisional hernia repair: an international questionnaire among hernia surgeons. Hernia. 2008;12(3):223-5.
14. Lauscher JC, Leonhardt M, Martus P, Zur Hausen G, Aschenbrenner K, Zurbuchen U, et al. [Watchful waiting vs surgical repair of oligosymptomatic incisional hernias: Current status of the AWARE study]. Chirurg. 2016;87(1):47-55.
15. Lauscher JC, Rieck S, Loh JC, Grone J, Buhr HJ, Ritz JP. Oligosymptomatic vs. symptomatic incisional hernias--who benefits from open repair? Langenbecks Arch Surg. 2011;396(2):179-85.
16. Fitzgibbons RJ, Jr., Ramanan B, Arya S, Turner SA, Li X, Gibbs JO, et al. Long-term results of a randomized controlled trial of a nonoperative strategy (watchful waiting) for men with minimally symptomatic inguinal hernias. Ann Surg. 2013;258(3):508-15.
17. O'Dwyer PJ, Norrie J, Alani A, Walker A, Duffy F, Horgan P. Observation or operation for patients with an asymptomatic inguinal hernia: a randomized clinical trial. Ann Surg. 2006;244(2):167-73.
18. Vaos G, Gardikis S, Kambouri K, Sigalas I, Kourakis G, Petoussis G. Optimal timing for repair of an inguinal hernia in premature infants. Pediatr Surg Int. 2010;26(4):379-85.
19. Lautz TB, Raval MV, Reynolds M. Does timing matter? A national perspective on the risk of incarceration in premature neonates with inguinal hernia. J Pediatr. 2011;158(4):573-7.

20. Gonzalez Santacruz M, Mira Navarro J, Encinas Goenechea A, Garcia Ceballos A, Sanchez Zaplana H, Jimenez Cobo B. Low prevalence of complications of delayed herniotomy in the extremely premature infant. Acta Paediatr. 2004;93(1):94-8.

21. Lee SL, Gleason JM, Sydorak RM. A critical review of premature infants with inguinal hernias: optimal timing of repair, incarceration risk, and postoperative apnea. J Pediatr Surg. 2011;46(1):217-20.

22. Poley MJ, Brouwer WB, Busschbach JJ, Hazebroek FW, Tibboel D, Rutten FF, et al. Cost-effectiveness of neonatal surgery: first greeted with scepticism, now increasingly accepted. Pediatr Surg Int. 2008;24(2):119-27.

23. Deerenberg EB, Harlaar JJ, Steyerberg EW, Lont HE, van Doorn HC, Heisterkamp J, et al. Small bites versus large bites for closure of abdominal midline incisions (STITCH): a double-blind, multicentre, randomised controlled trial. Lancet. 2015;386(10000):1254-60.

24. Millbourn D, Cengiz Y, Israelsson LA. Risk factors for wound complications in midline abdominal incisions related to the size of stitches. Hernia. 2011;15(3):261-6.

25. van 't Riet M, Steyerberg EW, Nellensteyn J, Bonjer HJ, Jeekel J. Meta-analysis of techniques for closure of midline abdominal incisions. Br J Surg. 2002;89(11):1350-6.

List of publications

Incidence, risk factors, and treatment of incisional hernia after kidney transplantation: An analysis of 1,564 consecutive patients
Verhelst J, Ooms LS, Jeekel J, Ijzermans JN, Lange JF, and Terkivatan T
Surgery; 2016: May, 159(5):1407-11

Emergency repair of inguinal hernia in the premature infant is associated with high direct medical costs
Verhelst J, de Goede B, van Kempen BJ, Langeveld HR, Poley MJ, Kazemier G, Jeekel J, Wijnen RM, and Lange JF
Hernia; 2015:

Very low birth weight is an independent risk factor for emergency surgery in premature infants with inguinal hernia
Verhelst J, de Goede B, van Kempen BJ, Baartmans MG, Langeveld HR, Halm JA, Kazemier G, Lange JF, and Wijnen RM
J Am Coll Surg; 2015, 220(3): 347-52

Open incisional hernia repair with a self-gripping retromuscular Parietex mesh: a retrospective cohort study
Verhelst J, de Goede B, Kleinrensink GJ, Jeekel J, Lange JF, and van Eeghem KH
Int J Surg; 2015, 13: 184-8

Watchful waiting in incisional hernia: is it safe?
Verhelst J, Timmermans L, van de Velde M, Jairam A, Vakalopoulos KA, Jeekel J, and Lange JF
Surgery; 2015, 157(2): 297-303

Letter to the Editor on the article “Open ventral hernia repair using ProGrip self-gripping mesh”
Kroese LF, **Verhelst J,** Jeekel J, Kleinrensink GJ, and Lange JF
Int J Surg; 2015: May, 27:190

