Closing gaps - risk factors, occurrence, and treatment of abdominal wall hernias

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CHAPTER 1

General introduction and outline of this thesis

General introduction

The human abdominal wall consists of all structures that surround the abdominal cavity, including the abdominal muscles, fat, fasciae, and skin. The term 'abdominal wall hernia' generally refers to a defect in the connective tissue of the abdominal wall, most often at the midline (linea alba) between the rectus abdominis muscles and more rarely like the Spighelian hernia at the level of the lateral muscles (external oblique, internal oblique, and transverse abdominis muscles). An abdominal wall hernia is a protrusion of preperitoneal fat or abdominal contents (fat, bowel, liver) through the abdominal wall. It can occur at any weakened spot of the abdominal wall.

Abdominal wall hernias can be divided into two categories. One category of hernias: primary hernias, can be found at natural weak spots of the abdominal wall that are present from birth. These weak spots are either formed at a location where structures go from inside the abdominal cavity to outside the abdominal cavity (causing umbilical or inguinal hernias), or they are formed by weakness in the connective tissue at the junction of different muscles (causing either epigastric or Spigelian hernias). The most frequently seen inguinal hernia occurs at one of these weak spots, the foramen of Fruchaud.

The second category of hernias is caused by weak spots due to surgery. When such hernias occur after an incision (laparotomy), they are called incisional hernia and when they occur after stoma creation, are called parastomal hernias.

Hernia biology

To understand hernia biology, it is important first to know the biology in healthy patients. In healthy connective tissue, degradation of old proteins and synthesis of new proteins are in balance.[1] One of the most important proteins in connective tissue is collagen. Collagen is synthesized by fibroblasts and it eventually forms mature fibrils.[2] Currently, more than twenty different subtypes of human collagen are known.[3] In the human fascia, collagen types I and III are predominant.[4] Type I collagen is mature, mechanically stable collagen, whereas type III is immature and mechanically unstable.[5] In healthy people, these two types of collagen are in balance. In hernia patients however, less type I collagen is found in connective tissue, leading to a smaller collagen type I/III ratio. This decreased ratio can be found in connective tissue throughout the whole body. It leads to thinner collagen fibers with less tensile strength. In areas subject to repetitive strain, such as the abdominal wall, this results in the stretching of connective tissue, eventually leading to hernia formation.[6, 7]

Risk factors

Several factors are associated with a higher risk of incisional hernia development. These factors can be divided into three categories: pre-, per-, and postoperative factors. Although divided into separate categories, it must be kept in mind that these factors interact and can

influence each other.

Preoperative factors concern patient related factors. Well known preoperative risk factors are age, obesity, high America Society of Anesthesiologists score, diabetes mellitus, malnutrition, smoking, and steroid use.[8-15]

Apart from the surgeon-related quality of the closure of the fascial layers of the laparotomy peroperative risk factors are factors mainly linked to the complexity of surgery. Operation time often a reflects of a larger, more complex operation, leading to more complications and incisional hernia occurence.[8-10] Apart from operating time itself, emergency surgery is also known to lead to more complications and hernia formation. In emergency patients, more wound infections are found, leading to more hernias months after surgery.[8-10]

In addition to these factors, several postoperative factors have been identified as risk factors for incisional hernia. So called surgical site occurrences like infection, ischemia, seroma, and wound dehiscence can lead to a threefold increased risk of hernia occurrence.[16] Of these factors, surgical site infection is the most important factor.[17, 18]

Hernia prevention

Current research on prevention of incisional hernias has focused on two main subjects: 1) improvement of results by optimizing the suture technique (for example by altering the distance between sutures and the distance to the fascial edge)[19, 20] and 2) reinforcement of the closed incision with mesh augmentation.[21, 22]

Research on suture technique has covered several topics. One of the most important ones was the establishment of the suture length to wound length ratio (SL:WL) of at least 4:1. [23-25] It has been demonstrated that this ratio reduces the tension on the suture and by doing so it reduces the chance of incisional hernia development.[24, 25]

Research on mesh augmentation has mainly focused on patients undergoing elective abdominal aortic aneurysm surgery.[21, 22] This group of patients is often chosen because they are thought to be at higher risk of incisional hernia development. Both their aneurysms and their incisional hernias can be considered as expressions of altered collagen metabolism.

Hernia treatment

Since the existence of wounds closure was attempted with several techniques and materials. Over the last decades, various suture materials came available. Sutures can be resorbable or non-resorbable, they can be treated with aseptic agents, and finally different patterns or techniques can be used when suturing. A great revolution came with the invention of nylon and the use of this new product in the production of suture material. This led to a paradigm shift in hernia surgery: the use of prosthetic meshes. Before the introduction of synthetic meshes, hernia recurrence rates after surgical repair were up to 60%.[24] The first mesh used in hernia surgery was the Marlex™ mesh in the 1950s by Usher.[25] It consisted of a combination of polypropylene and high-density polyethylene. Currently, 60 years after

this milestone, more than 200 meshes are commercially available for hernia surgery. They cover a wide range of shapes, materials, weaving patterns, and costs. Besides the mesh characteristics, there are several ways to incorporate meshes. The main difference is the anatomical location of the mesh. This can be intraperitoneal, preperitoneal, retromuscular (sublay), or onlay.[29] Although meshes have improved outcomes of hernia surgery in terms of hernia recurrence, they are also associated with postoperative complications like infection, enterocutaneous fistulas, and bulging.[26] In this thesis, the use of different meshes and their complications will be addressed.

Complex hernias

Small, simple abdominal wall hernias can be treated with simple techniques using sutures or meshes. However, in case of larger hernia's and comorbidity surgical repair can be technically challenging. In these cases, surgery is associated with prolonged hospital stay, high rates of reoperations and readmissions, impaired wound healing, and high recurrence rates.[27-31]

In complex ventral hernia repair, loss of domain is an important principle. In a study evaluating volumetric measurements on CT imaging to predict tension-free closure, Sabbagh et al. stated that a ratio of incisional hernia volume/ peritoneal volume (IHV/PV) <20 % is predictive of tension free fascial closure. When IHV/PV is greater than 20 %, tension free closure without resection cannot be achieved in over 80% of the patients.[32] Additionally, loss of domain can cause complications like severe postoperative pain, abdominal hypertension, wound dehiscence, ventilatory and/or pulmonary problems, and higher risk of hernia recurrence.[33-35]

To classify these patients, Slater et al. defined criteria, based on clinical findings, to classify ventral hernias as complex.[36] With higher complexity, the number of perioperative measures, risk of complications, and costs will rise.

Although suggested in the title of this thesis, there is no such thing as the abdominal wall hernia. The group of patients is extremely heterogeneous. For research purposes and for communication, it is often easy to assume that all hernias are alike. Although there are many shared characteristics, great differences exist, not only in hernia characteristics, but also in patient characteristics. This is probably the explanation for the great variation found in the results of publications on hernia prevention or hernia repair. One of the aims of this thesis is to make a relevant differentiation between the types of hernia based on the mentioned factors. The rationale behind this differentiation is that hernia prevention and hernia treatment should be based on patient, hernia, and (mesh)material characteristics in order to achieve better results.

Outline of this thesis

This thesis covers a broad spectrum of new developments in abdominal wall hernia research. Prevention and recurrence, and the treatment of simple as well as complex hernias will be addressed.

Part I of this thesis focuses on prevention and risk factors for development of incisional and parastomal hernias.

Chapter 2 is a review of the literature on hernia prevention and laparotomy closure. Risk factors, different suture modalities and materials, and prophylactic mesh augmentation will be addressed.
Chapter 3 is a systematic review of the literature on several different modalities for diagnosing incisional hernia. In 2015 the European Hernia Society (EHS) has published guidelines on the closure of abdominal wall incisions.[37] In these guidelines it is recommended to use ultrasound or CT-scan for incisional hernia diagnosis. However, the incisional hernia prevalence found by the different modalities is not well studied. This chapter investigates the accuracy of different diagnostic modalities.
Chapter 4 is a systematic review and meta-analysis of the literature comparing extraperitoneal colostomy with transperitoneal colostomy with regard to parastomal hernia occurrence. Secondary outcomes are stoma prolapse and stoma necrosis.

Part II focuses on the treatment of simple abdominal wall hernias.

In **Chapter 5** a registry-based, large-scale, prospective cohort is used to compare primary and incisional hernias in terms of patient characteristics, surgical characteristics, and postoperative complications. Patients with incisional hernias and primary ventral hernias are often pooled in studies.[38] This chapter analyzes whether this is justified or whether these two types of hernias should be studied and reported on separately.
In **Chapters 6 and 7** the European Hernia Society Classification of primary and incisional abdominal wall hernias[39] is studied as a risk factor for postoperative complications following hernia repair in a registry-based, large-scale, cohort. The classification is analyzed amongst patient characteristics, surgical characteristics, and hernia characteristics. Primary hernias are discussed in **Chapter 6** and incisional hernias are discussed in **Chapter 7**.
In **Chapter 8** all available evidence on prevention and treatment of parastomal hernias is used to compose the European Hernia Society guidelines. A group of international hernia experts conformed to the AGREE II standards[40] and GRADE methodology[41] when writing these guidelines. Questions regarding diagnosis, surgical technique, mesh repair, and type of mesh will be answered.

In **Chapter 9** non-operative treatment is studied and compared with surgical treatment as a strategy for patients with parastomal hernia. This treatment strategy has been studied for patients with inguinal or incisional hernia,[42, 43] but not yet for patients with parastomal hernia. Patients who presented with a parastomal hernia between 2007 and 2012 are analyzed. Non-operative treatment and surgical treatment are compared in terms of patient characteristics, hernia size and symptoms, cross-over rates, and complications.

Part III focuses on the treatment of complex incisional or primary hernias.

Chapter 10 describes the long-term outcomes of patients with complex ventral hernias undergoing hernia repair with the use of a self-gripping mesh. This mesh has been used before in inguinal hernia surgery and has been analyzed previously for short-term results after repair of complex incisional hernias. In this chapter results after at least one year are presented.

In **Chapter 11** a case series is presented of patients with Ehlers-Danlos syndrome, who undergo ventral hernia repair. Given the impaired collagen metabolism of these patients, a higher recurrence rate is expected. Therefore, these patients were treated as if they had larger hernias by implanting larger meshes. The results of this strategy are presented and discussed in this chapter.

Chapter 12 describes a prospective study that focuses on the use of a biosynthetic, slowly resorbable mesh in patients with Ventral Hernia Working Group Grade 3 hernias. This group is prone to postoperative complications. Therefore it is hypothesized that a non-synthetic mesh could be beneficial in this group of patients.

Part IV focuses on new developments in hernia research.

Chapter 13 describes a completely new device: the AbdoMAN, that has been developed to study abdominal wall surgery. The AbdoMAN was developed to enable standardized, repeated testing without the use of laboratory animals or human subjects. In this chapter the AbdoMAN is presented and it is tested for physiological simulation and repeatability.

The results described in all chapters will be summarized and discussed in **Chapter 14.**

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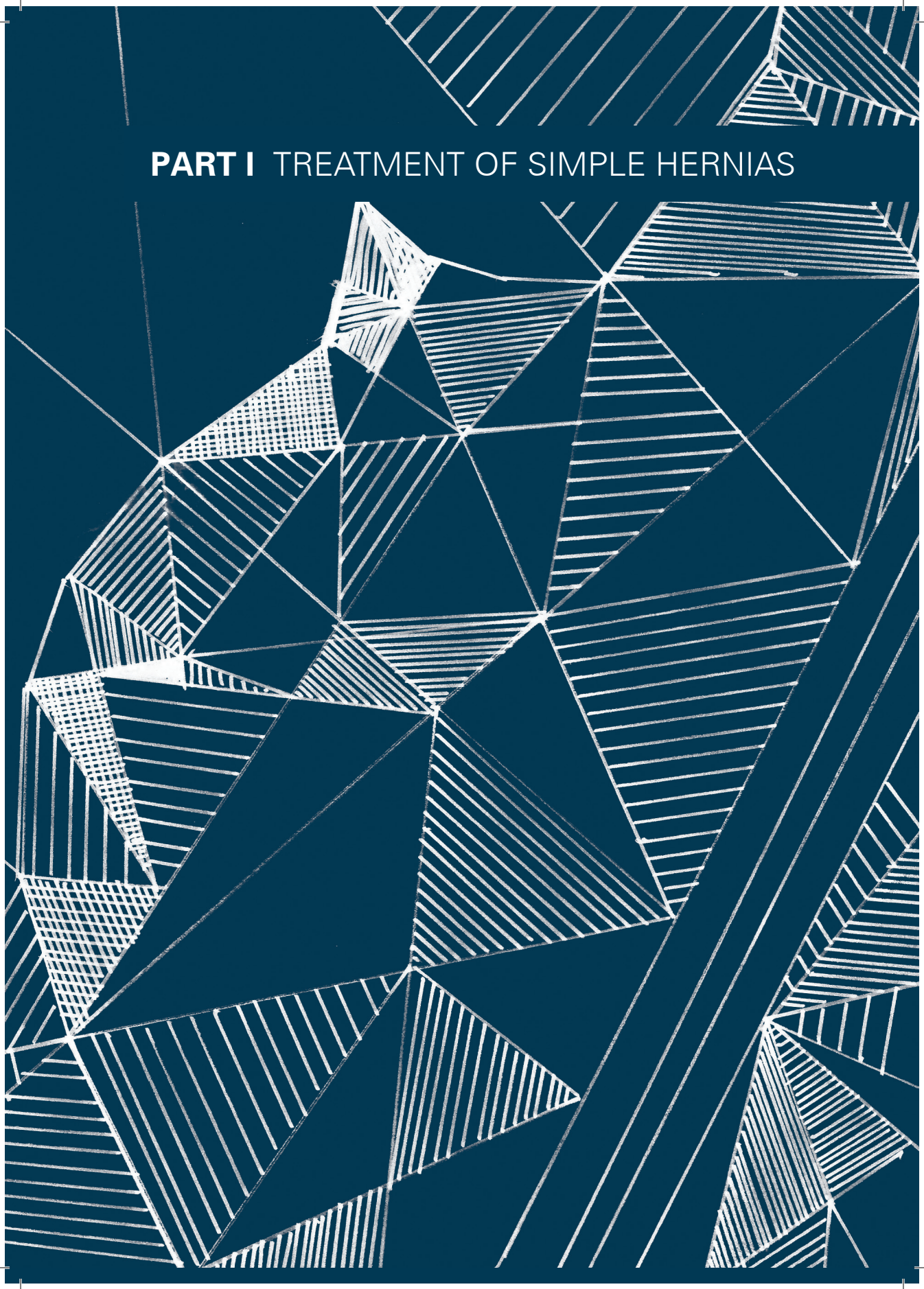
PART I TREATMENT OF SIMPLE HERNIAS



CHAPTER 2

Hernia Prevention and the importance of laparotomy closure

L.F. Kroese, J.F. Lange, J. Jeekel
Textbook of Hernia by William W. Hope, William S. Cobb, and Gina L. Andrales

Abstract

Incisional hernia remains a major complication after abdominal surgery associated with high morbidity and costs. Several risk factors have been identified. To reduce incisional hernia, attention should be paid to laparotomy closure. Closure should be performed using continuous sutures using mass closure with small bite size (5mm) and 5mm between stitches, resulting in a suture length to wound length ratio of ≥4. Absorbable suture material should not be chosen, slowly absorbable sutures are preferred. Prophylactic mesh augmentation is recommended in high risk patients, like patients undergoing abdominal aortic aneurysm surgery or obese patients.

Onlay mesh position is as effective as sublay mesh position in preventing incisional hernia. For mesh augmentation, a synthetic mesh should be chosen.

Introduction

Incisional hernia is an important complication of abdominal surgery with an incidence of 10–23%, after midline laparotomy increasing up to 38% in specific risk groups.[1-8] In the USA up 4 million to 5 million laparotomies are performed annually, leading to a calculated potential 400 000–500 000 incisional hernias to occur every year. Incisional hernia can lead to pain, discomfort and cosmetic complaints, resulting in a decreased quality of life.[9] Moreover, incisional hernia can cause incarceration and strangulation of abdominal contents, requiring emergency surgery, with associated morbidity and mortality.[10, 11] About 348 000 operations for incisional hernia are done every year in the USA with US$ 3.2 billion in annual associated costs.[12] Because of the abovementioned, prevention of incisional hernia occurrence is of vital importance.

In the past decades, abdominal surgery has moved from midline laparotomies to laparoscopic or other minimally invasive techniques. This shift however, has resulted in a higher risk population of patients that still undergo midline laparotomies.

Given the morbidity and costs associated with incisional hernia occurrence and repair, focus should be on treatment as well as prevention. Therefore, this chapter will focus on different closure techniques and other considerations that may prevent the development of incisional hernia.

After discussing different risk factors, different suture techniques and materials will be outlined. The recent development of prophylactic mesh placement will also be addressed. Finally, some future perspectives will be mentioned.

Risk factors

Several risk factors for the occurrence of incisional hernia have been identified. They include patient factors and operative factors.

Patient related risk factors

Known patient factors are overweight, male sex, abdominal distension, postoperative respiratory failure and previous wound infection.[13-16] Also, reoperations through the same laparotomy scar increase the risk of incisional hernia.[17, 18] A well-known risk factor is smoking.[19] Apart from these, older age, diabetes mellitus, malignancy, malnutrition, history of chemotherapy, jaundice and glucocorticosteroid use are also associated with higher incisional hernia rates.[13-15, 17, 20, 21] Patients operated for abdominal aortic aneurysm (AAA) have an increased risk of incisional hernia.[22, 23] In patients with AAA it is thought that the connective tissue with its collagen metabolism, and the ratio between mature and immature collagen in particular, is compromised.[24, 25] This compromised collagen plays an important role in aortic distention leading to AAA. It is thought that this is also of key importance in the formation of incisional

hernia after laparotomy.[26, 27] An important feature of collagen is the ratio of collagen type I and type III. Collagen type I is larger in diameter than collagen type III and is responsible for maintaining tensile strength. Collagen type III is an immature collagen and is found in early wound healing. A reduced type I/III collagen ratio is an indication of reduced mechanical stability of connective tissue, and it is associated with impaired wound healing. This impaired wound healing leads to higher incisional hernia incidence.

In obese patients, increased intra-abdominal pressure is thought to increase stress on the suture line, promoting incisional hernia formation. This is not the only contributing factor of obesity. Obesity is associated with complicated wound healing, caused by decreased vascularity of adipose tissue. This can lead to local hypoxia. Hypoxic wound can have impaired mature collagen synthesis, causing weaker connective tissue and deficient overall wound healing.[8, 14]

Operative factors

The type of laparotomy incision has often been debated. In several studies, reviewed in two meta-analyses,[28, 29] midline laparotomy has a higher risk of incisional hernia than transverse laparotomy. Paramedian incision leads to considerable lower incisional hernia rates. It is therefore advised to use non-midline incisions whenever possible.[30]

Too much tension on the sutures can weaken the wound, impairing collagen synthesis and increasing risk of wound infection and incisional hernia.[31-33]

To estimate individual patient risk, a risk model was developed by Van Ramshorst et al. in 2010.[34] This model combines several risk factors such as age, gender, pulmonary disease, ascites, jaundice, anaemia, coughing, type of surgery and wound infection. This model ranges from low scores resulting in almost 0% risk of abdominal wound dehiscence, to high scores resulting in >60% risk. The importance of these risk factors has recently been acknowledged by Fischer *et al.*[21] by constructing a risk model which combines all these risk factors. By making a combined score of all risk factors, they stratified patients in four risk groups, resulting in 0.5% (low risk), 2.6% (moderate risk), 8.9% (high risk) and 20.6% (extreme risk) incisional hernia after almost three years.

Methods of closure

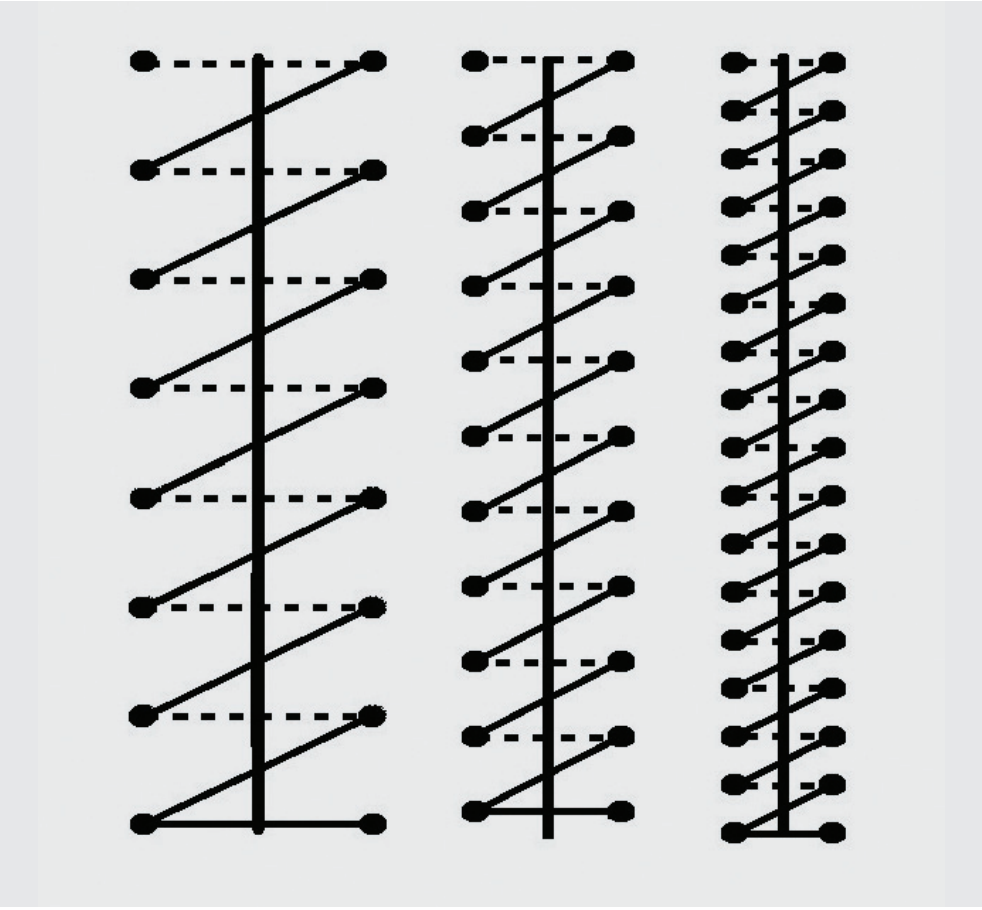
Continuous or interrupted sutures

When closing the abdominal wall after laparotomy, suturing can be performed using continuous or interrupted sutures. Continuous sutures are found to result in lower incisional hernia rates,[3, 11, 35] but this finding is not confirmed by other studies.[36, 37] Apart from this, continuous suturing provides a more time saving way and might therefore be preferred.

Suture length to wound length ratio

First described in 1976,[38] the suture length to wound length ratio (SL/WL ratio) is calculated by dividing the length of the used suture thread by the length of the incision, reflecting the relation between the size of the stitches used and the distance between two stitches.[39] Different SW/WL ratios are displayed in Figure 1. Research has shown a beneficial effect of a SL/WL ratio ≥4.[40-42] A SL/WL ratio <4 can triple the risk of incisional hernia occurrence.[39] Since there is a limited number of RCT's on this topic, no strong recommendations can be made.[30] The limitation of studies describing the SL/WL ratio is that it is often not mentioned in detail how the ratio is determined. Differences can occur when including or excluding knots or when only the remaining suture length is determined.

Figure 1 Suture length to wound length ratio



To maintain a suture length to wound length ratio of >4, the number of stitches should increase when they are placed closer to the wound edges

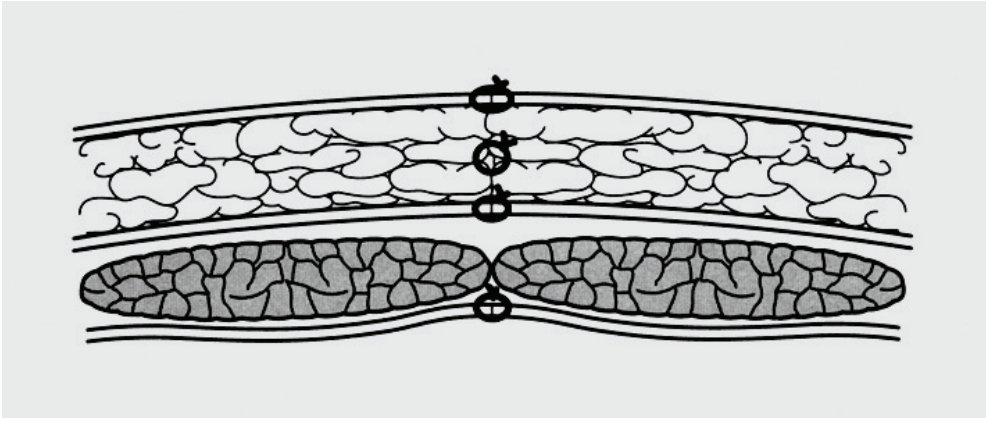
Layered closure or mass closure

The laparotomy can be closed with a layered closure or a mass closure (Figure 2). Several studies have compared layered closure (closure of the incision with more than one separate layer of fascial closure) with mass closure (closure of the incision with a suture bite that includes all layers of the abdominal wall except the skin). Meta-analyses on this topic showed a favourable result when using mass closure.[43, 44]

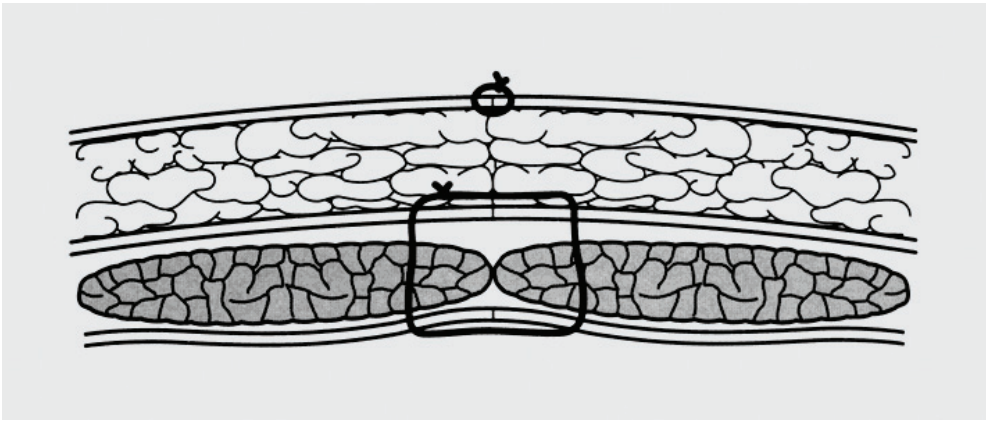
Figure 2 Layered closure versus mass closure

Adapted from: DeLancey, J, Hartman, R, Glob. libr. women's med., (ISSN: 1756-2228) 2008; DOI 10.3843/GLOWM.10038

A Layered closure: all layers are sutured separately



B: Mass closure: all layers of the abdominal wall except the skin are sutured in one bite



Stitch size

In the past, closing laparotomy wounds with larger tissue bites was considered to be the most effective in terms of incisional hernia incidence.[38, 45] Since 2009 however, new evidence, both experimental and clinical, has shown that smaller bite size (being 5 mm bites every 5 mm) increases the laparotomy closure strength and decreases the incisional hernia incidence rate.[39, 46] This has been recently confirmed in a large multicentre randomized controlled trial: the STITCH trial.[47] The smaller bite size reduces incisional hernia incidence after one year from 21% to 13%. The difference in bite size is shown in Figure 1.

Suture material

Suture materials have two main variables: duration of absorption (rapidly absorbable, slowly absorbable, non-absorbable) and fabric type (monofilament, multifilament).

Rapidly absorbable sutures have been found to lead to more incisional hernia compared to slow or non-absorbable sutures,[3, 11] the use of rapidly absorbable sutures is therefore not advised.

No difference was found in incisional hernia rate between slowly absorbable and non-absorbable sutures.[11] However, prolonged wound pain and suture sinus formation incidence are increased when using non-absorbable sutures.[11, 48] Therefore, the use of slowly absorbable sutures is suggested.

Monofilament sutures are associated with lower surgical site infection rates.[49] However, no clear evidence for the use in laparotomy closure has been found. Nevertheless, with all slowly absorbable suture materials currently being monofilament, this is no actual topic of discussion.

No studies have been conducted to compare different suture thicknesses. Although recent studies[39, 47] investigating bite size use a USP 2-0 suture for small bites closure, no evidence exists on which suture should be chosen.

Prophylactic mesh augmentation

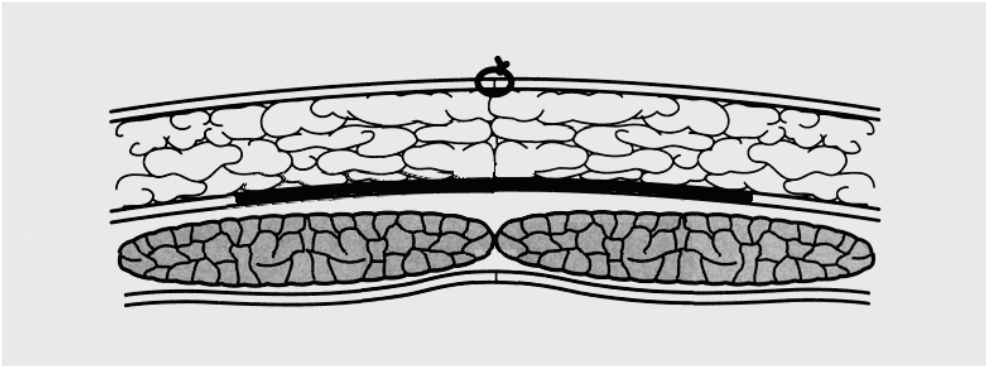
Mesh placement is well known for incisional hernia repair, reducing recurrence rates compared to primary suture closure.[50, 51] Mesh augmentation to prevent incisional hernia was first described in 1995.[52] The mesh can be placed in different positions; onlay, sublay or preperitoneal (Figure 3). In the onlay position, the mesh is placed ventrally to the anterior rectus fascia. In the sublay position, the mesh is placed dorsally to the rectus muscles and ventrally to the posterior rectus fascia. In the preperitoneal position, the mesh is placed caudally to the semicircular line of Douglas dorsally to the posterior rectus fascia and ventrally to the peritoneum.

Since 1995, multiple studies have been performed, mainly in high risk patients like patients undergoing AAA surgery of obese patients. Overall data of these studies show a decreased incidence of incisional hernia after prophylactic mesh placement in high risk patients.[53, 54]

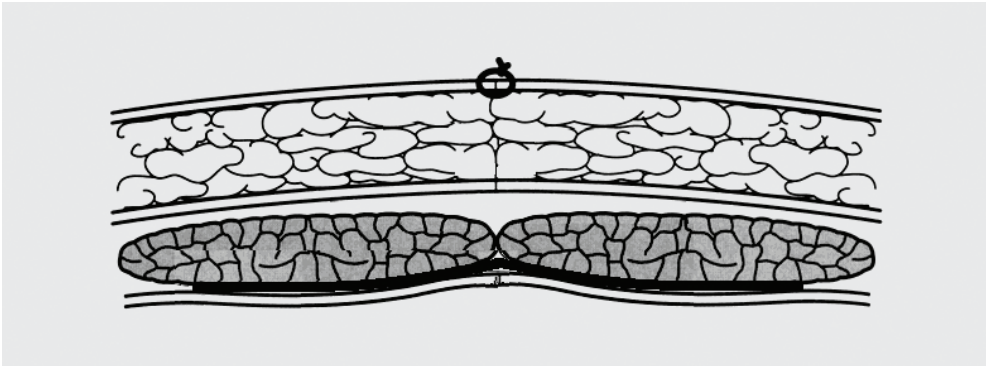
Figure 3 Mesh positions

Adapted from: DeLancey, J, Hartman, R, Glob. libr. women's med., (ISSN: 1756-2228) 2008; DOI 10.3843/GLOWM.10038

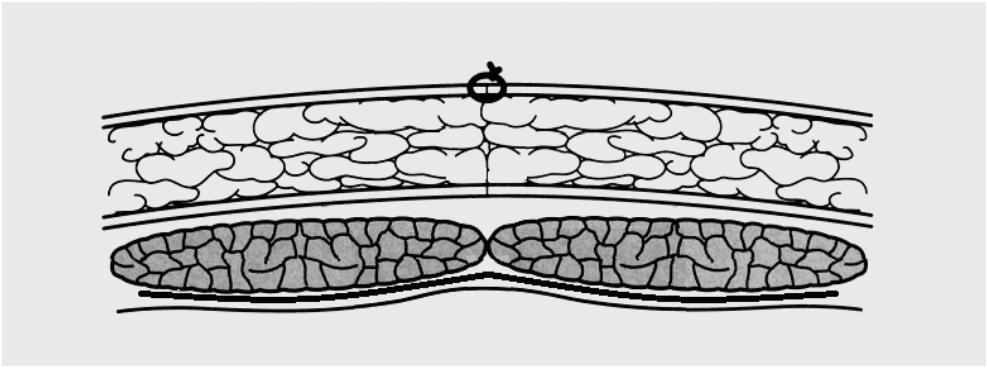
A: Onlay position



B: Sublay position



C: Preperitoneal position



Although not always significant, there seems to be a trend showing slightly higher seroma formation rates in mesh groups.

Recent research like the Dutch PRIMA trial has focused on prophylactic mesh augmentation to prevent incisional hernia after midline laparotomy using both onlay and sublay technique.[55, 56] Short term results after one month show that mesh augmentation is a safe procedure without increased complications such as surgical site infection.[55] After two years of follow up, mesh augmentation showed significant lower rates of incisional hernia. Sublay position resulted in 18% incisional hernia and onlay position resulted in 13% incisional hernia compared to 30% in the primary suture group. There was no difference in complication rates between groups. Although not significantly different, onlay position seems to be preferable in terms of incisional hernia rate and applicability.

The recently published Belgium PRIMAAT trial has also focused on prophylactic mesh placement in patients undergoing AAA surgery. This study found 0% incisional hernia after two years of follow up, compared to 28% in the suture group.[57] One key feature of this study, was that laparotomy closure was always performed by a dedicated abdominal wall surgeon.

Based on these recent studies, an onlay mesh augmentation technique should be used in high risk patients to prevent incisional hernia.

Future directions

Although the number of laparotomies for abdominal surgery is decreasing with laparoscopic surgery being used increasingly, incisional hernia remains a major complication after midline laparotomy. In the future, we expect the population of patients still undergoing midline laparotomy to be higher risk patients. For these patients, the risk of incisional hernia development is even greater. Until now, laparotomies are almost always closed using the big bite suture technique. Recent data provide evidence that the midline laparotomy should be closed with small bite 5x5mm suture technique. The choice of laparotomy closure techniques depends on the patients risk profile.[21] Recent studies show that prophylactic mesh placement significantly lowers the incidence of incisional hernia. Therefore prophylactic mesh placement, enforcing the closed midline, should be applied in high risk patients.

Finally, with incisional hernia remaining one of the most serious complications of the abdominal surgeon, it might require a dedicated abdominal wall surgeon to perform the laparotomy closure.

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CHAPTER 3

Comparing different modalities for the diagnosis of incisional hernia, a systematic review

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Abstract

Purpose: Incisional hernia (IH) is the most frequent complication after abdominal surgery. The diagnostic modality, observer, definition, and diagnostic protocol used for the diagnosis of IH potentially influence the reported prevalence. The objective of this systematic review is to evaluate the diagnostic accuracy of different modalities used to identify IH.

Methods: Embase, MEDLINE OvidSP, Web of Science, Google Scholar, and Cochrane databases were searched to identify studies diagnosing IH. Studies comparing the IH detection rate of two different diagnostic modalities or inter observer variability of one modality were included. Quality assessment of studies was done by Cochrane Collaboration's tool. Article selection and data collection was performed independently by two researchers. PROSPERO registration: CRD42017062307.

Results: Fifteen studies representing a total of 2,986 patients were included. Inter observer variation for CT-scan ranged from 11.2 to 69% (n=678). Disagreement between ultrasound and CT-scan ranged between 6.6 and 17% (n=221). Ten studies compared physical examination to CT-scan or ultrasound. Disagreement between physical examination and imaging ranged between 7.6 and 39% (n=1602). Between 15% and 58% of IHs were solely detected by imaging (n=483). Relative increase in IH prevalence for imaging compared to physical examination ranged from 0.92 to 2.4 (n=1922).

Conclusions: Ultrasound or CT-scan will result in substantial additional IH diagnosis. Lack of consensus regarding the definition of IH might contribute to the disagreement rates. Both the observer and diagnostic modality used, could be additional factors explaining variability in IH prevalence and should be reported in IH research.

Introduction

Incisional hernia (IH) is the most frequent complication after open abdominal surgery. IH prevalence rates in published cohorts vary substantially: prevalence rates between 10 and 32% have been reported[1,2]. Several factors explaining the variability in IH rate have been brought forward such as: age, obesity, abdominal aortic aneurysms, and previous abdominal surgery [1]. Most studies investigating the treatment or prevention of IH use IH prevalence as their primary endpoint. The diagnostic modality, observer, definition, and diagnostic protocol used for the diagnosis of IH are infrequently identified as factors associated with the IH prevalence rate. However, all four of these elements regularly differ within and between studies.

Many diagnostic modalities are used for the diagnosis of IH including physical examination, ultrasound, computed tomography scan (CT-scan), magnetic resonance imaging (MRI), and per-operative diagnosis. In IH research, the use of imaging modalities is considered important to achieve more reliable results. This is accentuated by the recommendation in the 'European Hernia Society guidelines on the closure of abdominal walls' to use ultrasound or CT-scan in the follow-up of prospective studies [3]. This approach deviates from every day clinical practice, in which clinicians mainly focus on the diagnosis of symptomatic IHs that might require treatment [4].

In general, it is believed that the use of radiologic imaging will increase the detection rate of IH compared to physical examination alone. However, not all published cohorts show this trend [3-6].

The choice of diagnostic modality is often dictated by multiple factors such as cost, availability, safety, and especially in a research setting the detection rate, and reliability. However, the latter remains unclear, as the evidence concerning these factors is limited and sometimes contradictory [7,8]. In IH research, the IH definition is not always uniform. The definition of IH as stated by Korenkov *et al.* [9]: 'any abdominal wall gap with or without bulge in the area of a postoperative scar perceptible or palpable by clinical examination or imaging', is acknowledged in the European Hernia Society (EHS) classification of primary and incisional abdominal wall hernias [9,10]. Although IH is usually defined as an 'abdominal wall gap or fascial defect' some nuances with regard to this definition circulate as the term 'abdominal wall weakness' may also be used. Furthermore, bulging or a positive Valsalva maneuver may or may not be a diagnosing symptom [11,12]. The place of imaging techniques within the diagnostic protocol often differs: some studies use a more clinical approach, reserving imaging techniques for cases with an inconclusive physical examination, whereas other studies only consider 'radiologically confirmed' diagnosis [2,13,14].

We hypothesize that the use of different diagnostic modalities, observers, definitions, and diagnostic protocols might influence the number of IHs identified. The objective of our systematic review is to evaluate the diagnostic accuracy of the different modalities used to

identify IH after open abdominal surgery and after IH repair surgery. We provide a qualitative synthesis of the available data on the diagnostic accuracy of physical examination, CT-scan, and ultrasound for the identification of IH.

Methods

The study protocol was registered in the PROSPERO database (International Prospective Register of Systematic Reviews, www.crd.york.ac.uk/prospero) prior to the start of the systematic review with the registration number CRD42017062307. All aspects of the PRISMA statement (Preferred Items for Reporting of Systematic Reviews and Meta-analyses), were followed .

Search strategy

Embase, Medline ovid, Web-of-science, Cochrane, PubMed publisher, and Google scholar databases were searched on 28 March 2017. Full search details and syntax are presented in Appendix 1. The syntax construction and database search were performed in collaboration with a medical librarian specialized in conducting systematic reviews.

Studies reporting on IH diagnosis after primary laparotomy and after IH repair surgery were included. There was no limit in language or date of publication.

Studies were first evaluated for inclusion based on title and abstract by two independent researchers (LK and DS) and finally evaluated independently based on full text. Differences in article selection were discussed and articles were included or excluded after reaching agreement. Studies were included if they met the following criteria:

1. Inclusion of patients that underwent abdominal or IH repair surgery that were followed for the development of IH.
2. Studies assessing the performance of a diagnostic modality (physical examination, abdominal CT-scan, abdominal MRI-scan, abdominal ultrasound or surgery) used for the diagnosis of IH.

Studies assessing only laparoscopy patients, non-consecutive patient populations (e.g. patients with prior IH diagnosis), Spigelian, or occult hernias were excluded. Discrepancies in inclusion were resolved by discussion between reviewers and a senior author (JFL or FM).

Data collection

Data collection was performed independently by two different researchers (LK and DS) using standard forms covering study characteristics (study design, year, location and level of evidence); patient baseline characteristics (type of intervention, number of patients, age, sex, open or laparoscopic surgery, duration of follow up, and reason for surgery). Outcome characteristics concerning diagnostic performance comprise: definition of IH, inter observer variation, CT-scan vs ultrasound, CT-scan vs physical examination, ultrasound vs physical

examination, diagnostic modalities vs per-operative diagnosis, and diagnostic performance in obese patients. Extracted data consisted of absolute data in four by four contingency tables, prevalence rates, kappa values, or intra-class correlation coefficients.

Assessment of study quality

The level of evidence of each paper was established according to the Oxford Centre for Evidence-based Medicine levels of evidence [16]. The possible risk of bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias [17]. Risk of bias was assessed separately for each outcome since the quality of different outcomes in papers with a wide scope might differ.

Results

Search and study characteristics

The PRISMA flow diagram of the complete search strategy is shown in Figure 1. The initial search resulted in 4,855 articles (3,010 after duplicates removal). After screening, 135 articles were selected for full-text reading. After full-text reading, 15 articles were selected for inclusion [2,4-8,11,12,14,18-23]. Characteristics of included studies are summarized in Table 1.

Study quality

Risk of bias and applicability concerns of included studies per outcome are summarized in Figure 2. Overall major concerns in patient selection, execution and comparison of diagnostic tests and patient flow were present in 25% to 50% of the review sample (Figure 3). Major applicability concerns were present in 10 % of the review sample (Figure 3). Specific methodological concerns are presented in Appendix 2.

Definition of IH

A clear definition for IH was reported in seven of the included studies (Appendix 3) [2,4,7,11,12,20,22]. IH was defined as any 'abdominal wall gap' or 'defect' in the proximity of the postoperative scar, by five out of seven studies [2,4,7,12,22]. Two of these studies included 'a protrusion of abdominal contents' in the definition and incorporated the terms 'weakness' as well as 'defect' of the abdominal wall in their definition [12,22]. One study defined IH as a 'palpable protrusion' under the laparotomy scar [11]. One study defined IH as 'fascial defect' in the proximity of the scar [20]. Three studies referred to a proposed universal definition [2,4,12]. One study that did not clearly define IH, reported that in case of disagreement between two or more observers, this was due to the lack of a clear definition among the observers in 35% of the patients (n=42) [23].