Implementing a clinical pathway for hip fractures; effects on hospital length of stay and complication rates in five hundred and twenty six patients
Burgers PT, Van Lieshout EM, **Verhelst J**, Dawson I, and de Rijcke PA
Int Orthop; 2014, 38(5): 1045-50

Dankwoord

Beste professor Lange, allereerst wil ik u bedanken voor de kansen en het vertrouwen dat u mij heeft gegeven. U heeft altijd onze eigen ideeën en initiatieven voor nieuw onderzoek aangemoedigd en ondersteund. Tijdens de REPAIR vergaderingen op vrijdagmiddag wordt altijd geopend met een portie wekelijkse cultuur. U refereerde dan vaak aan Jazz muziek. Het doen van onderzoek is daar treffend mee te vergelijken denk ik. In het begin klinkt het vooral chaotisch en onrustig. Maar gaandeweg kom je er achter dat wanneer alle disciplines samen in harmonie spelen, er daadwerkelijk sprake is van muziek. Hoe beter je het leert begrijpen, des te meer leer je het waarderen en des te leuker ga je het vinden. Er zit zeker nog veel (jazz-) muziek in onderzoek en de REPAIR.

Om in het thema muziek te blijven, ben ik natuurlijk u, professor Jeekel, ook veel dank verschuldigd. Ik weet nog goed dat ik bij u kwam solliciteren op uw kamer Ee-1459, het hart van de REPAIR. Waarna ik, met uw begeleiding, het avontuur bij Eurotape ben aangegaan. Uw passie voor het vak chirurgie en onderzoek in het bijzonder, zijn niet alleen voor mij een belangrijke inspiratie, maar ook voor vele anderen. Door uw netwerk heb ik veel belangrijke mensen kunnen ontmoeten en met hen kunnen samenwerken. Ik ben erg trots dat ik met u als mentor mijn onderzoek heb kunnen voltooien.

Beste professor Berrevoet, met de eerste winnaar van de Award vernoemd naar bovenstaande co-promotor in mijn commissie, die nota bene op zijn verjaardag de internationale glans aan mijn promotie wil geven, ben ik u vanzelfsprekend erg erkentelijk.

Beste professor Wijnen, de samenwerking met u en de afdeling kinderchirurgie heeft geleid tot een belangrijk deel van dit proefschrift. Naast het feit dat u zitting wilt nemen in mijn leescommissie wil ik u ook voor die samenwerking bedanken.

Beste professor Verhagen, ook met u heb ik mogen samenwerken aan een hoofdstuk van dit proefschrift. Daarvoor dank en natuurlijk ben ik vereerd dat u zitting wilt nemen in mijn leescommissie

Beste professor Bouvy en beste professor Tilanus, ik wil u beiden bedanken dat u de moeite wil nemen mijn proefschrift te beoordelen en bij mijn verdediging plaats te nemen in de grote commissie.

Beste professor van Eijck, op 8NW heb ik van u veel geleerd. Niet alleen vakinhoudelijk, maar nog veel meer over patiëntenzorg. In een topteam met dr. Kok en dr. Erdmann was

de persoonlijke aandacht voor individuele patiënten en hun naasten misschien wel het belangrijkste onderdeel van die patiëntenzorg. Tot slot dank dat u plaats wil nemen in mijn commissie en voor het telefoontje destijds aan het adres van professor Jeekel. Daardoor stond ik bij mijn sollicitatie voor deze onderzoeksplaats reeds met 1-0 voor.

Beste professor Kleinrensink, één van de drie giganten van de REPAIR onderzoeksgroep. Ongekend hoe u altijd van iedere tegenslag weer iets positiefs weet te maken. Daarbij zorgt u altijd voor de nodige vrolijke inbreng tijdens de vergaderingen. Met name het onderzoek voor een “Prix des Amis” met een Franse delegatie in de snijzaal is bijgebleven.

Beste Barry, iets met laag hangend fruit, hard klussen en gezelligheid. Jij hebt me wegwijs gemaakt in de wereld van het onderzoek en schrijven van artikelen. Hetgeen geresulteerd heeft in een paar mooie stukken. En hoe mooi is het dat we nu samen aan het begin staan van de opleiding chirurgie in Rotterdam. Het beloven nog zes mooie jaren te worden. Niet voor niets ben ik blij dat je bij mijn verdediging aan mijn zijde staat.

Lieve Liesbeth, niet zomaar een kamergenoot, co-autheur, maar vooral een goed vriendinnetje. Je zorgde er altijd voor dat mijn werkplek er piekfijn uitzag, genoeg ruimte voor een dansje op de stoelen op vrijdagmiddag om het weekend in te luiden. Met wat ontspannende Ibiza-lounge kon af toe de druk weer van de ketel worden gehaald. Ik ben blij dat ook jij mijn paranymf wil zijn tijdens mijn verdediging, en onthoud: alles komt uiteindelijk toch wel goed!