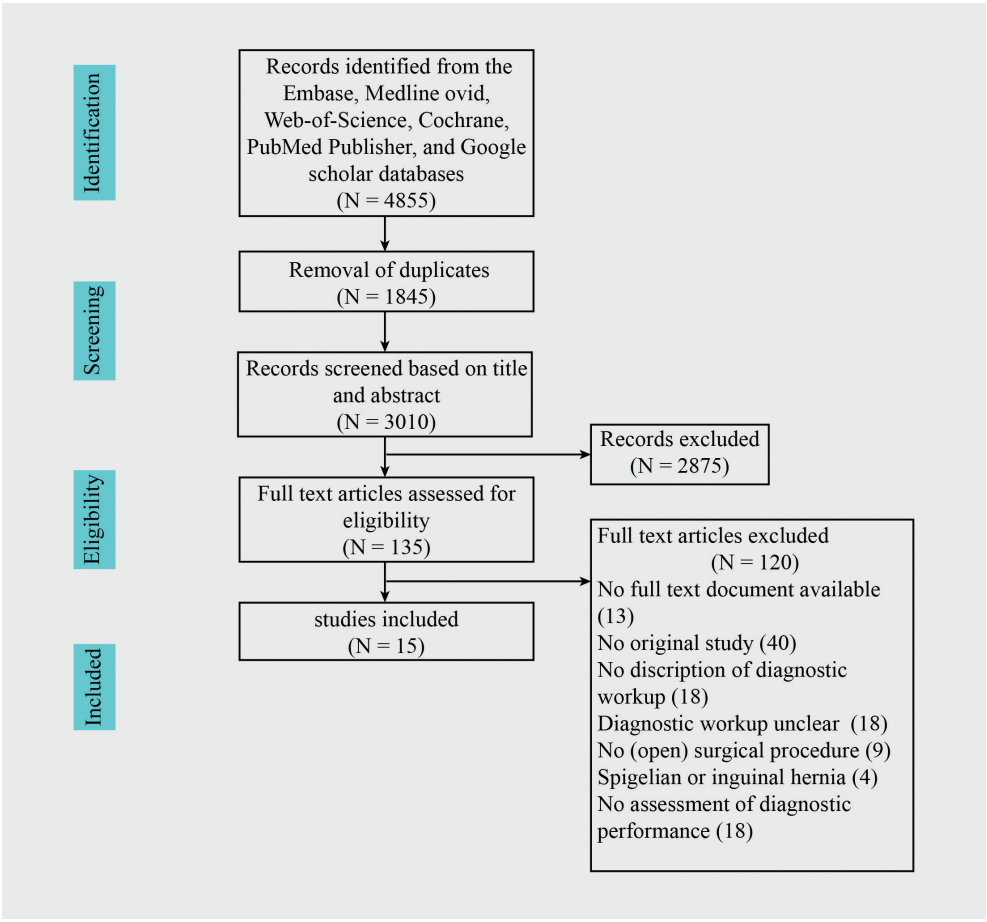

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram

Inter observer variation

Inter observer variation was reported in five of the included studies concerning a total of 698 patients [8,12,18,20,23]. Four out of five studies included in this comparison had one or more methodological concerns [12,18,19,23]. Results obtained by these studies are summarized in Table 2. Reported disagreement between two observers ranged from 11.2 to 14.4 %, corresponding kappa values ranged from 0.71 to 0.74 (n = 578) [8,12,18]. One study comparing the inter observer variation in a group of six radiologists and three surgeons reported disagreement rates of 69 and 27% respectively (kappa: 0.38 and 0.62; n = 100) [23]. One other study used a panel of five independent surgeons and reported an intra class correlation coefficient of 0.85 (n = 20) [20]. The inter observer variation of ultrasound was assessed in one study that used a panel of three independent surgeons, an intra class correlation coefficient of 0.79 (n = 17) was reported [7].

Table 1: overview of included studies

Study	journal	Modalities included	Surgical procedure	N	Age in years Mean; SD; (range)	BMI (Mean; SD; (range))	Follow up in months (Mean; SD; (range))
Baucom *et al.* [14] 2014	J Am Coll Surg	Physical examination and CT-scan	Abdominal/ some laparoscopic cases	181*	54; SD 13	31.3; SD 6,7	> 6
Baucom *et al.* [18] 2014	Am Surg	CT-scan	Abdominal/ some laparoscopic cases	181*	54; SD 13	31.3; SD 6,7	> 6
Baucom *et al.* [19] 2014	JAMA surgery	Ultrasound and CT-scan	Abdominal/ some laparoscopic cases	109*	54; SD 13	32.2; SD 6.7	> 6
Baucom *et al.* [20] 2016	Ann Surg Oncol	CT-scan	Abdominal/ some laparoscopic cases	491	59.5; SD 12.1	28.6; SD 6.1	13.2; SD 7.7
Beck *et al.* [7] 2013	J Am Coll Surg	Ultrasound and CT	Abdominal/ some laparoscopic cases	181*	54; SD 13	31.3; SD 6,7	> 6
Bloemen *et al.* [4] 2012	Hernia	Physical examination and Ultrasound	Midline open	456	63.3; SD 13.9	25.5; SD 4.4	33.8; (31.8-35.8)
Caro-Tarrago *et al.* [11] 2014	World j Surg	Physical examination and CT-scan	Midline open	160	Group 1: 64.32; SD 14.27 Group 2: 67.32; SD 11.11	NR	Group 1: 14.8; SD 8.3 Group 2: 12.5; SD 8.5
Claes *et al.* [12] 2014	Hernia	Physical examination and CT-scan	Colorectal cancer surgery	448	69.8 SD 11.8	NR	Clinical: 33 (0.5-90) CT: 30 (0.1-94)
Deerenberg *et al.* [2] 2015	The Lancet	Physical examination and ultrasound	Midline open	545	Group 1: 63; (54–71) Group 2: 62; (53–72)	24; (22–27)	(12-15)
Den Hartog *et al.* [8] 2014	Ultrasound Med Biol	CT-scan and ultrasound	Abdominal aneurysm (abdominal open)	40	72.5; SD 8,9	NR	40.8; SD 19,2
Goodenough *et al.* [5] 2015	J Am Coll Surg	Physical examination and CT-scan	Abdominal open	439	60.8; SD 11.4	28.1; SD 5.7	41 (0.3-64)
Hřjer *et al.* [22] 1997	Eur Radiol	CT-scan and surgery	Incisional hernia repair	24	62; (19-90)	NR	NR
Gutiérrez de la Peńa *et al.* [6] 2001	Eur Radiol	Physical examination, CT-scan and surgery	Incisional hernia repair	50	58;	NR	NR
Holihan *et al.* [23] 2016	JAMA Surg	Physical examination and CT-scan	Incisional hernia repair	100	51.0; SD 12.6	10.2; (0.2-48.8)	12,5; (2-1711)
Baucom *et al.* [21] 2016	Am J Surg	Physical examination and Ultrasound	Incisional hernia repair	52	52; SD 12	33 6; SD 6.5	46; SD 13

*Legend: NR: not reported, SD: standard deviation; *identical source population*

Figure 2: Risk of bias and applicability concerns summary

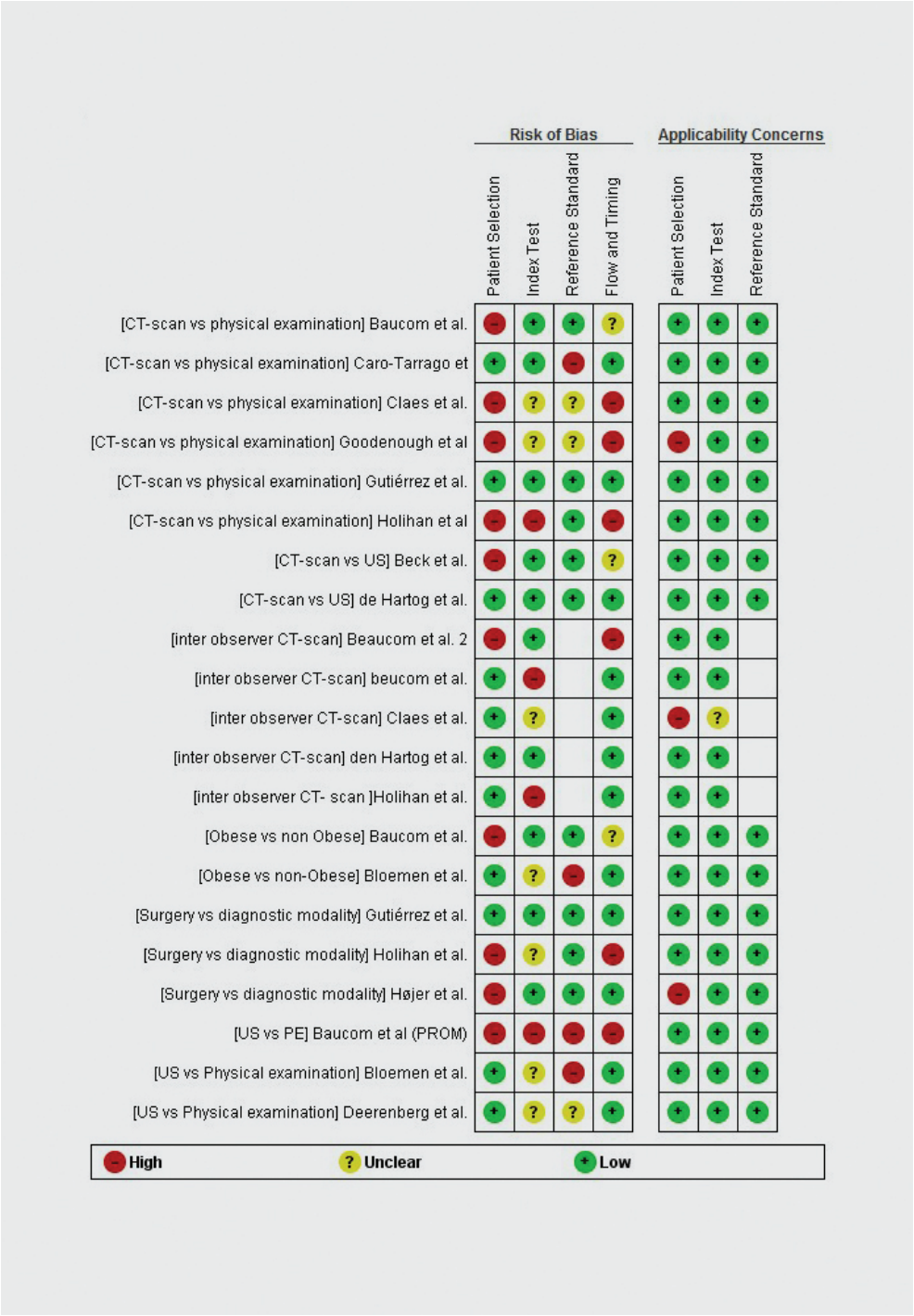

Figure 3: Overall risk of bias and applicability concerns

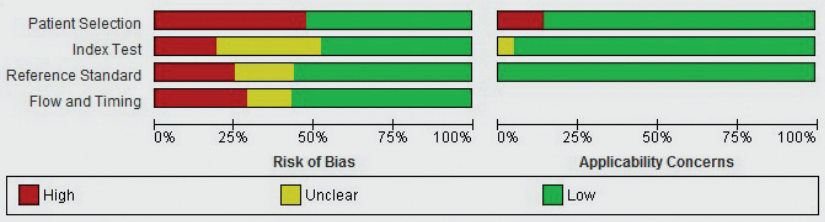

Table 2: inter observer variation

Den Hartog *et al.* [8] 2014	Risk of bias	+++	Radiologist B		Radiologist A		
	Level of evidence	2B			CT +	CT -	Total
	Agreement	87,50%		CT +	21	1	22
	Disagreement	12,50%		CT -	4	14	18
	Kappa	0,74		Total	25	15	40
Baucom *et al* [18] 2014	Risk of bias	++	Surgeon		Radiology report		
	Level of evidence	2B			CT +	CT -	Total
	Agreement:	85,60%		CT +	78	21	99
	Disagreement:	14,40%		CT -	5	77	82
	Kappa:	0,71		Total	83	98	181
Claes et al [12] 2014	Risk of bias	++	Radiologist B		Radiologist A		
	Level of evidence	2B			CT +	CT -	Total
	Agreement:	88,80%		CT +	84	21	105
	Disagreement:	11,20%		CT -	19	233	252
	Kappa:	0,73		Total	103	254	357
Holihan *et al.* [23] 2014	Risk of bias:	++	N = 100			Disagreement	Kappa
	Level of evidence:	2B	10 observers			73%	0,44
	10 observers: 3 surgeons, 6 radiologist and radiology report		9 observers			71%	0,44
			Surgeons (n=3)			27%	0,62
			Radiologists (n=6)			69%	0,38
Baucom *et al.* [21] 2016	Risk of bias:	+	Panel of 5 surgeons evaluated a random sample of 20 CT-scans. **Intra class correlation coefficient: 0.85.**				
	Level of evidence:	3B					

CT-scan versus ultrasound

The prevalence rate of IH after ultrasound and CT-scan was reported in two studies concerning a total of 221 patients [7,8]. The study by Beck *et al.*[7] had methodological problems concerning patient selection and patient flow. Results obtained by these studies are summarized in Table 3. These two studies obtained contradictory results. Den Hartog *et al.*[8] reported a higher prevalence rate when using ultrasound whereas Beck *et al.*[7] reported unchanged prevalence rates. Relative increase in prevalence rate when comparing CT-scan to ultrasound was 1.41 and 0.93. Disagreement between ultrasound and CT-scan was reported in 7/40 (17.5%) and 12/181 (6.6%) cases.

CT-scan versus physical examination

The prevalence rates of IH after CT-scan and physical examination were reported in six studies concerning a total of 1,378 patients [5,6,11,12,14,23]. Five out of six studies included in this comparison had one or more methodological concerns [5,11,12,14,23]. Results obtained by these studies are summarized in Table 4. Four studies reported higher prevalence rates and two studies reported lower prevalence rates when using CT-scan for the diagnosis of IH. The relative increase in prevalence rates when comparing CT-scan to physical examination ranged from 0.92 to 1.8 (n = 1,378). Disagreement between diagnosis by CT-scan compared to physical examination was quantifiable in four studies and ranges from 7.8 to 32% (n = 770). Between 15% and 48% of the reported IH diagnosis were solely established with use of CT-scan (N=267) [5,6,14,23].

Table 3: CT-scan vs ultrasound

Den Hartog *et al.* [8] 2014	Risk of bias	++++	4x4 table			
	Level of evidence	2B		CT +	CT -	Total
	Prevalence CT	60%	US+	17	0	17
	Prevalence US	43%	US -	7	16	23
	Relative increase	1.41	Total	24	16	40
Beck *et al.* [7] 2013	Risk of bias	++	4x4 table			
	Level of evidence	2B		CT +	CT -	Total
	Prevalence CT	55%	US+	97	10	107
	Prevalence US	59,1%	US -	2	72	74
	Relative increase	0.93	Total	99	82	181

Legend: US: ultrasound

Table 4: CT-scan vs Physical examination

Gutiérrez de la Peña *et al.* [6] 2001	Risk of bias	++++	4x4 table			
	Level of evidence	2B		PE +	PE -	Total
	Prevalence PE	18%	CT+	6	3	9
	Prevalence CT	17%	CT -	4	37	41
	Relative increase	0,92	Total	10	40	50
Baucom *et al.* [14] 2014	Risk of bias	++	4x4 table			
	Level of evidence	2B		PE +	PE -	Total
	Prevalence PE	44%	CT+	76	23	99
	Prevalence CT	55%	CT -	4	78	82
	Relative increase	1,24	Total	80	101	181
Holihan *et al.* [23] 2016	Risk of bias	++	4x4 table			
	Level of evidence	2B		PE +	PE -	Total
	Prevalence PE	30%	CT+	26	28	54
	Prevalence CT	54%	CT -	4	42	46
	Relative increase	1,80	Total	30	70	100
Goodenough *et al.* [5] 2015	Risk of bias	??	4x4 table			
	Level of evidence	2B		PE +	PE -	Total
	Prevalence PE	18%	CT+	59	14	73
	Prevalence CT	17%	CT -	20	346	366
	Relative increase	0,92	Total	79	360	439
Caro-Tarrago *et al.* [11] 2015	Risk of bias	+++	N =160			
	Level of evidence	2B				
	Prevalence PE	14%				
	Prevalence CT	20%				
	Relative increase	1,45				
Claes *et al.* [12] 2014	Risk of bias	+++	N =160			
	Level of evidence	2B				
	Prevalence PE	17%				
	Prevalence CT	30%				
	Relative increase	1,71				

Legend: PE: physical examination

Ultrasound versus physical examination

The prevalence rate of IH after ultrasound and physical examination were reported in four studies concerning a total of 1,013 patients [2,4,7,14,21]. All studies included in this comparison had one or more methodological concerns [2,4,7,14,21]. Results obtained by these studies are summarized in Table 5. Three studies reported higher prevalence rates and one study reported a similar prevalence rate when using ultrasound for the diagnosis of IH. The relative increase in prevalence rates when comparing ultrasound to physical examination ranges from 1 to 2.4 (n = 1,013). Disagreement between diagnosis by ultrasound compared to physical examination was quantifiable in three studies. Disagreement between the two modalities was reported in 41/456 (9%), 44/338 (13%) and 15/38 (39%) of the cases. IH diagnosis was solely established with us of ultrasonography in 21/103 (20%), 41/87 (47%) and 15/26 (58%) of IH diagnosis [2,4,21].

Table 5: Ultrasound vs physical examination

Bloemen *et al.* [4] 2015	Risk of bias	+++	4x4 table			
	Level of evidence	2B		PE +	PE -	Total
	Prevalence PE	18,0%	US+	62	21	83
	Prevalence US	18,2%	US -	20	353	373
	Relative increase	1,0	Total	82	374	456
Deerenberg *et al.* [2] 2015	Risk of bias	++	4x4 table			
	Level of evidence	2B		PE +	PE -	Total
	Prevalence PE	13,6%	US+	43	41	84
	Prevalence US	24,9%	US -	3	251	254
	Relative increase	1,8	Total	46	292	338
Baucom *et al.* [21] 2016	Risk of bias	3B	4x4 table			
	Level of evidence	----		PE +	PE -	Total
	Prevalence PE	28,9%	US+	11	15	26
	Prevalence US	68,4%	US -	0	12	12
	Relative increase	2,4	Total	11	27	38
Baucom/ Beck *et al.* [7,14] 2014	Risk of bias	++	n = 181			
	Level of evidence	2B				
	Prevalence PE	14%				
	Prevalence US	20%				
	Relative increase	1,45				

Legend: PE: physical examination

Table 6: peroperative diagnosis

CT-scan VS per operative diagnosis						
Gutiérrez de la Peña *et al.* [6] 2001	Risk of bias	++++	4x4 table			
	Level of evidence	2B		Surgery +	Surgery -	Total
			CT+	8	1	9
			CT -	0	41	41
			Total	8	42	50
Hřjer *et al.* [22] 1997	Risk of bias	+++	4x4 table			
	Level of evidence	3B		Surgery +	Surgery -	Total
			CT+	6	1	7
			CT -	2	3	5
			Total	8	4	12
Holihan *et al.* [23] 2016	Risk of bias	+	4x4 table			
	Level of evidence	3B		Surgery +	Surgery -	Total
			CT+	14	1	15
			CT -	0	3	3
			Total	14	4	18
Physical examination vs peroperative diagnosis						
Gutiérrez de la Peña *et al.* [6] 2001	Risk of bias	++++	4x4 table			
	Level of evidence	2B		Surgery +	Surgery -	Total
			PE+	6	4	10
			PE -	2	38	40
			Total	8	42	50
Holihan *et al.* [23] 2016	Risk of bias	+	4x4 table			
	Level of evidence	3B		Surgery +	Surgery -	Total
			PE+	11	1	12
			PE -	3	3	6
			Total	14	4	18

Legend: PE: physical examination

Peroperative diagnosis

The diagnosis obtained through physical examination or CT-scan was compared to the per-operative findings in three studies concerning 80 patients. Results obtained by these studies are summarized in Table 6 [6,22,23]. only one of the studies included in this comparison was of good methodological quality. All reports on this outcome were flawed by small sample sizes. Gutiérrez de la Peña *et al.*[6] reported a true positive rate of 100% and a false positive rate of

98% (n = 50) for diagnosis with CT-scan. For the diagnosis with physical examination, a true positive rate of 75% and a false positive rate of 90% (n = 50) were reported [6].

Impact of obesity

The impact of obesity on the diagnosis of IH was reported in three studies concerning two different patient populations [4,14,19]. Baucom *et al.*[14] compared CT-scan as diagnostic modality to physical examination in obese and non-obese patients. The disagreement rate between the two modalities was 21% (n = 96) in obese patients compared to 13% in non-obese patients (n = 85) [14]. Bloemen *et al.*[4] compared ultrasound as diagnostic modality to physical examination in patients with a body mass index (BMI) >25 and in patients with a BMI < 25. The disagreement rate between the two modalities was 10% (n = 228) in the BMI > 25 patients compared to 8% in BMI < 25 patients (n = 228) [4]. One other study compared the mean surface area of incisional hernias detected with ultrasound in obese and non-obese patients and did not find a significant difference between the two [19].

Discussion

In this systematic review on diagnostic modalities for IH diagnosis, great variance between modalities and between different studies was found. The diagnosis of IH remains challenging, as no objective gold standard is present.

All included studies were of retrospective design, had multiple methodological concerns, or presented a small sample of patients (GRADE quality: low or very low). Therefore, the results of included studies should be interpreted with caution. Compared to peroperative diagnosis CT-scan seems to be reasonably accurate in one study presenting a small sample of patients [6]. However, considerable inter observer variability has been reported [8,12,18,20,23]. Moreover, multiple studies report considerable discrepancy between CT-scan and physical examination and between CT-scan and ultrasonography results [2,4-7,11,12,14,23]. No study compares ultrasound to the peroperative diagnosis. Two studies compare ultrasound to CT-scan and find contradictory results [7,8]. Inter observer variability for ultrasound and physical examination has not been assessed thoroughly however, we may assume inter observer variability will be present due to the dynamic nature of these diagnostic modalities.

One prospective study of decent methodological quality provides a comparison between physical examination and the peroperative diagnosis in a small sample of 50 patients. Although the sample size was limited, this is the only report that provides some reliable insight in the sensitivity and specificity of physical examination, a sensitivity of 75% and a specificity of 90% being reported [6]. Considerable discrepancies were reported between diagnosis by physical examination and ultrasound or CT-scan [2,4-7,11,12,14,23]. Most studies report higher prevalence rates when using imaging modalities for the diagnosis of IH. However, not all studies show this trend [4,6]. Relative increase in IH prevalence

compared to physical examination ranged from 0.92 to 1.8 for CT-scan and 1 to 2.4 for ultrasound [2,4-7,11,12,14,23]. Strikingly, studies that report similar prevalence rates for physical examination and ultrasound or CT-scan still show considerable disagreement between the two imaging modalities [4,6]. The diagnostic performance of CT-scan is more thoroughly investigated compared to physical examination and ultrasound. CT-scan will likely provide the most sensitive and reproducible diagnosis of IH followed by ultrasound and physical examination. The definition of IH differed slightly in those studies that reported a definition. No study reported an IH definition specifically adapted for the diagnostic modality used. Disagreement between observers might in part be due to lack of consensus with regard to the IH definition [23].

It is important to stress that all the above-mentioned concerns relate to the research setting. For clinical studies, objective comparable measures should be used to report endpoints. The choice of diagnostic modality in a clinical setting might be relatively straightforward as most clinicians are mainly focused on identifying symptomatic incisional hernias that might require treatment. Therefore, in asymptomatic patients a full diagnostic workup would often not be necessary. For a surgeon, detection rate is not the only argument to choose one modality over the other. In this case, costs, availability, patient safety, and patient comfort are important factors to take into account. It is understandable that a stepwise incremental approach is often chosen, in which physical examination will be the first modality used, followed by imaging in case of doubt.

In IH research the diagnostic follow-up is challenging as no diagnostic gold standard exists and imaging will often be applied for non-IH related indications or in patients with an inconclusive physical examination, potentially causing for selection bias. The choice of diagnostic modality and the number of observers might influence the IH prevalence found. When different modalities and observers are unequally distributed over study cohorts, internal study validity could be compromised. This is especially of concern in studies of observational retrospective design since many observers and different diagnostic modalities are present in every day clinical practice. Moreover, the aims of the clinician (identifying symptomatic IHs) often deviate from the aims of the researcher (identifying all IHs). Varying definitions for IH among observers are likely to cause a part of the observed disagreement [23].

Use of a universal definition such as the definition as proposed by Korenkov *et al.*[9]: 'any abdominal wall gap with or without bulge in the area of a postoperative scar perceptible or palpable by clinical examination or imaging', might be imperative. Based on current data, restricting the definition of IH to radiologically confirmed hernia's only, is not advisable, illustrated by the substantial inter observer variation in CT-scan examinations and reports of false negative and false positive CT-scan diagnosis [6,8,18,22,23]. Although our knowledge with

regard to inter observer variation in IH diagnosis is mainly based on diagnosis by CT-scan, we may assume that these variations are of even more concern when applying ultrasound or physical examination, due to the more dynamic nature of these diagnostic modalities and the fact that in both modalities subjectivity plays a larger role. The series presented by Holihan *et al*. [23] (CT-scan only) suggested that at least part of the observed inter observer variation was due to subtle differences in the applied definition and methodology of operators. An IH definition specifically altered for the (radiologic) diagnostic modality of use, accompanied by a standardized systematic approach, might further improve the accuracy and consistency of IH diagnosis [7,23]. For ultrasound examination a systematic approach in which the midline area is examined first, followed by the abdominal areas next to the midline and finally the more lateral abdominal areas as suggested by Beck *et al*. [7] could be considered. This approach could be applied similarly for abdominal palpation. Since the diameter of the fascial defect and hernia sac significantly enlarge during a Valsalva maneuver, routine use of the Valsalva maneuver during physical examination and radiologic evaluation of the postoperative scar might be of added diagnostic value [24].

The clinical relevance of IHs detected solely by radiologic imaging remains unclear. Only one study to date attempts to answer this question. Bloemen *et al*. [4] reported 26/103 of IH patients with discomfort, 3/26 of these IHs were detected by ultrasound alone and 1/13 IHs that were treated surgically were detected by ultrasound alone. Based on current literature the proportion of IHs solely detected by radiologic imaging that requires treatment or will progress through time remains unclear. Future research concerning the diagnosis of IHs should emphasize more on these factors.

Limitations

Our systematic review has some limitations. First, all included studies were of low quality: most were of retrospective design, and some studies presented small samples. Therefore, the data should be interpreted with caution. We assume that between study variation is present: follow-up, indication for abdominal surgery, BMI, and age differed between studies. Additionally, some studies included a small proportion of laparoscopic patients [7,12,14,18-20]. IH prevalence rates in patients operated laparoscopically differ from patients undergoing open abdominal surgery. Therefore, the proportion of patients operated laparoscopically will influence the total IH prevalence. Although these factors influence the comparability of reported IH prevalence, these factors might be of less concern when assessing the diagnostic accuracy. The majority of included studies had multiple methodological concerns. Risks for either reporting or selection bias was found frequently (Appendix 2). Most methodological concerns will mainly influence the overall prevalence rates; however, the diagnostic accuracy will be influenced by the prevalence rate to some degree. Additionally, a number of studies did not compare the diagnostic modalities in a blinded fashion, potentially diluting the presented results and diminishing generalizability [2,4,5,11,12,18].

Conclusion

Great variance between different diagnostic modalities and between different observers was found. Use of imaging modalities will usually cause for additional/increasing numbers of IH diagnosis and increase the IH prevalence compared to use of physical examination alone. When comparing different imaging modalities, CT-scan provides the most accurate diagnosis. Lack of consensus with regard to the IH definition among observers might in part explain the inter observer variation. The observer, diagnostic modality, and diagnostic approach could be additional factors explaining variability in IH prevalence and should therefore be reported with detail in IH research. To achieve internally valid study results proper distribution of different observers and diagnostic modalities across study cohorts is imperative.

Conflict of Interest:
LFK, DS, GJK and JFL declare that they have no conflict of interest.
FM declares conflict of interest not related to the submitted work, grants and personal fees from Medtronic and Dynamesh.

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Appendix 1: literature search syntax

Embase.com

('incisional hernia'/exp OR 'abdominal wall hernia'/mj OR (((incision* OR scar* OR cicatri*) NEAR/3 (herni*)) OR postoperat*-herni* OR post-operat*-herni*):ab,ti OR ((abdom* OR ventral*) NEAR/3 (herni*)):ti) AND ('sensitivity and specificity'/exp OR 'diagnostic value'/exp OR 'interrater reliability'/exp OR 'reproducibility'/de OR 'observer variation'/exp OR 'observer bias'/exp OR 'diagnostic error'/exp OR 'diagnostic accuracy'/de OR 'diagnostic test accuracy study'/exp OR 'differential diagnosis'/exp OR 'predictive value'/de OR 'kappa statistics'/de OR (sensitiv* OR specific* OR ((diagnos* OR imaging OR ct OR tomograph* OR resonance OR mri OR predicti*) NEAR/6 (value* OR useful* OR challeng* OR pitfall* OR contribution* OR effect* OR efficac* OR error* OR erron* OR accura* OR different*)) OR (false NEXT/1 (negative* OR positive*)) OR ppv OR npv OR reliab* OR reproduc* OR interrat* OR observer* OR interobserver* OR intraobserver* OR (kappa NEXT/1 (value OR test OR statistic*))):ab,ti OR ((('diagnosis'/de OR 'computer assisted diagnosis'/exp OR 'diagnosis':lnk OR 'imaging and display'/exp OR 'computer assisted tomography'/exp OR 'nuclear magnetic resonance imaging'/exp OR radiodiagnosis/de OR 'diagnostic imaging'/exp OR tomography/exp OR 'nuclear magnetic resonance'/exp OR 'physical examination'/exp OR 'ultrasound'/de OR 'echography'/exp OR 'Valsalva maneuver'/de OR 'patient-reported outcome'/exp OR (diagnos* OR radiodiagnos* OR misdiagnos* OR imaging OR (compute* NEAR/3 tomogra*) OR ((ct OR cat OR mr OR nmr) NEXT/3 (scan* OR imag*)) OR mri OR (magnet* NEAR/3 resonan*) OR (physical* NEAR/3 examinat*) OR ultraso* OR sonogra* OR echogra* OR patient-report* OR palpat* OR Valsalva):ab,ti) AND ('intermethod comparison'/exp OR 'comparative study'/de OR 'instrument validation'/de OR 'validation process'/de OR 'validation study'/de OR 'evaluation study'/de OR (compare* OR comparative* OR comparison* OR comparing* OR validat* OR evaluat*):ab,ti))))

Medline Ovid

("Incisional Hernia"/ OR * "Hernia, Ventral"/ OR (((incision* OR scar* OR cicatri*) ADJ3 (herni*))).ab,ti,kf. OR ((abdom* OR ventral*) ADJ3 (herni*)).ti.) AND ("Sensitivity and Specificity"/ OR "Reproducibility of Results"/ OR "observer variation"/ OR exp "diagnostic errors"/ OR "Diagnosis, Differential"/ OR "kappa statistics"/ OR (sensitiv* OR specific* OR ((diagnos* OR imaging OR ct OR tomograph* OR resonance OR mri OR predicti*) ADJ6 (value* OR useful* OR challeng* OR pitfall* OR contribution* OR effect* OR efficac* OR error* OR erron* OR accura* OR different*)) OR (false ADJ (negative* OR positive*)) OR ppv OR npv OR reliab* OR reproduc* OR interrat* OR observer* OR interobserver* OR intraobserver* OR (kappa ADJ (value OR test OR statistic*))).ab,ti,kf. OR ((("diagnosis"/ OR exp "Diagnosis, Computer-Assisted"/ OR "diagnosis".xs. OR exp "Magnetic Resonance Imaging"/ OR exp "diagnostic imaging"/ OR exp tomography/ OR "Magnetic Resonance

Spectroscopy"/ OR exp "physical examination"/ OR "Ultrasonics"/ OR exp "Ultrasonography"/ OR "Valsalva Maneuver"/ OR "Patient Reported Outcome Measures"/ OR (diagnos* OR radiodiagnos* OR misdiagnos* OR imaging OR (compute* ADJ3 tomogra*) OR ((ct OR cat OR mr OR nmr) ADJ3 (scan* OR imag*)) OR mri OR (magnet* ADJ3 resonan*) OR (physical* ADJ3 examinat*) OR ultraso* OR sonogra* OR echogra* OR patient-report* OR palpat* OR Valsalva).ab,ti,kf.) AND ("Comparative Study"/ OR "Validation Studies"/ OR "evaluation studies"/ OR (compare* OR comparative* OR comparison* OR comparing* OR validat* OR evaluat*).ab,ti,kf.))))

Cochrane CENTRAL

((((incision* OR scar* OR cicatri*) NEAR/3 (herni*)) OR postoperat*-herni* OR post-operat*-herni*):ab,ti OR ((abdom* OR ventral*) NEAR/3 (herni*)):ti) AND ((sensitiv* OR specific* OR ((diagnos* OR imaging OR ct OR tomograph* OR resonance OR mri OR predicti*) NEAR/6 (value* OR useful* OR challeng* OR pitfall* OR contribution* OR effect* OR efficac* OR error* OR erron* OR accura* OR different*)) OR (false NEXT/1 (negative* OR positive*)) OR ppv OR npv OR reliab* OR reproduc* OR interrat* OR observer* OR interobserver* OR intraobserver* OR (kappa NEXT/1 (value OR test OR statistic*))):ab,ti OR ((((diagnos* OR radiodiagnos* OR misdiagnos* OR imaging OR (compute* NEAR/3 tomogra*) OR ((ct OR cat OR mr OR nmr) NEXT/3 (scan* OR imag*)) OR mri OR (magnet* NEAR/3 resonan*) OR (physical* NEAR/3 examinat*) OR ultraso* OR sonogra* OR echogra* OR patient-report* OR palpat* OR Valsalva):ab,ti) AND ((compare* OR comparative* OR comparison* OR comparing* OR validat* OR evaluat*):ab,ti))))

Web of science

TS=(((((incision* OR scar* OR cicatri*) NEAR/2 (herni*)) OR postoperat*-herni* OR post-operat*-herni*)) AND ((sensitiv* OR specific* OR ((diagnos* OR imaging OR ct OR tomograph* OR resonance OR mri OR predicti*) NEAR/5 (value* OR useful* OR challeng* OR pitfall* OR contribution* OR effect* OR efficac* OR error* OR erron* OR accura* OR different*)) OR (false NEAR/1 (negative* OR positive*)) OR ppv OR npv OR reliab* OR reproduc* OR interrat* OR observer* OR interobserver* OR intraobserver* OR (kappa NEAR/1 (value OR test OR statistic*))) OR ((((diagnos* OR radiodiagnos* OR misdiagnos* OR imaging OR (compute* NEAR/2 tomogra*) OR ((ct OR cat OR mr OR nmr) NEAR/2 (scan* OR imag*)) OR mri OR (magnet* NEAR/2 resonan*) OR (physical* NEAR/2 examinat*) OR ultraso* OR sonogra* OR echogra* OR patient-report* OR palpat* OR Valsalva)) AND ((compare* OR comparative* OR comparison* OR comparing* OR validat* OR evaluat*))))))

Google scholar

"incisional|scar|cicatrical hernia" diagnosis|radiodiagnosis|imaging|tomography|mri|"physical examination"|ultrasonography|echography validation|sensitivity|specificity|"diagnostic value|error|accuracy"

Systematic review and meta-analysis of extraperitoneal versus transperitoneal colostomy for preventing parastomal hernia

CHAPTER 4

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Abstract

Background: Parastomal hernia remains a frequent problem after constructing a colostomy. Current research mainly focuses on prophylactic mesh placement as an addition to transperitoneal colostomies. However, for constructing a colostomy, extraperitoneal or transperitoneal route can be chosen.

Objective: The aim of this meta-analysis is to investigate which technique results in lower parastomal hernia rates in patients undergoing end colostomy.

Data Sources: A meta-analysis was conducted according to PRISMA and MOOSE guidelines. Embase, Medline, Web-of-science, Scopus, Cinahl ebsco, Cochrane, PubMed-publisher and Google scholar databases were searched. The study protocol was registered in the PROSPERO database, number CRD42015025373.

Study Selection: Studies comparing extraperitoneal and transperitoneal colostomy were included. Only studies written in English were included. Quality of studies and risk of bias were assessed using Cochrane risk of bias tool. Quality of non-randomized studies was assessed using the Newcastle-Ottawa Scale.

Intervention: Intervention was colostomy formation.

Main Outcome Measures: Main outcome measure was parastomal hernia incidence. Secondary outcome measures were stoma prolapse, stoma necrosis and operating time.

Results: Of 401 articles found, a meta-analysis was conducted of ten studies (two RCTs, eight retrospective studies) comprising 1048 patients (347 extraperitoneal and 701 transperitoneal). Extraperitoneal colostomy led to significantly lower parastomal hernia rates (22 out of 347 (6.3%) for extraperitoneal versus 125 out of 701 (17.8%) for transperitoneal, RR 0.36, 95% CI 0.21-0.62, I2=26%, P<0.001) and significantly lower stoma prolapse rates (2 out of 185 (1.1%) for extraperitoneal versus 13 out of 179 (7.3%) for transperitoneal, RR 0.21, 95% CI 0.06-0.73, I2=0%, P=0.01). Differences in stoma necrosis were not significant. Operating time data was insufficient to analyze.

Limitations: Most studies were non-randomized and some of them were not recent publications.

Conclusions: Although the majority of studies included were retrospective, extraperitoneal colostomy was observed to lead to a lower rate of parastomal hernia and stoma prolapse.

Introduction

Colostomy is still a common procedure, with an estimated 120 000 new colostomies performed each year in the United States.[1] Parastomal hernia is the most common complication after stoma construction, especially after end colostomy.[2, 3] Although techniques in colorectal surgery have developed in the past decades, parastomal hernia incidence after end colostomy is still high, occurring in 3-39% of all patients.[3-5] Many parastomal hernias remain asymptomatic, but symptoms can vary from discomfort, esthetical complaints, hygienic problems, pain and bowel obstruction to incarceration.[4]

Traditionally, a colostomy is constructed using the transperitoneal route. In contrast, in the extraperitoneal route, the remaining colon after resection is mobilized and tunneled between the peritoneum and the abdominal wall muscles to the future stoma location. Then, an incision is made in the skin and muscles to create the stoma aperture. First reported in 1958 by Goligher,[6] extraperitoneal stoma formation has been used before, but it has never been widely used, especially not after the introduction and increase of laparoscopic colorectal surgery. In laparoscopic surgery, extraperitoneal stoma formation is still possible, but it requires new techniques.[7, 8]

Previously, research has been done studying different techniques of stoma formation and parastomal hernia repair,[4, 9] but this research only focused on the classic transperitoneal route for stoma formation. Recent research on the prevention of parastomal hernia has focused on prophylactic mesh placement. First performed in 2004 by Jänes et al.,[10] synthetic or biologic mesh placement around the stoma has shown promising results with regard to parastomal hernia incidence.[11-14] Despite these results, prophylactic mesh placement requires the implantation of a prosthetic device in all patients, including patients that will not develop parastomal hernia, with its possible side effects and higher costs. Therefore, using a different surgical technique may result in more favorable results.

Meta-analyses studying the extraperitoneal route have been performed before,[15, 16] however, these studies were incomplete, because only a limited number of literature databases was searched and no systematic review with a complete published search strategy syntax was performed, or they only focused on laparoscopic surgery.

The aim of this study is to compare the extraperitoneal and (the more frequently used) transperitoneal route for colostomy in both open and laparoscopic colorectal surgery, comparing data on parastomal hernia and other complications (stoma prolapse and stoma necrosis) and operating time.

Materials and Methods

The study protocol was registered in the PROSPERO database (International Prospective Register of Systematic Reviews, www.crd.york.ac.uk/prospero/) with the registration number CRD42015025373. All aspects of the PRISMA statement (Preferred Items for Reporting of Systematic Reviews and Meta-analyses),[17] and MOOSE guideline (Meta-analysis Of Observational Studies in Epidemiology)[18] were followed.

Search strategy

Embase, Medline, Web-of-science, Scopus, Cinahl ebsco, Cochrane, PubMed publisher and Google scholar databases were searched on July 22nd, 2015. Full search details and syntax are presented in Appendix 1. The syntax construction and database search were performed in collaboration with a medical librarian specialized in conducting systematic reviews.

Studies comparing extraperitoneal and transperitoneal colostomy were included. There was no limit in date of publication.

Studies were first evaluated for inclusion based on title and abstract by two independent researchers (LK and GS) and finally evaluated independently based on full text. Differences in article selection were discussed and articles were included or excluded after reaching agreement. Only English articles were included. Studies were included if they met the following criteria: 1) participants: adult patients undergoing colorectal surgery with end colostomy, 2) interventions: extraperitoneal colostomy or transperitoneal colostomy, 3) outcome measure: parastomal hernia, 4) secondary outcome measures: stoma prolapse, stoma necrosis and operating time. Discrepancies in inclusion were resolved by discussion between reviewers and the senior author (JL).

Data collection

Data collection was performed independently by two different researchers (LK and GS) using standard forms covering study characteristics (study design, year, location and evidence); patient baseline characteristics (type of intervention, number of patients, age, sex, open or laparoscopic surgery, duration of follow up and reason for surgery); type of colostomy (extraperitoneal versus transperitoneal), colostomy-related complications (parastomal hernia, stoma prolapse, stoma necrosis) and operating time.

Assessment of study quality

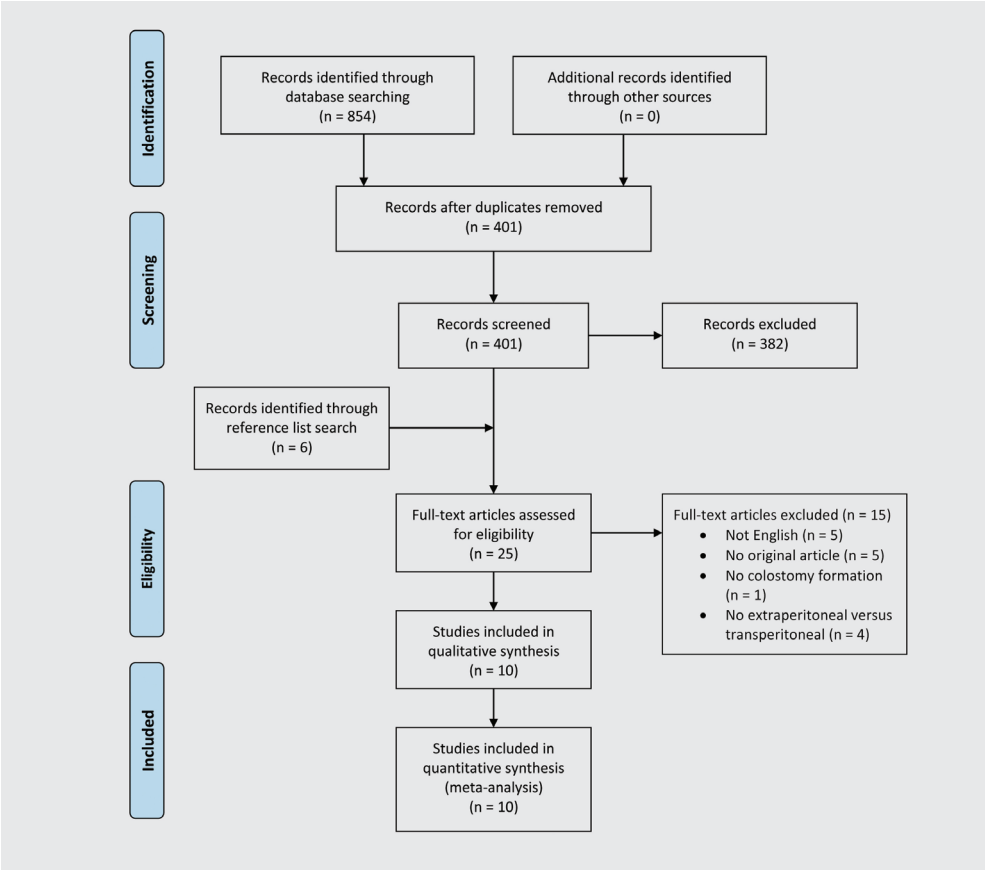
The level of evidence of each paper was established according to the Oxford Centre for Evidence-based Medicine levels of evidence.[19] The possible risk of bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias.[20] Methodological quality of included non-randomized studies was assessed using the Newcastle Ottawa Scale (NOS) criteria.[21]

Statistical analysis

To pool data and to calculate a pooled mean for each patient level outcome, the Mantel-Haenszel random-effects model was used, which takes into account the variance between studies and the variance within a study.[22] Risk ratios (RRs) with 95 per cent confidence intervals (CIs) were calculated to evaluate the statistical difference between outcomes following extraperitoneal or transperitoneal colostomy. Statistical heterogeneity was assessed for incidence of parastomal hernia, stoma prolapse and stoma necrosis by calculating the Q statistics and the I^2 statistic.