Lieve kamergenoten van Z-358, lieve dames, dank voor alle hulp maar vooral plezier op kamer 1 van de hunkerbunker. Zaar, voor het regelen van een gespreid bed zodat ik direct van start kon gaan; Mirel, voor alle ins en outs, en niet alleen die voor onderzoek van belang zijn; Marcia, voor al het groen op de kamer, je bent de leukste Eskimo die ik ooit heb ontmoet.

Beste Z-flatters, Niels Legend!, Inez dank voor alle interesse en steun, Jeff voor al je IT-oplossingen, Coebergh binnenkort heb ik meer tijd voor 18 holes, Bo succes met je skireis, Joey, weliswaar geen Z-flatter maar wel zo gezellig, Kirstin, mijn nieuwe collega in het Ikazia, wordt hoe dan ook weer gezellig, Shiro voor al je organisatorische hoogtepuntjes, Michael voor bloedstollende verhalen over de internistendagen, Kirsten voor je enthousiasme, en Mussie voor de Ramadan. Maar vooral dank voor alle gezelligheid binnen en buiten kantoortijden!

Beste REPAIRDERS, sowieso de mooiste onderzoeksgroep binnen het Erasmus MC, achteraf realiseer je je pas hoeveel kansen je hebt gekregen binnen de onderzoeksgroep. Niet alleen de kansen geboden door de professoren, maar ook door je collega-onderzoekers. Zonder jullie hulp was dit boekje er niet geweest. An, tegelijk in het diepe bij de REPAIR en beiden

in de Z terecht gekomen. Jij op de PRIMA, ik bij Eurotape. Iedere vrijdag samen de lange wandeling naar prof. Jeekel. Mooie reizen/congressen bezocht. Nog even volhouden en dan krijg ook jij hopelijk wat je wilT. Beste Simone, mijn kamergenoot twee maal per week in de Oval Office van het Eurotape Paleis in Soest. Mooie experimenten gedaan en alles aan elkaar gelijmd. Wat je allemaal niet kan krijgen voor twee appeltaarten. Beste Ruth, Zhouqiao, Sandra, Leonard en Lucas; ook jullie allen ben ik vanzelfsprekend erkentelijk voor alle hulp en/of gezelligheid.

Beste collegae van Eurotape uit Soest. Dank voor het vertrouwen in mij voor een vruchtbare samenwerking met het Erasmus MC. Binnen jullie bijzondere bedrijf in Soest heb ik me altijd heel welkom gevoeld, ik kon overal binnenwandelen en iedereen was altijd vriendelijk. Zowel bij de Frontoffice, de Productie als de R&D. Alles was mogelijk en geen idee was te gek of werd afgeschoten. De samenwerking met het LUMC, de projectgroep uit Delft en samenwerking met dermatologie in het Maasstad waren stuk voor stuk mooie projecten. Ik weet zeker dat onze samenwerking op het gebied van de SoClose ook nog zijn vruchten gaat afwerpen.

Beste chirurgen en assistenten uit het Maasstad. Een supermooie hechte groep die allen keihard voor elkaar werken. Wat gaat een jaar dan toch alweer snel. Heb veel van jullie mogen leren en dank voor alle steun, niet alleen rondom het schrijven van mijn boekje naar met name rondom de sollicitatie. Zou voor iedere differentiatie nog graag terugkomen.

Beste chirurgen en collega's uit het IJsselland, beste IJsvogels. In Capelle werd de basis gelegd voor mijn keuze voor de chirurgie en dat is niet voor niets. Ik heb echt een supermooie tijd gehad en wanneer ik jaarlijks tijdens skiweekend een keer het fort mag bewaken voelt dat altijd een beetje als thuiskomen op het oude nest.

Beste chirurgen en collega's uit het Ikazia. Ik ben erg blij dat ik het grootste deel van mijn opleiding in het Ikazia mag doorlopen. Ik heb er ontzettend veel zin in en heb me vanaf het begin heel welkom gevoeld.

Beste Eduard, Friso en Wouter, dank voor al jullie interesse rondom mijn promotietraject. Maar ik wil jullie met name bedanken voor alle ontspanning tussendoor. Etentjes, rondjes golf, vaaruitjes op de Rotte en de Ourthe en avonden met wijn en Catan. Wat mij betreft gewoon zo door!

Beste Bert, maatje van het eerste uur. Jij bent er hoe dan ook in deze drukke tijden het meest bij ingeschoten. Altijd heb je belangstelling gehad in mijn promotie. Ik beloof je dat we die tijd ook weer inhalen in Rotterdam, of het zuiden van het land.