Individual study effects on the results were examined by removing the studies one at a time to determine whether removing a particular study would change the significance of the pooled effect. Two-sided $P \leq 0.05$ was considered statistically significant. Analyses were performed using Review Manager software (RevMan 5.3; The Nordic Cochrane Centre, Copenhagen, Denmark).

Figure 1: PRISMA 2009 flow diagram



Results

Search and study characteristics

A PRISMA flow diagram of the complete search strategy is shown in Figure 1. The initial search resulted in 854 articles (401 after duplicates removal). After screening, 25 articles were selected for full-text reading. After full-text reading, ten articles were selected for inclusion2, 23-31. Two articles were RCT's, eight were retrospective. All non-randomized studies scored 5 out of 9 or higher on the NOS criteria and were included in the quantitative analysis. Complete study details are listed in Table 1. The summary of risk of bias assessment is presented in Table 2.

Parastomal hernia

Ten studies[2, 23-31] comprising 1048 patients (347 patients with extraperitoneal colostomy and 701 patients with transperitoneal colostomy) investigating the parastomal hernia rate were included in the meta-analysis (Figure 2). The parastomal hernia rate was significantly lower in the extraperitoneal group (22 out of 347, 6.3%) compared to the transperitoneal group (125 out of 701, 17.8%) (RR 0.36, 95% CI 0.21-0.62, I2=26%, P<0.001).

Figure 2: Forest plot of parastomal hernia results

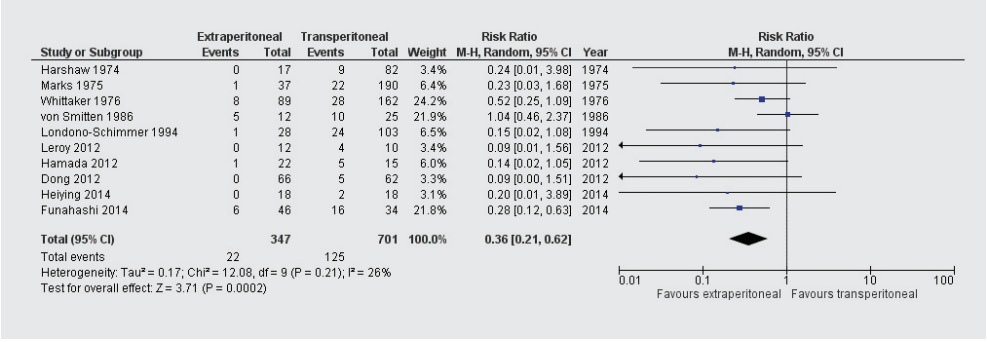


Figure 3: Forest plot of stoma prolapse results

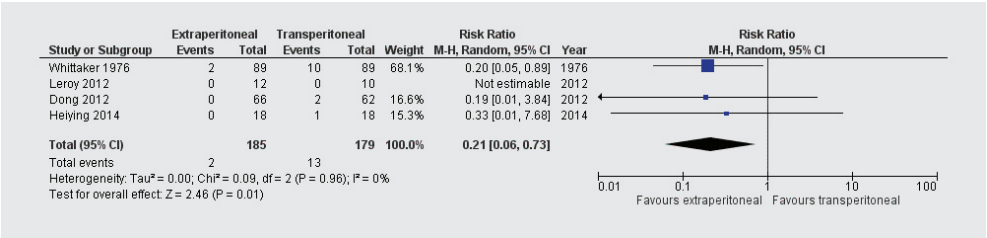


Table 1: Study characteristics

Reference	Type of study	LoE	NOS	n		Age (years)*	Men (%)	Primary surgery(n)	Open / laparoscopic	Follow up (months)	Outcome measures
Harshaw *et al.*[23] (1974)	Retro	2b	5	Total EPS TPS	99 17 82	-	-	APR	Open	-	PSH
Marks *et al.*[24] (1975)	Retro	2b	6	Total EPS TPS	227 37 190	62.1 (50-79)† - -	66.9 - -	APR	Open	60	PSH
Whitakker *et al.*[25] (1976)	Retro	2b	6	Total EPS TPS	251 89 162	-	59.4	APR	Open	24	PSH, prolapse
von Smitten *et al.*[26] (1986)	Retro	2b	6	Total EPS TPS	37 12 25	62.4 (36-83)† - -	40.7 - -	APR	Open	54 (12-96)†	PSH
Londono-Schimmer *et al.*[2] (1994)	Retro	2b	6	Total EPS TPS	131 28 103	62 (23-86)† - -	60.4 - -	APR (127), Hartmann (4)	Open	66 (2-250)†	PSH
Dong *et al.*[27] (2012)	RCT	1b	-	Total EPS TPS	128 66 62	- 56.4 (11.0) 57.9 (10.3)	53.9 54.5 53.2	APR	-	60	PSH, prolapse, OT
Hamada *et al.*[28] (2012)	Retro	2b	9	Total EPS TPS	37 22 15	- 67 (10) 68 (12)	64.9 50.0 86.7	APR	Laparoscopic	 24‡ 14‡	PSH, Necrosis, OT
Leroy *et al.*[29] (2012)	Retro	2b	9	Total EPS TPS	22 12 10	- 66.6 (8.9) 75 (8.7)	63.6 66.7 60.0	APR	Laparoscopic	- 22.25 (27.94)* 36.3 (20.02)*	PSH, prolapse, necrosis, OT
Funahashi *et al.*[30] (2014)	Retro	2b	6	Total EPS TPS	80 46 34	66 (33-90) - -	73.8 - -	APR (67), TPE (13)	Both	31 (0.5-91)‡	PSH
Heiying *et al.*[31] (2014)	RCT	1b	-	Total EPS TPS	36 18 18	- 59.7 (14.4) 61.4 (11.4)	44.4 38.9 50.0	APR	Laparoscopic	17 (12-24)‡	PSH, prolapse, OT

*Values are means (standard deviation); † values are mean (range); ‡ values are median (range)

LoE, Oxford Centre for Evidence-based Medicine levels of evidence; NOS, Newcastle-Ottawa Score; EPS, extraperitoneal stoma; TPS, transperitoneal stoma; Retro, retrospective study; RCT, randomized controlled trial; APR, abdominoperineal resection; TPE, total pelvic exenteration; PSH, parastomal hernia; OT, operating time

Stoma prolapse

Four studies[25, 27, 29, 31] comprising 437 patients (185 patients with extraperitoneal colos-tomy and 252 patients with transperitoneal colostomy) investigating the stoma prolapse rate were included in the meta-analysis (Figure 3). The stoma prolapse rate was significantly lower in the extraperito-neal group (2 out of 185, 1.1%) compared to the transperitoneal group (13 out of 179, 7.3%) (RR 0.21, 95% CI 0.06-0.73, I2=0%, P=0.01).

Stoma necrosis

Two studies[28, 29] comprising 59 patients (34 patients with extraperitoneal colostomy and 25 patients with transperitoneal colostomy) investigating the stoma necrosis rate were included in the meta-analysis (Figure 4). There was no statistically significant difference in stoma necrosis rate between extraperitoneal (2 out of 34, 5.9%) and transperitoneal (2 out of 25, 8.0%) route (RR 0.76, 95% CI 0.04-14.69, I2=50%, P=0.86).

Operating time

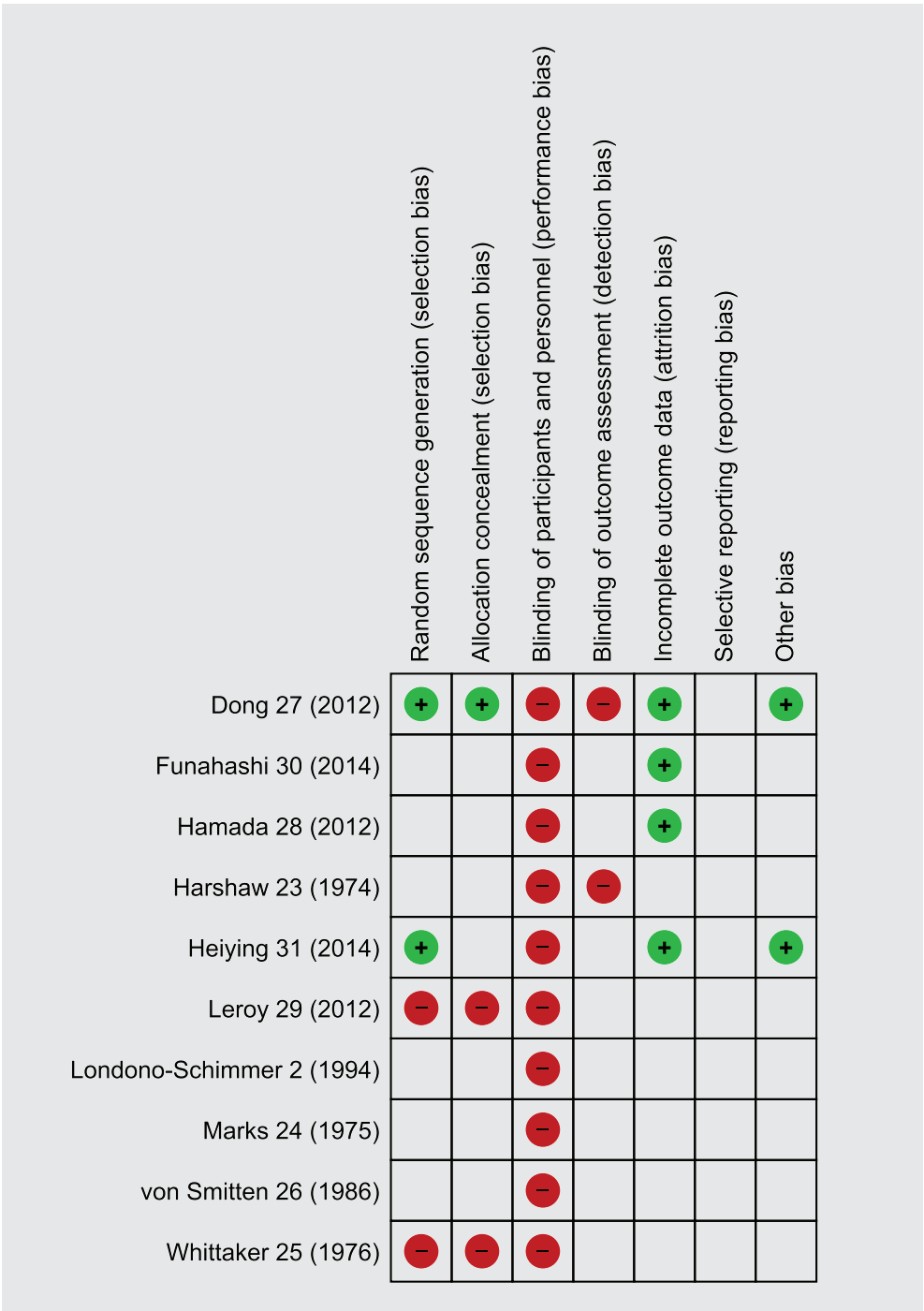
Four studies[27-29, 31] reported on operating time. However, definitions of operating time seem to range from full operating time to stoma construction time, making it impossible to make a fair comparison of the data.

Figure 4: Forest plot of stoma necrosis results

Discussion

Parastomal hernia still remains a frequent complication after stoma formation, occurring in 3-39% of all end colostomies.[3-5] Traditionally, a colostomy is constructed transperitoneally. To reduce the incidence of parastomal hernias, colostomy through the extraperitoneal route has been used as an alternative technique.[6] Recent publications suggest beneficial effects of this extraperitoneal stoma formation.[15, 16] However, these studies are incomplete and unclear about their methods. To provide a clear insight on all literature so far, this meta-analysis was performed showing that the use of the extraperitoneal route for stoma creation results in a significantly lower parastomal hernia rate compared to the transperitoneal route (22 out of 347 (6.3%) extraperitoneal versus 125 out of 701 (17.8%) in transperitoneal). This is

Table 2


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Dong 27 (2012)
Funahashi 30 (2014)
Hamada 28 (2012)
Harshaw 23 (1974)
Heiying 31 (2014)
Leroy 29 (2012)
Londono-Schimmer 2 (1994)
Marks 24 (1975)
von Smitten 26 (1986)
Whittaker 25 (1976)

consistent with evidence provided before.[15, 16] Also, a significantly lower incidence of stoma prolapse was found in the extraperitoneal group (2 out of 185 (1.1%) extraperitoneal versus 13 out of 179 (7.3%) transperitoneal). No significant differences could be found in stoma necrosis rates.

Although described before,[15, 16] this meta-analysis is the first to systematically search all available literature, providing a complete overview of all research until this moment. Also, by using PRISMA and MOOSE guidelines, an attempt for standardization was made.

It is possible that by creating an extraperitoneal colostomy, forces on the abdominal wall (both pressure and tension) are more evenly spread compared to the transperitoneal route where forces are concentrated on one created defect through all layers of the abdominal wall. Secondly, apart from factors such as malnutrition, obesity, raised intra-abdominal pressure, corticosteroid use and increased age, the presence of lateral space, defined as space between the lateral side of the colon and the abdominal wall muscle or fascia, is thought to be an important factor in parastomal hernia occurrence.[4] In the extraperitoneal route, the colon is tunneled laterally towards the stoma, preventing lateral space to occur.

Also, with transperitoneal colostomies, rises in intra-abdominal pressure may cause intra-abdominal contents to be forced laterally to the colostomy. When pressure rises with extraperitoneal colostomies, the higher pressure pushes the sigmoid lateral to the stoma, preventing intra-abdominal contents to herniate.

Recent literature suggests beneficial effects of the use of prophylactic biological or synthetic meshes.[11-14] Despite these promising results, mesh placement has its potential disadvantages such as obstruction, infection, fistulas or erosion. Secondly, a majority of patients will not develop a parastomal hernia.[3-5] Prophylactic mesh placement would mean potential side effects in this otherwise unaffected group.

One of the difficulties of parastomal hernia literature research is the lack of clear definitions of parastomal hernia and how to diagnose it. The included studies are not always clear on this matter. Four articles have no description of diagnosis,[23, 24, 31, 32] two articles have physical examination only[25-28] and two articles used physical examination combined with computed tomography,[29, 30] This heterogeneity however, is expected to influence parastomal hernia incidence equally in both groups. For future RCT's, a combination of physical examination and imaging techniques such as ultrasonography or computed tomography should be used, as is common use in incisional hernia research.[33]

A potential disadvantage of extraperitoneal could be a more difficult situation for parastomal hernia repair. Taking this fact into account, laparoscopic mesh repair using the Sugarbaker technique as used for parastomal hernia repair[34, 35] could be chosen for this matter.

Limitations

To minimize the possibility of bias and heterogeneity between studies, a meta-analysis ideally

consists of a number of high quality studies with comparable populations and interventions.[36] This study only contains two RCTs, the rest being retrospective studies.
As displayed in table 2, four of the more recent studies[27, 28, 30, 31] show a smaller risk of bias than the older studies. Despite this fact, the same beneficial effect on outcome measures was found in all studies.

Secondly, all included studies cover a broad period of time (1974-2014). Within this period, major changes have taken place in both operative and perioperative care, such as the introduction of neoadjuvant therapy and laparoscopic surgery. Although these changes are not expected to be favorable to one of both techniques, the wide timespan should be considered when interpreting the results.

With laparoscopic surgery being the first choice of care in colorectal surgery nowadays, it is suggested that the extraperitoneal route might not be practical.[11] The practical aspect could not be investigated in this study, but in this meta-analysis, both open and laparoscopic surgery was performed in different studies. The results show that all included publications tend towards the same direction in favor of the extraperitoneal route, regardless of the surgery being open or laparoscopic.

Unfortunately, only a small number of the studies investigated potential complications of extraperitoneal colostomy; Hamada *et al.*[28] and Leroy *et al.*[29] mentioned necrosis, Heiying *et al.*[31] investigated ischemia, Whittaker *et al.*[25] reported obstruction and Dong *et al.*[27] and Leroy *et al.*[29] studied stoma prolapse. To make a fair comparison, these should also be studied thoroughly in future research.

Even with these remarks taken to account, extraperitoneal colostomy may favor transperitoneal colostomy with regard to parastomal hernia incidence.

Conclusion

Although the majority of the studies included are retrospective, the extraperitoneal route seems preferable for colostomy with respect to parastomal hernia and stoma prolapse occurrence.

A prospective, randomized controlled trial is recommended comparing extraperitoneal colostomy with transperitoneal colostomy.

Acknowledgments

We would like to thank Wichor Bramer for his assistance on the search strategy and syntax.

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Appendix 1: Search syntax

Embase.com 222

(colostomy/exp OR 'rectum resection'/exp OR 'colon resection'/exp OR stoma/exp OR (colostom* OR ((abdominoperin* OR abdomino-perineal OR colon* OR colorect* OR rectum OR rectal OR sigmoid OR transvers*) NEAR/6 (resection* OR excision*)) OR stoma OR stomas OR stomata OR transversostom*):ab,ti) AND (retroperitoneum/exp OR (retroperiton* OR extraperiton* OR ((retro* OR extra) NEXT/1 periton*)):ab,ti) AND ('comparative study'/exp OR (transperiton* OR intraperiton* OR ((trans* OR intra) NEXT/1 periton*) OR conventional* OR comparativ* OR intermethod*):ab,ti)

Medline ovid 162

(colostomy/ OR "Colectomy"/ OR "Surgical Stomas"/ OR (colostom* OR ((abdominoperin* OR abdomino-perineal OR colon* OR colorect* OR rectum OR rectal OR sigmoid OR transvers*) ADJ6 (resection* OR excision*)) OR stoma OR stomas OR stomata OR transversostom*).ab,ti.) AND ("Retroperitoneal Space"/ OR (retroperiton* OR extraperiton* OR ((retro* OR extra) ADJ periton*)).ab,ti.) AND ("comparative study"/ OR (transperiton* OR intraperiton* OR ((trans* OR intra) ADJ periton*) OR conventional* OR comparativ* OR intermethod*).ab,ti.)

Cochrane 7

((colostom* OR ((abdominoperin* OR abdomino-perineal OR colon* OR colorect* OR rectum OR rectal OR sigmoid OR transvers*) NEAR/6 (resection* OR excision*)) OR stoma OR stomas OR stomata OR transversostom*):ab,ti) AND ((retroperiton* OR extraperiton* OR ((retro* OR extra) NEXT/1 periton*)):ab,ti) AND ((transperiton* OR intraperiton* OR ((trans* OR intra) NEXT/1 periton*) OR conventional* OR comparativ* OR intermethod*):ab,ti)

Web-of-science 97

TS=(((colostom* OR ((abdominoperin* OR abdomino-perineal OR colon* OR colorect* OR rectum OR rectal OR sigmoid OR transvers*) NEAR/5 (resection* OR excision*)) OR stoma OR stomas OR stomata OR transversostom*)) AND ((retroperiton* OR extraperiton* OR ((retro* OR extra) NEAR/1 periton*))) AND ((transperiton* OR intraperiton* OR ((trans* OR intra) NEAR/1 periton*) OR conventional* OR comparativ* OR intermethod*)))

Scopus 249

TITLE-ABS-KEY(((colostom* OR ((abdominoperin* OR abdomino-perineal OR colon* OR colorect* OR rectum OR rectal OR sigmoid OR transvers*) W/5 (resection* OR excision*)) OR stoma OR stomas OR stomata OR transversostom*)) AND ((retroperiton* OR extraperiton* OR ((retro* OR extra) W/1 periton*))) AND ((transperiton* OR intraperiton* OR ((trans* OR intra) W/1 periton*) OR conventional* OR comparativ* OR intermethod*)))

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(MH colostomy+ OR MH "Colectomy+" OR "Surgical Stomas+" OR (colostom* OR ((abdominoperin* OR abdomino-perineal OR colon* OR colorect* OR rectum OR rectal OR sigmoid OR transvers*) N5 (resection* OR excision*)) OR stoma OR stomas OR stomata OR transversostom*)) AND (MH "Retroperitoneal Space+" OR (retroperiton* OR extraperiton* OR ((retro* OR extra) N1 periton*))) AND (MH "comparative studies+" OR (transperiton* OR intraperiton* OR ((trans* OR intra) N1 periton*) OR conventional* OR comparativ* OR intermethod*))

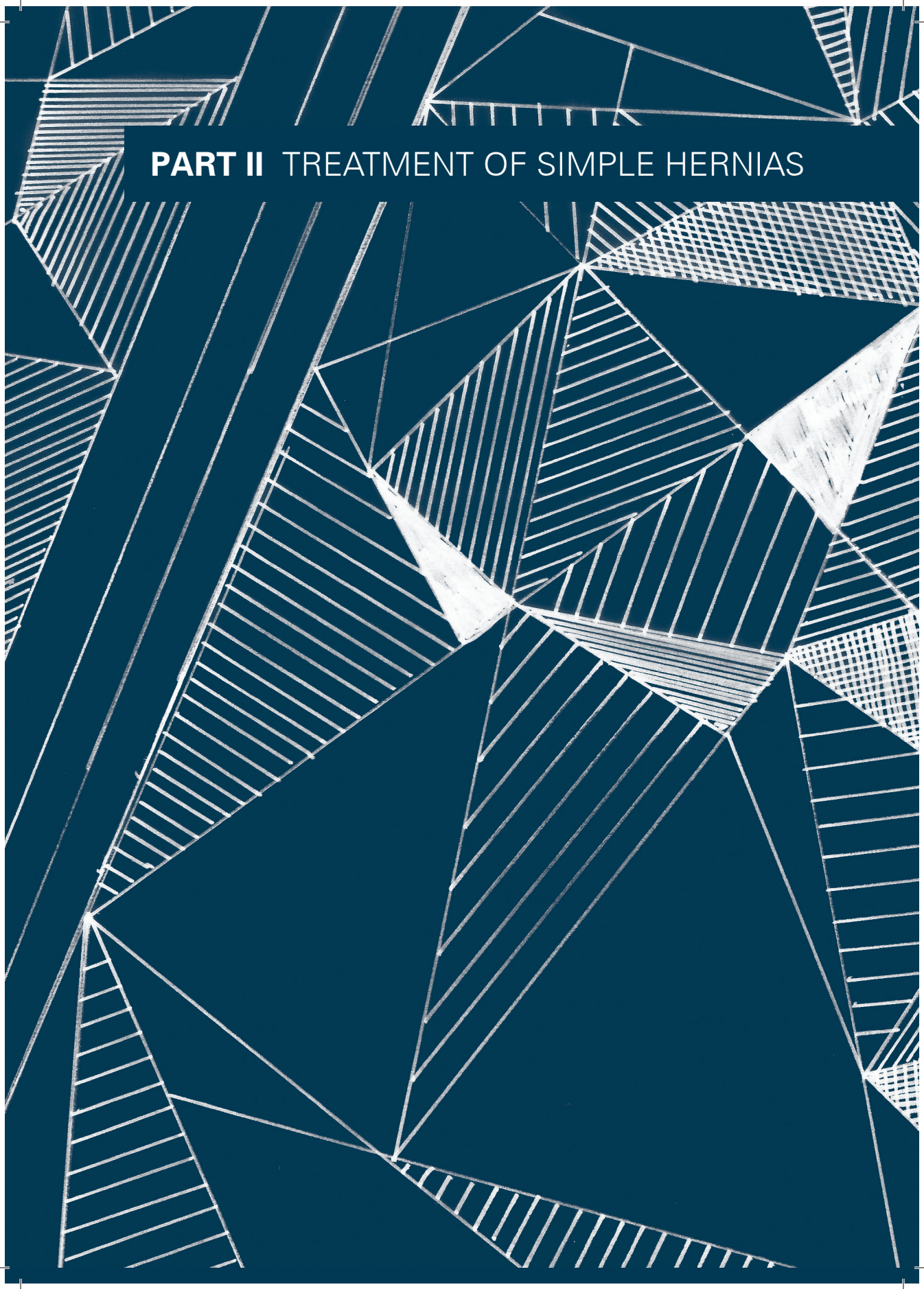
Pubmed publisher 7

(colostomy[mh] OR "Colectomy"[mh] OR "Surgical Stomas"[mh] OR (colostom*[tiab] OR ((abdominoperin*[tiab] OR abdomino-perineal OR colon*[tiab] OR colorect*[tiab] OR rectum OR rectal OR sigmoid OR transvers*[tiab]) AND (resection*[tiab] OR excision*[tiab])) OR stoma OR stomas OR stomata OR transversostom*[tiab])) AND ("Retroperitoneal Space"[mh] OR (retroperiton*[tiab] OR extraperiton*[tiab] OR retro periton*[tiab] OR extra periton*[tiab])) AND ("comparative study"[pt] OR (transperiton*[tiab] OR intraperiton*[tiab] OR trans periton*[tiab] OR intra periton*[tiab] OR conventional*[tiab] OR comparativ*[tiab] OR intermethod*[tiab])) AND (publisher[sb] OR inprocess [sb])

Google scholar

Colostomy|Colostomies|"abdominoperineal|colon|colorectal|rectum|rectal|sigmoid|transverse resection|resections|excision|excisions"|stoma|stomas retroperitoneal|extraperitoneal transperitoneal|intraperitoneal|conventional|comparative|intermethod

PART II TREATMENT OF SIMPLE HERNIAS



CHAPTER 5

Primary and incisional ventral hernias are different in terms of patient characteristics and postoperative complications - A prospective cohort study of 4,565 patients

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Abstract

Background: Primary and incisional hernias are often pooled in publications studying hernia symptoms, treatment, or surgical outcomes. The question rises whether this is justified or if primary and incisional hernia should be considered as two separate entities. The aim of this prospective cohort study is to compare primary and incisional ventral hernias regarding patient characteristics, hernia characteristics, surgical characteristics, and postoperative complications.

Materials and methods: A registry-based, prospective cohort study was performed. All patients undergoing primary or incisional hernia repair surgery between September 1st 2011 and February 29th 2016 were included. Patient baseline characteristics, hernia characteristics, surgical characteristics, and postoperative outcomes were collected and analyzed.

Results: A total of 4,565 patients were included, of whom 2,374 had a primary hernia and 2,191 had an incisional hernia. All patient, hernia, and surgical characteristics were statistically significantly different between primary and incisional hernias except for corticosteroid use, history of inguinal hernia, incarceration, and emergency surgery. Overall complication rates (wound, surgical, and medical) were significantly different (105/2,374 (4.4%) for primary hernia versus 323/2,191 (15%) for incisional hernia, $p<0.001$).

Conclusion: Primary and incisional hernia are statistically significantly different for almost all patient, hernia, surgical, and postoperative characteristics analyzed. Given these differences, data on primary hernias and incisional hernias should not be pooled in studies reporting on hernia repair.

Introduction

Primary (PH) and incisional ventral hernias (IH) are very common conditions. In the USA alone, over 300,000 ventral hernia repairs are performed annually.[1] Around 75% of these hernia repairs are performed for primary ventral hernias (mainly epigastric and umbilical hernias) and around 25% are performed for incisional hernias.[2] The associated costs of these hernia repairs are estimated to be US$3.2 billion a year.[1] Currently, incisional hernias occur in 10-30% of all patients undergoing midline laparotomies, depending on risk factors.[3-8]

Primary and incisional ventral hernias have many similarities. They are both abdominal wall defects predominantly located in the linea alba, and share similar symptoms like discomfort, pain, and potentially incarceration.[9] However, despite these similarities, the etiology of both types of hernias is thought to be different. Primary hernias can be considered as a congenital condition, whereas incisional hernias represent an iatrogenic technical or wound healing problem.

Regardless of these potential differences, primary and incisional ventral hernias are most often pooled in publications reporting on hernia surgery outcomes.[10-15] Stirler *et al.*[16] and Köckerling *et al.*[17] addressed this issue of pooled data analysis. Stirler *et al.* compared the characteristics and outcomes of patients undergoing laparoscopic ventral hernia repair. Köckerling *et al.* compared surgical techniques and complication rates of primary and incisional hernia surgery. Both studies found statistically significant differences. These articles are an important first step in comparing both types of hernias, but unfortunately, almost no patient characteristics were included in the comparison between both groups. These characteristics are among the most important features to take into account because they are associated with postoperative outcomes: many patient characteristics, like age, American Society of Anesthesiologists (ASA) score, smoking, and steroid use, but also factors like operative time and emergency surgery, are associated with postoperative complications and recurrences.[18-21]

The objective of this study was to compare primary and incisional hernias regarding patient characteristics, hernia characteristics, surgical characteristics, and postoperative complications after hernia repair surgery, by using a large-scale database.

Material and methods

Study design

A registry-based, prospective cohort study was performed. All adults undergoing ventral hernia surgery in the French Hernia-Club registry from September 1, 2011, until February 29, 2016, were compared.

The Hernia-Club registry is approved by the French 'Commission Nationale de l'Informatique et des Libertés' (CNIL; registration number 1993959v0). Because the study is a registry-based study, and patient data is anonymized, additional participant consent and

institutional review board approval were not required in accordance to the French and Dutch national ethical standards.

STROBE (Strengthening the Reporting of Observational studies in Epidemiology) recommendations for the reporting of observational studies, STROCSS criteria, as well as the European Registry of Abdominal Wall Hernias (EuraHS) recommendations were used for this study.[22-24]

Hernia-Club registry

The Hernia-Club registry is a collaborative, prospective, anonymized online database of all the hernia surgery procedures performed by 42 French surgeons (both public and private, academic and non-academic) with a specific interest in abdominal wall surgery. Each participating surgeon must accept and sign the Charter of Quality, which states that: ''all input must be registered in a consecutive, unselected, and exhaustive manner and in real time''. The registration is performed before outcomes are known. A total of 164 parameters are collected prospectively from screening, pre-, peri- and postoperative periods. Parameters are directly collected online by the operating surgeon in real time. Participants consent to random peer review of original medical charts. Postoperative outcomes are collected by the surgeon and are further checked by an independent clinical research associate (CRA) during the 2-year follow-up. In case of discrepancies, the medical record is checked.

The collected parameters in this database are compatible with the European Hernia Society (EHS) classification of primary and incisional abdominal wall hernias[25] and the EuraHS international online platform.[26]

Data collection

Patient characteristics extracted from the registry included patient age, sex, body mass index (BMI), smoking habits, diabetes mellitus (DM), corticosteroid use, preoperative radio- or chemotherapy, history of aneurysm of the abdominal aorta (AAA), connective tissue disorders, anticoagulants use or coagulopathies, previous history of hernias, and American Society of Anesthesiologists (ASA) score. Hernia characteristics included location, width, length, EHS width class, primary or recurrent hernia, and symptoms., Surgical characteristics included open or laparoscopic approach, emergency surgery, mesh use and technique of mesh placement, duration of surgery, and Altemeier wound classification[27]. Finally, postoperative data (admission duration, complications, and reoperations) were also collected. Postoperative complications (wound, surgical, and medical) were graded using the Clavien-Dindo grading system.[28]

Statistical methods

SPSS 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. IBM Corp, Armonk, NY, USA) was used for all statistical analyses. To test normal distribution of

continuous variables, Levene's test for equality of variances was used. Continuous variables are presented as means with standard deviations (SDs). Categorical variables are presented as numbers with percentages. Missing data are presented in all Tables. Mann-Whitney U (continuous data) and chi-squared tests (categorical data) were used to compare primary and incisional hernia patients. In case of small groups (n<5), Fisher's exact test was used. P-values <0.05 were considered statistically significant. To demonstrate the overall comparison and to avoid emphasis on one particular factor, it was chosen to do this by performing univariate analysis without additional multivariate or sensitivity analysis.

Results

A total of 4,565 patients were included. Of these patients, 2,374 (52%) had a PH and 2,191 (48%) had an IH. The rate of missing data for a single variable was no more than 3.7% (Tables 1, 2, and 3).

Baseline patient characteristics

All baseline patient characteristics are presented in Table 1. PH and IH patients were statistically significantly different for thirteen of the sixteen baseline characteristics analyzed. Most notable different factors were age (55.61 for PH versus 62.86 for IH, p<0.001), sex (61% males for PH versus 48% males for IH, p<0.001), smoking (22% for PH versus 18% for IH, p=0.001), diabetes mellitus (6.1% for PH versus 12% for IH, p<0.001), and a family history of abdominal wall hernia (4.3% for PH versus 0.8% for IH, p<0.001).

The only factors that were not different were corticosteroid use (3.4% for PH versus 3.5% for IH, p=0.867), presence of ascites (0.9% for PH versus 0.6% for IH, p=0.344), and a history of inguinal hernia (9.4% for PH versus 11% for IH, p=0.248).

Hernia and surgical characteristics

Hernia and surgical characteristics are presented in Table 2. Hernia width (1.62±1.50 cm for PH versus 4.85±4.22 cm for IH, p<0.001) and hernia length (1.79±1.73 cm for PH versus 6.10±5.59 cm for IH, p<0.001) were statistically significantly different.

PH patients had more asymptomatic hernias (22% for PH versus 15% for IH, p<0.001) and fewer hernias causing pain (69% for PH versus 73% for IH, p<0.001).

The duration of surgery was significantly longer for IH patients (24.45±16.58 minutes for PH versus 65.04±52.20 minutes for IH, p<0.001), PH patients had more laparoscopic procedures (29% for PH versus 26% for IH, p=0.037), and PH patients had more primary suture repairs (33% for PH versus 11% for IH, p<0.001). Mesh location (p<0.001), Altemeier wound class (p=0.010), and antibiotic treatment (P<0.001) were also significantly different between PH and IH, demonstrating that IH patients had more contaminated or dirty wounds and received more antibiotic treatment than PH patients. The rate of emergency procedures was not significantly different between the two groups.

Table 1. Baseline patient characteristics

	Primary hernia (n=2374)	*N missing (%)*	**Incisional hernia (n=2191)**	*N missing (%)*	**p-value**
Age in years (SD)	55.61 (14.69)	*9 (0.4)*	62.86 (14.12)	*10 (0.5)*	<0.001
Male sex (%)	1445 (61)	*0*	1044 (48)	*0*	<0.001
BMI, kg/m^2 (SD)	27.67 (7.09)	*0*	29.13 (7.04)	*0*	<0.001
Smoking (%)	529 (22)	*51 (2.1)*	389 (18)	*119 (5.4)*	0.001
Diabetes mellitus (%)	145 (6.1)	*28 (1.2)*	269 (12)	*47 (2.1)*	<0.001
Corticosteroid use (%)	81 (3.4)	*28 (1.2)*	76 (3.5)	*47 (2.1)*	0.867
Radiotherapy (%)	22 (0.9)	*28 (1.2)*	38 (1.7)	*47 (2.1)*	0.015
Chemotherapy (%)	30 (1.3)	*28 (1.2)*	132 (6.0)	*47 (2.1)*	<0.001
AAA (%)	6 (0.3)	*17 (0.7)*	18 (0.8)	*17 (0.8)*	0.008
Connective tissue disorder (%)	1 (0.0)	*17 (0.7)*	7 (0.3)	*17 (0.8)*	0.032
Anticoagulants use or coagulopathy (%)	198 (8.3)	*28 (1.2)*	361 (17)	*47 (2.1)*	<0.001
Ascites (%)	21 (0.9)	*23 (1.0)*	14 (0.6)	*24 (1.1)*	0.344
History of abdominal wall hernia (%)					
Inguinal hernia (%)	224 (9.4)		229 (11)		0.248
Ventral hernia (%)	84 (3.5)		343 (16)		<0.001
Incisional hernia (%)	20 (0.8)		392 (18)		<0.001
Other abdominal wall hernia (%)	8 (0.3)		54 (2.5)		<0.001
Missing (%)	17 (0.7)		17 (0.8)		
Hiatal hernia (%)	16 (0.7)	*17 (0.7)*	65 (3.0)	*17 (0.8)*	<0.001
Family history of hernia (%)	103 (4.3)	*17 (0.7)*	17 (0.8)	*17 (0.8)*	<0.001
ASA Class					<0.001
I-II (%)	1985 (84)		1500 (69)		
III-IV (%)	366 (15)		679 (31)		
Missing	23 (1.0)		12 (0.5)		

Data are mean (SD) or n (%).
SD, standard deviation; BMI, body mass index; AAA, aneurysm of the abdominal aorta; ASA, American Society of Anesthesiologists

Table 2: Hernia and surgical characteristics

Hernia characteristics	Primary hernia (n=2374)	*N missing (%)*	Incisional hernia (n=2191)	*N missing (%)*	p-value
Hernia width, cm (SD)	1.62 (1.50)	*38 (1.6)*	4.85 (4.22)	*73 (3.3)*	<0.001
Hernia length, cm (SD)	1.79 (1.73)	*58 (2.4)*	6.10 (5.59)	*111 (5.1)*	<0.001
Symptoms					
Asymptomatic (%)	520 (22)		337 (15)		<0.001
Pain (%)	1643 (69)		1611 (73)		<0.001
Incarceration, reducible (%)	106 (4.5)		93 (4.2)		0.846
Incarceration, not reducible (%)	83 (3.5)		79 (3.6)		0.724
Missing (%)	*22 (0.9)*		*71 (3.2)*		
Surgical characteristics					
Emergency surgery (%)	91 (3.8)	*6 (0.3)*	90 (4.1)	*12 (0.5)*	0.620
Duration of surgery, min (SD)	24.45 (16.58)	*27 (1.1)*	65.04 (52.20)	*49 (2.2)*	<0.001
Laparoscopic surgery (%)	685 (29)	*21 (0.9)*	568 (26)	*34 (1.6)*	0.037
Primary suture (%)	780 (33)	*55 (2.3)*	232 (11)	*84 (3.8)*	<0.001
Mesh placement	1539 (65)		1875 (86)		<0.001
Intraperitoneal (%)*	*1084 (71)*		*1250 (67)*		*0.022*
Sublay (%)*	*442 (29)*		*557 (30)*		*0.510*
Onlay (%)*	*12 (0.8)*		*57 (3.0)*		*<0.001*
Component separation with mesh (%)*	*0 (0)*		*7 (0.4)*		*0.016*
Altemeier wound classification[26]					0.010
Clean (%)	2267 (96)		2062 (94)		
Clean contaminated (%)	88 (3.7)		87 (4.0)		
Contaminated (%)	10 (0.4)		24 (1.1)		
Dirty (%)	4 (0.2)		11 (0.5)		
Missing (%)	*5 (0.2)*		*7 (0.3)*		
Antibiotic treatment					<0.001
None (%)	1177 (50)		443 (20)		
Prophylactic (%)	1166 (49)		1625 (74)		
Therapeutic (%)	27 (1.1)		108 (4.9)		
Missing (%)	*5 (0.2)*		*7 (0.3)*		

Data are mean (SD) or n (%).
**Percentages are within the group of patients that received a mesh.*
SD, standard deviation

Postoperative outcomes and complications

Mean admission duration (0.85±2.90 days for PH versus 4.32±4.70 days for IH, p<0.001) was significantly different. In the PH group, 105 patients (4.4%) developed one or more postoperative complications compared with 323 patients (15%) in the IH group (p<0.001). Additionally, patients in the IH group underwent more reoperations (13 (0.6%) for PH versus 45 (2.1%) for IH, p<0.001). An overview of all postoperative complications is given in Table 3.

Table 3: Outcomes

	Primary hernia (n=2374)	*N missing (%)*	**Incisional hernia (n=2191)**	*N missing (%)*	**p-value**
Admission duration, days (SD)	0.85 (2.90)	*0*	4.32 (4.70)	*0*	<0.001
Complication within 30 days (%)	105 (4.4)		323 (15)		<0.001
Wound complications (%)	62 (2.7)		166 (7.7)		<0.001
Surgical complications (%)	9 (0.4)		93 (4.3)		<0.001
Medical complications (%)	38 (1.6)		137 (6.4)		<0.001
Missing (%)	*83 (3.5)*		*55 (2.5)*		
Clavien Dindo grade[27]					<0.001
<III (%)	52 (2.3)		176 (8.5)		
≥III (%)	13 (0.6)		51 (2.5)		
Unknown (%)	40 (38)		96 (30)		
Reoperation (%)	13 (0.6)	*99 (4.2)*	45 (2.1)	*70 (3.2)*	<0.001

Data are mean (SD) or n (%).
SD, standard deviation; ICU, intensive care unit

Discussion

In this analysis of a large-scale, prospective, French database of 4,565 patients, statistically significant differences were found between primary ventral hernia (PH) and incisional hernia (IH) patients. Baseline patient characteristics, hernia characteristics, surgical characteristics, and postoperative complications all were statistically significantly different.

The data clearly show that PH and IH patients are considerably different groups. Some of the analyzed characteristics (age, ASA score, smoking, and operative time) have been associated with complications and hernia recurrences before.[18-21] Additionally, they are associated with incisional hernia occurrence after midline laparotomy.[7, 29] These factors

were present more frequently in IH patients than in PH patients. In accordance with this association, our study found a higher complication rate after IH surgery (15%) compared to PH surgery (4.4%).

Another important aspect of this study is the type of hernia symptoms: PH is more frequently asymptomatic (22% versus 15%) and IH causes pain more frequently (69% versus 73%). Interestingly, despite differences in symptoms and size (1.62±1.50x1.79±1.73 cm for PH versus 4.85±4.22x6.10±5.59 cm for IH), there were no differences in incarceration or emergency surgery rates.

Research on the comparison between PH and IH has been published before.[16, 17] In these studies, it is suggested that pooled data analysis PH and IH should not be performed. Their studies mainly investigated surgical techniques and postoperative outcomes. Although limited analysis of patient characteristics was performed, their conclusions are in line with the findings of the present study.

The differences found in this study confirm that PH and IH are two different entities and even more, they suggest that PH and IH have a different etiology. Several of the factors that were more present in IH patients, like higher age, higher BMI, diabetes mellitus, and preoperative radiotherapy or chemotherapy, are linked to wound healing problems. Where PH can be considered a congenital condition, IH represents a technical issue of failure and/or a wound healing disorder. This might pose clinical consequences: given the presence of factors related to impaired wound healing in patients with IH, the preoperative and operative treatment strategy should focus on the prevention of wound problems.

Limitations

This study has some limitations. First, the results of this study are not based on randomized data, leading to a potential risk of confounding by indication. However, the benefit of this kind of registry study is the translation to the real clinical situation: no artificial selection has been made in patient inclusion. The use of this kind of "big data" is an actual topic and it has been addressed recently for hernia research specifically.[30]

Second, this study focuses on the baseline differences between patients with the two types of hernias. We chose to use univariate analysis for this study to emphasize on the differences in patient characteristics. Because of this, some caution should be taken when looking at the postoperative complication rates. Nevertheless, the differences found are so clear that they definitely provide the evidence to separate PH and IH as different ventral hernia entities.

Third, in this study, around 50% of all patients had an incisional hernia. This is much higher than the expected 25% based on literature[2] and could be a potential source of selection bias. The reason of this higher percentage could be the fact that the Hernia-Club collaborators are surgeons with a special interest in hernia surgery. Moreover, the fact that they are experienced hernia surgeons could explain the relatively low rate of complications found.