Beste clubgenoten van JC Valiant. Al vele mooie mijlpalen met elkaar bereikt, nu zelfs een promotie. Nu altijd weer de vraag: wie wordt de volgende. Dank voor alle steun en op naar de volgende borrels en lustrumreis.

Lieve zusjes, Nu alle promotieperikelen bijna achter de rug zijn, is er weer meer tijd voor friet op vrijdag, kunnen we weer andere belangrijke zaken bespreken die er echt toe doen!

Lieve Papa en Mama, jullie zijn de enigen die letterlijk aan de wieg van dit proefschrift hebben gestaan. Dank dat jullie mij alle kansen hebben gegeven gedurende mijn studie, de weg naar deze promotie en opleiding.

Lieve Steef, je zegt soms zelf dat jouw bijdrage aan dit proefschrift misschien niet eens zo groot is geweest, ik denk echter dat je dat onderschat. Maar veel belangrijker ben je de grootste bijdrage in mijn leven, mijn lieve vriendinnetje en maatje. Ik ben ongelooflijk trots op jou en we gaan nog lang en veel genieten van alle mooie dingen in het leven. Ik hou van jou!

Curriculum Vitae

Joost Verhelst werd geboren op 4 oktober 1984 te Breda. Na zijn eindexamen VWO aan het Onze Lieve Vrouwe Lyceum in Breda begon hij in 2003 aan zijn studie Geneeskunde aan de Erasmus Universiteit in Rotterdam. Zijn wetenschappelijke stage heeft hij gelopen op de afdeling Anesthesiologie van het Auckland City Hospital in New-Zealand. De laatste fase van zijn coschappen liep hij in het Ekwendeni Mission Hospital in Malawi en op de afdeling Orthopedie van het Reinier de Graaf Gasthuis in Delft. In 2011 behaalde hij zijn artsexamen, waarna hij als arts-assistent is gaan werken op de afdeling Heelkunde van het IJsselland Ziekenhuis in Capelle aan den IJssel. Na een korte tijd werkzaam te zijn geweest op de afdeling Heelkunde van het Erasmus Medisch Centrum kreeg hij een promotietraject aangeboden door prof. dr. Lange en prof. dr. Jeekel. Deze promotie combineerde hij met zijn werkzaamheden op de research en development afdeling van een fabrikant van medische hulpmiddelen in Soest. Het onderzoek naar buikwandbreuken heeft uiteindelijk geleid tot de totstandkoming van dit proefschrift. Vanaf juni 2015 was hij een jaar werkzaam op de afdeling Heelkunde van het Maasstadziekenhuis te Rotterdam. Per 1 juli 2016 is hij gestart met de opleiding Heelkunde in het Ikazia Ziekenhuis te Rotterdam.

PhD portfolio / Summary of PhD training and teaching

Name PhD student: Joost Verhelst Erasmus MC department: Surgery	PhD period: June 2013- June 2016 Promotor: Prof. dr. J.F. Lange Co-promotor: Prof. dr. J.Jeekel	
1. PhD training		
	Year	Workload (ECTS)
General Courses BROK ('Basiscursus Regelgeving Klinisch Onderzoek') Course Endnote, Systematic Literature Retrieval and PubMed Basic Introduction Course on SPSS, Erasmus MC, Rotterdam Integrity in Research, Erasmus MC, Rotterdam	 2013 2013 2013 2015	 1.0 1.0 1.0 0.5
Specific courses Cursus dierproefkunde/Artikel 9	 2013	 3.0
Presentations (international conferences) European Hernia Society, (poster presentation) World Conference on Hernia Surgery, Milan (oral presentation) Annual Hernia Repair Symposium, Washington (oral presentation)	 2014 2015 2016	 2.0 2.0 2.0
Presentations (national conferences) WCS Wondcongres (oral presentation) Chirurgendagen NVvH (oral presentation) Najaarsvergadering NVvH (oral presentation) Najaarsvergadering NVvH (poster presentation) SEOHS (poster presentation)	 2013 2014 2014 2014 2014	 1.0 1.0 1.0 1.0 1.0
Conferences Rotterdam International Congress on Hernia Chirurgendagen NVvH	 2014 2013-2015	 1.0 1.0
2. Teaching		
	Year	Workload (ECTS)
Lecturing/Tutoring Examination Basic Life Support Research development Eurotape Soest Joint Master project TU Delft	 2012-2015 2013-2015 2015	 0.4 5.0 3.0
Supervising Master thesis Teddy Vijfwinkel		 2.0
3. Other		
	Year	Workload (ECTS)
Organisation Rotterdam International Congress on Hernia	2013-2014	3.0