Finally, the main postoperative outcome in this study is the number of patients with postoperative complications. This choice was made to focus on the baseline differences between the patients with the two types of hernias. Two important factors often used in hernia research, recurrences and patient reported outcomes, were not included in this study and should be studied in additional research. The results of this study indicate that this has to be done separately for PH and IH.

Conclusion

Primary ventral hernia and incisional hernia are statistically significantly different for almost every factor investigated in this study. This accounts for baseline, hernia, surgical, and postoperative characteristics. Therefore, primary ventral hernias and incisional hernias should be considered as separate entities and should not be combined in hernia research.

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Identification of risk factors for 30-day postoperative complications in patients undergoing primary ventral hernia repair - a prospective cohort study of 2,374 patients

CHAPTER 6

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SURGERY 2018

Structured abstract

Background: Primary ventral hernia is a common condition. Surgical repair is associated with complications, but no clear predictive risk factors are identified. The EHS classification offers a structured framework to describe hernias and to analyze postoperative complications. Given this structured nature, the EHS classification might prove useful for preoperative patient or treatment classification. The objective of this study is to investigate the EHS classification as a predictor for complications within 30 days after primary ventral hernia surgery.

Methods: A registry-based, prospective cohort study was performed, including all patients undergoing primary ventral hernia surgery between September 1st 2011 and February 29th 2016. Univariate analyses and multivariable logistic regression analysis were performed to identify risk factors for postoperative complications.

Results: A total of 2,374 patients were included, of whom 105 (4.4%) patients had one or more complications, either a wound, surgical, or medical complication. Factors associated with complications in univariate analyses ($p<0.10$) and clinically relevant factors were included into the multivariable analyses. In the multivariable analyses, age, BMI, and duration of surgery were independent risk factors. The hernia diameter was not an independent risk factor.

Conclusions: Primary ventral hernia repair is associated with 4.4% complications. No correlation was found between the EHS classification and postoperative complications. Age, BMI, and duration of surgery are correlated with postoperative complications. Therefore, age and BMI should be used in the preoperative risk assessment.

Introduction

Ventral hernia repair is a common surgical procedure, with over 300,000 repairs being performed each year in the United States alone.[1] Of these hernia repairs, around 75% are performed for primary ventral hernias (mainly epigastric and umbilical hernias).[2]

Primary ventral hernias can vary in type and size. To categorize these hernias, the European Hernia Society (EHS) classification was developed and published in 2009.[3] One of the aims of this classification was to use a uniform way of describing hernias in both scientific and clinical communication. The classification is partly based on the estimated risk of complications and recurrences. Although published several years ago, the EHS classification has not been externally validated thoroughly.

Recently, Kokotovic *et al.*[4] demonstrated that 11.2% of all patients undergoing primary ventral hernia repair develop short-term or long-term postoperative complications and that these complications are correlated with the successive readmission rate. This shows the importance of identifying risk factors for postoperative complications. Recognizing these risk factors could potentially lead to preoperative interventions or individual patient risk assessment.

The objective of this study was to evaluate the EHS classification amongst other factors, as a potential predictive tool for postoperative complications after primary ventral hernia surgery, by using a French large-scale database.

Methods

Study design

A registry-based, prospective cohort study was performed. All adults undergoing primary ventral hernia surgery in the French Hernia-Club registry between September 1, 2011, and February 29, 2016, were included.

The Hernia-Club registry is approved by the French 'Commission Nationale de l'Informatique et des Libertés' (CNIL; registration number 1993959v0). Because the study is a registry-based study, and patient data is anonymized, participant consent and institutional review board approval were not required in accordance to French and Dutch national ethical standards.

STROBE (Strengthening the Reporting of Observational studies in Epidemiology) and the European Registry of Abdominal Wall Hernias (EuraHS) recommendations were used for this study.[5, 6]

Hernia-Club registry

The Hernia-Club registry is a collaborative, prospective, anonymized online database of all abdominal wall hernia surgery procedures performed by 42 French surgeons specialised in abdominal wall surgery. Each participating surgeon must accept and sign the Charter of Quality, which states that: ''all input must be registered in a consecutive, unselected and exhaustive manner and in real time''. Participants consent to random peer review of original medical charts. A total of 164 parameters are collected prospectively from screening, pre-, peri- and postoperative periods. All parameters are collected by a blinded clinical research associate (CRA), independent of the individual participating surgeon. The collected parameters in this database are fully compatible with the European Hernia Society (EHS) classification of primary and incisional abdominal wall hernias[3] and the European Registry of Abdominal Wall Hernias (EuraHS) international online platform.[7]

Data collection

Data extracted from the registry included patient age, sex and other patient characteristics (body mass index (BMI), smoking habits, diabetes mellitus (DM), corticosteroid use, preoperative radio- or chemotherapy, history of aneurysm of the abdominal aorta (AAA), connective tissue disorders, anticoagulants use or coagulopathies, previous history of hernias, American Society of Anesthesiologists score (ASA)); hernia characteristics (location, width, length, EHS class, primary or recurrent hernia), and surgical characteristics (open or laparoscopic, emergency surgery, mesh use and technique of mesh placement, duration of surgery, and Altemeier wound class[8]).

Outcome

The primary outcome measure was the number of patients with one or more postoperative

complications within 30 days after surgery. Postoperative complications were graded using the Clavien-Dindo grading system.[9]

Statistics

SPSS 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. IBM Corp, Armonk, NY, USA) was used for all statistical analyses. To test normal distribution of continuous variables, Levene's test for equality of variances was used. Continuous variables are presented as means with standard deviations (SDs). Categorical variables are presented as numbers with percentages. Mann-Whitney U (continuous data) and chi-squared tests (categorical data) were used to compare risk factors for complications after primary hernia surgery. In case of small groups (n<5), Fisher's exact test was used. To prevent bias, multiple imputations were performed to compensate for missing data. Potential risk factors that were related to postoperative complications in the univariate analysis (p<0.10) and clinically relevant factors were included in the multivariable regression analysis. In the multivariable analysis, p-values <0.05 were considered as statistically significant.

Results

A total of 2,374 patients with a primary ventral hernia who underwent surgical repair were included. Baseline patient characteristics are presented in Table 1. Patients with postoperative complications were statistically significantly older (62.43±15.00 year versus 55.21±14.54, p<0.001), had a significantly higher BMI (30.21±8.70 kg/m2 versus 27.58±6.97 kg/m2, p<0.001), used significantly more anticoagulant medication (17% versus 8.0%, p<0.001), had more inguinal hernias in their medical history (16% versus 9.2%, p=0.019), and had a significantly higher ASA class (31% class III-IV versus 15% class III-IV, p<0.001). Other patient characteristics were not statistically significantly different.

Postoperative complications

Of the 2,374 included patients, 105 patients (4.4%) developed one or more of postoperative complications. Of these 105 patients, 62 (59%) had a wound complication, nine (8.6%) had a surgical complication, and 38 (36%) had a medical complication. In total, 13 patients (0.5%) were re-operated. All complications and postoperative outcomes are shown in Table 2.

Hernia characteristics

All hernia characteristics are presented in Table 3. More than 90% of all patients had an epigastric or umbilical hernia. This was not different between patients with or without complications. The EHS size class was significantly different between patients with or without postoperative complications, with more small hernias in the group of patients without complications and more medium or large hernias in the group of patients with complications (p=0.002).

Table 1: Baseline characteristics

Characteristic	No complication (n=2186)	*Missing (%)*	Any complication (n=105)	*Missing (%)*	p-value
Age in years (SD)	55.21 (14.54)	*8 (0.4)*	62.43 (15.00)	*0 (0)*	<0.001
Male sex (%)	1335 (61)	*0 (0)*	62 (59)	*0 (0)*	0.678
BMI, kg/m^2 (SD)	27.58 (6.97)	*0 (0)*	30.21 (8.70)	*0 (0)*	<0.001
Smoking (%)	493 (23)	*50 (2.3)*	19 (18)	*0 (0)*	0.235
Diabetes mellitus (%)	131 (6.0)	*24 (1.1)*	10 (9.5)	*1 (1.0)*	0.143
Corticosteroid use (%)	74 (3.4)	*24 (1.1)*	6 (5.7)	*1 (1.0)*	0.205
AAA (%)	6 (0.3)	*17 (0.8)*	0 (0)	*0 (0)*	1.000
Connective tissue disorder (%)	1 (0)	*17 (0.8)*	0 (0)	*0 (0)*	1.000
Anticoagulants use or coagulopathy (%)	174 (8.0)	*24 (1.1)*	18 (17)	*1 (1.0)*	0.001
Presence of ascites (%)	19 (0.9)	*20 (0.9)*	1 (1.0)	*0 (0)*	0.614
History of abdominal wall hernia (%)					
Inguinal hernia (%)	201 (9.2)		17 (16)		0.019
Ventral hernia (%)	79 (3.6)		2 (1.9)		0.585
Incisional hernia (%)	17 (0.8)		3 (2.9)		0.062
Other abdominal wall hernia (%)	8 (0.4)		0 (0)		1.000
Missing (%)	*17 (0.8)*		*0 (0)*		
Hiatal hernia (%)	15 (0.7)	*17 (0.8)*	1 (1.0)	*0 (0)*	0.532
Family history of hernia (%)	100 (4.6)	*17 (0.8)*	1 (1.0)	*0 (0)*	0.087
Previous abdominal surgery (%)	554 (26)	*17 (0.8)*	29 (28)	*2 (1.9)*	0.553
ASA Class					<0.001
I-II (%)	1842 (84)		71 (68)		
III-IV (%)	325 (15)		33 (31)		
Missing (%)	*19 (0.9)*		*1 (1.0)*		

Data are means (SD) or n (%).
SD, standard deviation; BMI, body mass index; AAA, aneurysm of the abdominal aorta; ASA, American Society of Anesthesiologists.

Table 2: Outcomes after 30 days

Characteristic	Frequency	N missing (%)
Admission duration, days (SD)	0.85 (2.90)	*0 (0)*
Patients with ≥1 complication within 30 days (%)	105 (4.4)	*0 (0)*
Wound complications (%)	62 (2.6)	
Surgical complications (%)	9 (0.4)	
Medical complications (%)	38 (1.6)	
Clavien Dindo grade[9]		
<III (%)	52 (50)	
≥III (%)	13 (12)	
Unknown (%)	40 (38)	

Data are means (SD) or n (%).
SD, standard deviation.

Surgical characteristics

Surgical characteristics are presented in Table 4. Patients with complications underwent more emergency procedures (8.6% versus 3.6%, p=0.010) and had a different Altemeier wound class, with more clean wounds in the group of patients without complications (p<0.001). The rate of laparoscopic procedures and the rate of primary suture closure did not differ between both groups. Other surgical characteristics were not significantly different.

Multivariable analysis

After univariate analysis, ten imputations were performed to reduce bias, caused by missing data. The highest percentage of missing data for a single variable was 2.4%. The imputed data was then used for logistic regression analysis. All factors with a p-value <0.10 and all clinically relevant factors were used for the multivariable analysis. The hernia diameter was analyzed in two different ways: 1) by using the EHS size class and 2) by using the diameter as a continuous variable. Tables 5 and 6 show the result of the multivariable analysis.

After using the EHS size class and correcting for possible confounding variables in the multivariable logistic regression analysis, the following factors remained statistically significant: Age (odds ratio (OR) 1.022 (95% confidence interval (CI) 1.006-1.038), p=0.008), BMI (OR 1.033 (95% CI 1.006-1.061), p=0.018), and duration of surgery (OR 1.021 (95% CI 1.011-1.030), p<0.001).

After using the diameter as a continuous variable and correcting for possible confounding variables in the multivariable logistic regression analysis, the following factors remained statistically significant: Age (OR 1.024 (95% CI 1.008-1.040), p=0.003), BMI (OR 1.039 (95% CI 1.013-1.066), p=0.003), and duration of surgery (OR 1.021 (95% CI 1.012-1.031), p<0.001).

Table 3: Hernia characteristics

Characteristic	No complications (n=2186)	Any complication (n=105)	p-value
Hernia type			0.318
Epigastric (%)	497 (23)	18 (17)	
Umbilical/subumbilical (%)	1587 (73)	82 (78)	
Epigastric and umbilical (%)	16 (0.7)	2 (1.9)	
Spigelian (%)	43 (2.0)	2 (1.9)	
Missing (%)	*43 (2.0)*	*1 (1.0)*	
EHS size classification			0.002
Small, <2 cm (%)	1323 (61)	48 (46)	
Medium, ≥2-4cm (%)	737 (34)	48 (46)	
Large, ≥4cm (%)	85 (3.9)	9 (8.6)	
Missing (%)	*41 (1.9)*	*0 (0)*	

Data are means (SD) or n (%).
EHS, European Hernia Society.

Discussion

In this analysis of a large-scale, prospective French database of 2,374 patients undergoing primary ventral hernia surgery, age, BMI, and duration of surgery were independent risk factors for 30-day postoperative complications.

In contrast to incisional hernias, the EHS class and the hernia size are not correlated with an increased rate of postoperative complications. There are three possible explanations for this finding: 1) other factors might be more important for the development of postoperative complications, 2) the number of patients with complications might be relatively low in this study, and 3) the hernia size, compared to incisional hernia, is relatively limited.

The current division in size made in the EHS classification could be open for debate. In the classification, no rationale is given for the chosen cut-off values. One possible alternative division could be to make two instead of three categories. The smaller could be the category in which primary suture repair is still possible.

BMI had the strongest association with postoperative complications. The association has been demonstrated before[10, 11] and is important in the preoperative patient assessment. Although the exact mechanism behind this association is unknown, it is hypothesized to be a combination of altered biomechanics and an altered metabolic status. Given the higher risk of complications, patients should be encouraged to lose weight before surgery and surgery

Table 4: Surgical characteristics primary

Characteristic	No complications (n=2186)	*N missing (%)*	Any complication (n=105)	*N missing (%)*	p-value
Emergency procedure (%)	79 (3.6)	*5 (0.2)*	9 (8.6)	*0 (0)*	0.010
Incarceration (%)	72 (3.3)	*40 (1.8)*	8 (7.6)	*2 (1.9)*	0.020
Laparoscopic procedure (%)	616 (28)	*18 (0.8)*	29 (28)	*2 (1.9)*	0.955
Primary closure (%)	730 (33)	*49 (2.2)*	29 (28)	*3 (2.9)*	0.232
Duration of surgery, minutes (SD)	23.98 (15.76)	*13 (0.6)*	34.21 (28.60)	*1 (1.0)*	<0.001
Altemeier classification[8]					<0.001
Clean (%)	2102 (96)		92 (88)		
Clean contaminated (%)	71 (3.2)		10 (9.5)		
Contaminated (%)	8 (0.4)		2 (1.9)		
Dirty (%)	2 (0.1)		1 (1.0)		
Missing (%)	*3 (0.1)*		*0 (0)*		
Antibiotic treatment					0.386
None (%)	1070 (49)		44 (42)		
Prophylactic (%)	1088 (50)		59 (56)		
Therapeutic (%)	26 (1.2)		1 (1.0)		
Missing (%)	*2 (0.1)*		*1 (1.0)*		

Data are means (SD) or n (%).
SD, standard deviation.

Table 5: Multivariable analysis with EHS hernia size class

	OR	95% CI	P-value
Age	1.022	1.006-1.038	0.008
BMI	1.033	1.006-1.061	0.018
Anticoagulants	1.393	0.762-2.548	0.282
History of inguinal hernia	1.693	0.954-3.002	0.072
History of incisional hernia	1.747	0.422-7.228	0.441
Family history of hernia	0.218	0.029-1.665	0.142
ASA III&IV vs I&II	1.329	0.811-2.178	0.259
EHS type			
Epigastric	1.000		
Umbilical/subumbilical	1.255	0.725-2.174	0.417
Epigastric and umbilical	1.547	0.259-9.227	0.631
Spigelian	0.663	0.137-3.212	0.610
EHS size class			
Small, <2 cm	1.000		
Medium, ≥2-4cm	1.287	0.829-1.998	0.261
Large, ≥4cm	1.023	0.406-2.582	0.961
Emergency procedure	1.282	0.413-3.978	0.667
Incarceration	0.891	0.277-2.870	0.847
Duration of surgery	1.021	1.011-1.030	<0.001
Altemeier wound classification[8]			
Clean	1.000		
Clean contaminated	1.574	0.663-3.740	0.304
Contaminated	2.618	0.438-15.643	0.291
Dirty	7.323	0.627-85.566	0.112

OR, odds ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists; EHS, European Hernia Society.

might have to be postponed until sufficient weight loss is achieved.[11]

Some of the factors were expected to be associated with complications, but were not found to be different in this study: hernia size, incarceration, smoking, and Altemeier wound class. This finding might be partly explained by the relatively low rate of postoperative complications (4.4%), leading to small subgroups. It is possible that some of these factors will

Table 6: Multivariable analysis with hernia diameter as a continuous variable

	OR	95% CI	P-value
Age	1.024	1.008-1.040	0.003
BMI	1.039	1.013-1.066	0.003
Anticoagulants	1.399	0.765-2.558	0.276
History of inguinal hernia	1.691	0.953-2.999	0.073
History of incisional hernia	1.448	0.346-6.051	0.612
ASA III&IV vs I&II	1.413	0.866-2.307	0.166
Hernia diameter	1.020	0.901-1.154	0.758
Emergency procedure	1.191	0.389-3.647	0.759
Incarceration	0.978	0.311-3.078	0.970
Duration of surgery	1.021	1.012-1.031	<0.001
Altemeier wound classification[8]			
Clean	1.000		
Clean contaminated	1.532	0.643-3.651	0.336
Contaminated	2.413	0.394-14.781	0.341
Dirty	7.307	0.624-85.565	0.113

OR, odds ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists.

prove to be associated with complications in larger cohorts than the one used in this study. Registries like Hernia-Club, EuraHS[7], or AHSQC[12] are excellent means to study this. Regarding smoking, it might be possible that hernia repair was performed less frequently in smoking patients compared to non-smoking patients.

Limitations

There are several limitations to this study. First, although prospective, the results of this study are not based on randomized data. This gives a potential risk of selection bias. However, the benefit of this kind of registry study is the translation to the actual clinical situation: no artificial selection has been made in patient inclusion.

Second, this study focuses on 30-day postoperative complications and hence only covers part of the outcomes of hernia repair. A second, long-term analysis should study whether the EHS Classification could be used to predict recurrences or reoperations as well.

Finally, this cohort consists of a group of patients, operated on by dedicated hernia surgeons. These surgeons can be expected to have more experience than a general surgeon and thus, better results. However, it could also be argued that these surgeons would be operating the more challenging cases.

Conclusion

Age, BMI, and duration of surgery are correlated with postoperative complications after primary ventral hernia repair. No correlation was found between the EHS classification and postoperative complications. Given the correlation of age and BMI with postoperative complications, they should be considered in the preoperative patient assessment of patients with a primary hernia.

Collaborators

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External Validation of the European Hernia Society Classification for Postoperative Complications after Incisional Hernia Repair: A Cohort Study of 2,191 Patients

CHAPTER 7

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Abstract

Background: Incisional hernia is a frequent complication after midline laparotomy. Surgical hernia repair is associated with complications, but no clear predictive risk factors are identified. The European Hernia Society (EHS) classification offers a structured framework to describe hernias and to analyze postoperative complications. Because of its structured nature, it might prove to be useful for preoperative patient or treatment classification. The objective of this study was to investigate the EHS classification as a predictor for postoperative complications after incisional hernia surgery.

Study design: An analysis was performed using a registry-based, large-scale, prospective cohort study, including all patients undergoing incisional hernia surgery between September 1st 2011 and February 29th 2016. Univariate analyses and multivariable logistic regression analysis were performed to identify risk factors for postoperative complications.

Results: A total of 2,191 patients were included, of whom 323 (15%) patients had one or more complications. Factors associated with complications in univariate analyses ($p<0.20$) and clinically relevant factors were included into the multivariable analysis. In the multivariable analysis, EHS width class, incarceration, open surgery, duration of surgery, Altemeier wound class, and therapeutic antibiotic treatment were independent risk factors for postoperative complications. Third recurrence and emergency surgery were associated with fewer complications.

Conclusion: Incisional hernia repair is associated with 15% complications. The EHS width classification is associated with postoperative complications. To identify patients at risk for complications, the EHS classification is useful.

Introduction

Incisional hernia remains a frequent complication after abdominal surgery with incidence rates of 10-30% after midline laparotomies, depending on risk factors.[1-6] This incidence leads to a high number of hernia repair operations. In the USA alone, over 300,000 repairs are performed annually. The associated costs of these hernia repairs are estimated to be US$3.2 billion a year.[7] Incisional hernias can be surgically repaired for many reasons; patients can have cosmetic complaints, pain, bowel obstruction, mechanical complaints or incarceration. There is a great variety of incisional hernias with different locations, width, and length. To categorize these hernias, the European Hernia Society (EHS) developed and published the 'Classification of primary and incisional abdominal wall hernias' in 2009.[8] One of the aims of this classification was to use a uniform method of describing hernias in both scientific and clinical communication. It combines the location and size of the hernia. For location, differentiation between midline, lateral, or combined is made. For the size, the width of the hernia is used. This is divided into three subgroups: W1 (<4cm), W2 (4-10cm), and W3 (>10cm). The classification is partly based on the estimated risk of complications and recurrences. Although published several years ago, the EHS classification has not been externally validated thoroughly.

Several studies have addressed the issue of postoperative complications after incisional hernia repair,[9-11] but these studies did not correct for any risk factors or did not use any size classification such as the EHS classification.

The objective of this study was to evaluate the EHS classification amongst other factors, as a potential predictive tool for postoperative complications after incisional hernia surgery, by using a large-scale database. It was hypothesized that a higher hernia width class would lead to more postoperative complications.

Methods

Study design

A retrospective analysis of a registry-based, large-scale, prospective cohort was performed. Using the French Hernia-Club registry, all adult patients undergoing incisional hernia surgery between September 1, 2011, and February 29, 2016, were included. The Hernia-Club registry is approved by the French 'Commission Nationale de l'Informatique et des Libertés' (CNIL; registration number 1993959v0). Because the study is a registry-based study, and patient data is anonymized, additional participant consent and institutional review board approval were not required in accordance to the French and Dutch national ethical standards.

STROBE (Strengthening the Reporting of Observational studies in Epidemiology) recommendations for the reporting of observational studies as well as the European Registry of Abdominal Wall Hernias (EuraHS) recommendations were used for this study.[12, 13]

Hernia-Club registry

The Hernia-Club registry is a collaborative, prospective, anonymized online database of all abdominal wall hernia surgery procedures performed by 42 French surgeons with a specific interest in abdominal wall surgery. Each participating surgeon must accept and sign the Charter of Quality, which states that: ''all input must be registered in a consecutive, unselected, and exhaustive manner and in real time''. Participants consent to random peer review of original medical charts. A total of 164 parameters are collected prospectively from screening, pre-, peri- and postoperative periods. Parameters are directly collected online by the operating surgeon in real time. Postoperative outcomes are collected by the surgeon and are further checked by an independent clinical research associate (CRA) during the 2-year follow-up. The CRA is blinded for operative techniques used. In case of discrepancies, the medical record is checked.

All parameters collected in this database are fully compatible with the European Hernia Society (EHS) classification of primary and incisional abdominal wall hernias8 and the European Registry of Abdominal Wall Hernias (EuraHS) international online platform.[14]

Data collection

Data extracted from the registry included patient age, sex and other patient characteristics (body mass index (BMI), smoking habits, diabetes mellitus (DM), corticosteroid use, preoperative radio- or chemotherapy, history of aneurysm of the abdominal aorta (AAA), connective tissue disorders, anticoagulants use or coagulopathies, previous other abdominal wall hernias, American Society of Anesthesiologists score (ASA)); hernia characteristics (location, width, length, EHS width class, primary or recurrent hernia), and surgical characteristics (open or laparoscopic, emergency surgery, mesh use and technique of mesh placement, duration of surgery, and Altemeier wound classification[15] (clean/clean contaminated/contaminated/dirty)).

Outcome

The primary outcome measure was the number of patients with postoperative complications within 30 days after surgery. Postoperative complications were graded using the Clavien-Dindo grading system.[16]

Statistics

SPSS 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. IBM Corp, Armonk, NY, USA) was used for all statistical analyses. Normal distribution of continuous variables was assessed and Levene's test for equality of variances was used. Continuous variables are presented as means with standard deviations (SDs) or median with interquartile range (IQR). Categorical variables are presented as numbers with percentages. Mann-Whitney U (continuous data) and chi-squared tests (categorical data) were used to analyze risk factors for complications after incisional hernia surgery. In case of small groups ($n<5$),

Fisher's exact test was used. Potential risk factors that were related to postoperative complications in the univariate analysis ($p<0.20$) and clinically relevant factors often described in hernia publications were included in the multivariable logistic regression analysis. To prevent bias and to increase statistical power, multiple imputations were performed to compensate for missing data. In the multivariable analysis, p-values <0.05 were considered as statistically significant.

Results

A total of 2,191 patients with an incisional hernia were included in this study. Baseline patient characteristics are presented in Table 1. Most notable, age, BMI, smoking, diabetes mellitus, and ASA class were not statistically significantly different between patients with or without complications. Patients with a postoperative complication had statistically significantly fewer primary ventral hernias in their medical history (12% versus 17%, $p=0.021$). Other factors were not statistically significantly different.

Postoperative complications

Of the 2,191 patients, 323 patients (15%) developed one or more postoperative complications. Of these 323 patients, most patients had a wound complication (166 patients, 51% of all complications), followed by medical complications (137 patients, 42% of all complications) and surgical complications (93 patients, 29% of all complications). All 30-day postoperative outcomes are presented in Table 2.

Hernia characteristics

Hernia characteristics are presented in Table 3. There were significant differences in EHS width classification between patients with or without postoperative complications ($p<0.001$) with more W1 class hernias (<4 cm) in the group without complications and more W3 class hernias (>10 cm) in the group with complications. Most hernias were located in the midline. The location of hernias, the recurrences, and previous mesh placement were not significantly different between patients with or without postoperative complications.

Surgical characteristics

Surgical characteristics are presented in Table 4. Patients with complications had more incarcerated hernias (7.7% versus 3.0%, $p<0.001$), fewer laparoscopic procedures (12% versus 29%, $p<0.001$), and different mesh locations ($p<0.001$). Operating time was longer in the complication group (80 minutes (IQR 45-120) versus 45 minutes (IQR 24-75), $p<0.001$). Additionally, Altemeier wound class15 and antibiotic treatment were also significantly different (both $p<0.001$). Emergency surgery rates and primary suture rates were not significantly different.

Multivariable analysis

After univariate analysis, ten imputations were performed to reduce bias, caused by missing data and to increase statistical power. The imputed data was then used for logistic regression analysis. All factors with a p-value <0.20 and all clinically relevant factors were used for the multivariable analysis, identifying factors significantly associated with complications. The result of the multivariable analysis is shown in Table 5.

Table 1.Baseline Characteristics

Variable	No complication (n=1813)	Missing	Any complication (n=323)	Missing	p Value
Age, y, mean (SD)	62.77 (14.01)	6 (0.3)	63.94 (14.09)	2 (0.6)	0.155
Male sex, n (%)	865 (48)	0	151 (47)	0	0.750
BMI, kg/m^2, mean (SD)	29.03 (6.85)	0	29.94 (7.92)	0	0.069
Smoking, n (%)	315 (17)	98 (5.4)	63 (20)	20 (6.2)	0.319
Diabetes mellitus, n (%)	216 (12)	39 (2.2)	46 (14)	7 (2.2)	0.239
Corticosteroid use, n (%)	63 (3.5)	39 (2.2)	12 (3.7)	7 (2.2)	0.828
Radiotherapy, n (%)	33 (1.8)	39 (2.2)	5 (1.5)	7 (2.2)	0.733
Chemotherapy, n (%)	107 (5.9)	39 (2.2)	22 (6.8)	7 (2.2)	0.527
AAA, n (%)	12 (0.7)	15 (0.8)	5 (1.5)	2 (0.6)	0.100
Connective tissue disorder, n (%)	6 (0.3)	15 (0.8)	1 (0.3)	1 (0.3)	0.949
Anticoagulants use or coagulopathy, n (%)	289 (16)	39 (2.2)	65 (20)	7 (2.2)	0.062
Presence of ascites, n (%)	10 (0.6)	19 (1.0)	4 (1.2)	4 (1.2)	0.249
ASA Class, n (%)					0.096
I-II	1249 (69)		208 (64)		
III-IV	554 (31)		114 (35)		
Missing	10 (0.6)		1 (0.3)		
Previous other abdominal wall hernia, n (%)					
Inguinal hernia	196 (11)		28 (8.7)		0.242
Primary ventral hernia	299 (17)		37 (12)		0.021
Incisional hernia	313 (17)		68 (21)		0.105
Other abdominal wall hernia	46 (2.6)		8 (2.5)		0.945
Missing	15 (0.8)		2 (0.6)		
Hiatal hernia, n (%)	52 (2.9)	15 (0.8)	12 (3.7)	2 (0.6)	0.414
Family history of hernia, n (%)	15 (0.8)	15 (0.8)	2 (0.6)	2 (0.6)	0.696

AAA, aneurysm of the abdominal aorta; ASA, American Society of Anesthesiologists

Table 2. Outcomes

Characteristic	Frequency	N missing
Admission duration, d, mean (SD)	4.3 (4.6)	0
Patients with ≥1 complication within 30 days, n (%)	323 (15)	2 (0.09)
Wound complications	166 (7.6)	
Surgical complications	93 (4.2)	
Medical complications	137 (6.3)	
Clavien-Dindo grade [16], n (%)		
<III	176 (54)	
≥III	51 (16)	
Unknown	96 (30)	
30-day mortality, n (%)	2 (0.1)	

SD, standard deviation; ICU, intensive care unit

Table 3. Hernia Characteristics

Characteristic	No complication (n=1813)	Missing	Any complication (n=323)	Missing	p Value
Hernia location, n (%)					0.119
Midline	1037 (57)		209 (65)		
Lateral	194 (11)		27 (8.4)		
Combined	71 (3.9)		9 (2.8)		
Missing	511 (28)		78 (24)		
EHS width classification[8], n (%)					<0.001
W1: <4 cm	899 (50)		94 (29)		
W2: 4-10 cm	700 (39)		146 (45)		
W3: >10 cm	168 (9.3)		70 (22)		
Missing	46 (2.5)		13 (4.0)		
Recurrent hernia, n (%)	366 (20)	31 (1.7)	68 (21)	6 (1.9)	0.712
Number of recurrences, n (%)					0.051
First recurrence	268 (15)		52 (16)		
Second recurrence	63 (3.5)		7 (2.2)		
Third recurrence	31 (1.7)		5 (1.5)		
Fourth or more recurrence	4 (0.2)		4 (1.3)		
Missing	35 (1.9)		10 (3.1)		
Previous mesh, n (%)	610 (34)	25 (1.4)	113 (36)	6 (1.9)	0.597

EHS, European Hernia Society

After correcting for possible confounding variables in the multivariable logistic regression analysis, the following factors remained statistically significant: EHS width class (W2: odds ratio (OR) 1.448 (95% confidence interval (CI) 1.064-1.971), p=0.019; W3: OR 2.090 (95% CI 1.375-3.179), p=0.001), third recurrence (OR 0.369 (95% CI 0.144-0.941), p=0.037), emergency surgery (OR 0.207 (95% CI 0.068-0.631), p=0.006), incarceration (OR 3.187 (95% CI 1.199-8.467), p=0.020), open surgery (OR 2.060 (95% CI 1.408-3.015), p<0.001), duration of surgery (OR 1.006 (95% CI 1.004-1.009), p<0.001), Altemeier wound class (clean contaminated: OR 2.179 (95% CI 1.225-3.877, p=0.008; contaminated: OR 2.855 (95% CI 1.074-7.585, p=0.035; dirty: OR 6.346 (95% CI 1.442-27.938), p=0.015), and therapeutic antibiotic treatment (OR 2.391 (95% CI 1.289-4.438), p=0.006).

Discussion

In this analysis of a large-scale prospective French database of 2,191 patients undergoing incisional hernia surgery, EHS width class, incarceration, open surgery, duration of surgery, Altemeier wound class, and therapeutic antibiotic treatment were independent risk factors for postoperative complications. Emergency surgery and the presence of a third recurrence were found to be factors leading to a lower risk of postoperative complications. The complication rate of 15% found in this study was comparable to the 2009 study by Bisgaard *et al.* reporting complication rates of 10.7%.[11]

Hernia size has been identified as a risk factor for postoperative complications before.[10] Larger hernias mean more extensive dissection, larger meshes, and increased operating time. For ease of use, the EHS classification contains only three classes instead of the absolute size.

The EHS classification has previously been studied as a predictor for wound complications.[17] In this 2015 study by Baucom *et al.*, 538 patients were analyzed and compared, based on EHS location (midline or lateral). They found that postoperative complications were more likely to occur in midline hernias than in lateral hernias. However, the EHS classification was not used in more detail. Our study uses both the location of the hernia as well as the size class. After multivariable analysis, the hernia location was no statistically significant risk factor for postoperative complications. This different finding might be explained by the fact that Baucom *et al.* only performed univariate analyses and no multivariable analysis.

The other statistically significant findings; incarceration, open surgery, duration of surgery, Altemeier wound class, and therapeutic antibiotic treatment all reflect the situation of more complicated surgery. Especially wound contamination is more likely to lead to surgical site infections in these cases. In 2016, Petro *et al.*[18] suggested to include contamination in a hernia risk model. This is in line with the findings of this study.

Duration of surgery was associated with a higher risk of complications. It could be argued that duration of surgery could also be considered as a kind of an outcome measure.

Table 4. Surgical Characteristics

Characteristic	No complication (n=1813)	Missing	Any complication (n=323)	Missing	p Value
Emergency procedure, n (%)	69 (3.8)	7 (0.4)	18 (5.6)	3 (0.9)	0.133
Incarceration, n (%)	53 (3.0)	57 (3.1)	24 (7.7)	1 (3.4)	<0.001
Laparoscopic procedure, n (%)	519 (29)	26 (1.4)	37 (12)	6 (1.9)	<0.001
Primary suture closure, n (%)	183 (10)	55 (3.0)	40 (13)	22 (6.8)	0.137
Mesh location, n (5)					<0.001
Intraperitoneal	1084 (62)		136 (45)		
Sublay	447 (26)		101 (34)		
Onlay	37 (2.1)		20 (6.7)		
Component separation with mesh	4 (0.2)		3 (1.0)		
Missing	55 (3.0)		22 (6.8)		
Duration of surgery, min, median (IQR)	45 (25-75)	23 (1.3)	80 (45-120)	7 (2.2)	<0.001
Altemeier wound classification[15], n (%)					<0.001
Clean	1735 (96)		277 (86)		
Clean contaminated	57 (3.1)		28 (8.7)		
Contaminated	12 (0.7)		11 (3.4)		
Dirty	4 (0.2)		7 (2.2)		
Missing	5 (0.3)		0		
Antibiotic treatment, n (%)					<0.001
None	383 (21)		43 (13)		
Prophylactic	1355 (75)		240 (74)		
Therapeutic	66 (3.6)		37 (12)		
Missing	9 (0.5)		3 (0.9)		

IQR, interquartile range

Emergency surgery was associated with fewer complications in the multivariable analysis. However, this is possibly due to adjusting for confounders related to emergency surgery (incarceration, open surgery, Altemeier wound classification, and antibiotic treatment).

In general, there was a non-significant trend of fewer complications after more recurrent hernias. The only statistically significant difference in the third recurrence is probably associated with the relatively small group size (n=5 with third recurrences in the complications group) and does not reflect a clinically relevant finding.

This study demonstrates that there is a great variance within all patients with an incisional hernia. Although this might not sound surprising, it is of paramount importance to stress that

Table 5. Multivariable Analysis

Variable	OR	95% CI	p Value
Age	1.007	0.996-1.017	0.223
Female sex	1.138	0.870-1.488	0.345
BMI	1.013	0.994-1.033	0.168
Smoking	1.334	0.952-1.870	0.094
Diabetes	0.914	0.618-1.351	0.650
AAA	2.192	0.671-7.165	0.194
Anticoagulants	1.237	0.867-1.763	0.240
ASA III&IV vs I&II	1.090	0.807-1.473	0.573
History of primary ventral hernia	0.763	0.509-1.143	0.190
History of incisional hernia	1.009	0.654-1.554	0.969
EHS location			
Midline	1.000		
Lateral	0.718	0.440-1.170	0.180
Combined	0.514	0.252-1.045	0.066
EHS width class			
W1: <4cm	1.000		
W2: ≥4-10cm	1.448	1.064-1.971	0.019
W3: >10cm	2.090	1.375-3.179	0.001
Number of recurrences			
First recurrence	1.000		
Second recurrence	0.831	0.530-1.303	0.420
Third recurrence	0.369	0.144-0.941	0.037
Fourth or more recurrence	0.455	0.157-1.318	0.146
Emergency procedure	0.207	0.068-0.631	0.006
Incarceration	3.187	1.199-8.467	0.020
Open vs laparoscopic procedure	2.060	1.408-3.015	<0.001
Primary suture closure	0.893	0.581-1.373	0.607
Duration of surgery	1.006	1.004-1.009	<0.001
Altemeier wound classification[15]			
Clean	1.000		
Clean contaminated	2.179	1.225-3.877	0.008
Contaminated	2.855	1.074-7.585	0.035
Dirty	6.346	1.442-27.938	0.015
Antibiotic treatment			
None	1.000		
Prophylactic	1.251	0.865-1.808	0.234
Therapeutic	2.391	1.289-4.438	0.006

OR, odds ratio; AAA, aneurysm of the abdominal aorta; ASA, American Society of Anesthesiologists; EHS, European Hernia Society

hernia research should not investigate all patients with an incisional hernia as a homogeneous group. Given the great differences in outcomes, studies should divide their patients into subgroups, based on the EHS classification, or the EHS classification should be considered when determining inclusion or exclusion criteria for new studies. Using the EHS classification in research might reduce heterogeneity in results of studies on incisional hernia. It might also allow readers to appreciate results better by comparing different study populations based on the EHS classification. Although not evaluated in this study, the EHS classification might be a framework to use for tailored hernia care. An important step in this direction has recently been taken by Dietz *et al.*[19] by adjusting treatment based on a preoperative risk assessment. In this article, risk-adjusted procedure tailoring ensured that high-risk patients did not have a higher rate of postoperative complications. This research direction is an important one to investigate. Hernia surgery, especially when conducted electively, is considered to be relatively low-risk surgery. Fortunately, this is the case for most patients, but the results found in this study show that specific subgroups can have worse outcomes.

Limitations

There are several limitations to this study. First, the results of this study are not based on randomized data. This gives a potential risk of selection. However, the benefit of this kind of registry study is the translation to the real clinical situation: no artificial selection has been made in patient inclusion. Second, this study focuses on postoperative complications. However, this only covers part of the outcomes of hernia repair. A second, long-term analysis should study whether the EHS classification could be used to predict recurrences or reoperations as well. Such a study might require combining different large-scale cohort studies to achieve the statistical power needed.

Conclusion

The width classification of the EHS classification of incisional hernias is an independent risk factor for complications after incisional hernia repair. Therefore, the EHS classification should be used in studies reporting on incisional hernia repair. Surgeons should also use the classification for preoperative risk assessment. To achieve this, emphasis should be put on the simplicity of the classification. A next step will be to analyze different treatment strategies for patients from different EHS classes in an attempt to lower the overall postoperative complication rate effectively.

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European Hernia Society guidelines on prevention and treatment of parastomal hernias

CHAPTER 8

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Abstract

Background: International guidelines on the prevention and treatment of parastomal hernias are lacking. The European Hernia Society therefore implemented a Clinical Practice Guideline development project.

Methods: The guidelines development group consisted of general, hernia and colorectal surgeons, a biostatistician and a biologist, from 14 European countries. These guidelines conformed to the AGREE II standards and the GRADE methodology. The databases of MEDLINE, CINAHL, CENTRAL and the grey literature through OpenGrey were searched. Quality assessment was performed using Scottish Intercollegiate Guidelines Network checklists. The guidelines were presented at the 38th European Hernia Society Congress and each key question was evaluated in a consensus voting of congress participants.

Results: End colostomy is associated with a higher incidence of parastomal hernia, compared to other types of stomata. Clinical examination is necessary for the diagnosis of parastomal hernia, whereas computed tomography scan or ultrasonography may be performed in cases of diagnostic uncertainty. Currently available classifications are not validated, however we suggest the use of the European Hernia Society classification for uniform research reporting. There is insufficient evidence on the policy of watchful waiting, the route and location of stoma construction, and the size of the aperture. The use of a prophylactic synthetic non-absorbable mesh upon construction of an end colostomy is strongly recommended. No such recommendation can be made for other types of stomata at present. It is strongly recommended to avoid performing a suture repair for elective parastomal hernia. So far, there is no sufficient comparative evidence on specific techniques, open or laparoscopic surgery, and specific mesh types. However, a mesh without a hole is suggested in preference to a keyhole mesh when laparoscopic repair is performed.

Conclusion: An evidence-based approach to the diagnosis and management of parastomal hernias reveals the lack of evidence on several topics, which need to be addressed by multicentre trials. Parastomal hernia prevention using a prophylactic mesh for end colostomies reduces parastomal herniation.

Introduction

The European Hernia Society (EHS) has decided to implement a Clinical Practice Guideline development project on the prevention and treatment of parastomal hernias, in view of the lack of relevant summarized evidence and recommendations. The present guideline is based on a systematic and comprehensive literature review and takes into account both expected benefits and potential harms of prevention and treatment strategies. It applies to healthcare professionals (surgeons, general practitioners, stoma care nurses, physiotherapists), patients with a temporary or a permanent stoma, or patients expected to have a stoma, and policymakers. The target users of this guideline are healthcare professionals and policymakers within the European region, although with some limitations, because the feasibility of application in different countries may vary.

Clinical decisions are based not only on research evidence, but also on individual patients' preferences, specific characteristics, the clinician's perspective, available resources, and special circumstances. The present guideline should be viewed as a guide for clinical practice. However, clinical decision making is a much more complex process and cannot rely only on guidelines [1]. It is suggested that users of this guideline also inform their decisions through the aforementioned pathways, as well as from the current literature.

Methods

The coordinator and the supervisor of the project invited individuals from 14 European countries in December 2015 to participate, based on their published experience with the subject. Invited individuals and the steering committee, which consisted of members of the European Hernia Society, composed the guideline development group, which included general, hernia and colorectal surgeons, a biostatistician and a biologist. The group agreed on three introductory and nine key questions, which were determined and refined through e-mail communication. The guideline development protocol was formed by the coordinator and the supervisor in January 2016 (Appendix I). Every effort was made to conform to the AGREE II standards (Appraisal of Guidelines for Research and Evaluation) and the methodology proposed by the GRADE working group [2,3].

In brief, the key words for each question were defined by each subgroup in collaboration with the coordinator. The coordinator and a clinical librarian developed the search strategy (Appendix II) and the results of the first level screening of titles and abstracts were distributed to the subgroups in February 2016. A member of each subgroup cross-checked the first level search for potential omissions and all members scrutinized the search results to identify any missing articles. The search included the databases of MEDLINE (through PubMed), CINAHL (through OpenAthens) and CENTRAL (through Wiley Online Library) with no date or language restrictions. The grey literature was searched through OpenGrey (Exalead).

The second level screening was conducted by at least two members of each subgroup and it included the full texts of articles retrieved at first level screening. Relevant articles entered the quality assessment and grading of evidence process. These articles were assessed for their quality by at least two members of each subgroup, using the Scottish Intercollegiate Guidelines Network (SIGN) checklists [4]. Articles of unacceptable quality were discarded. Study data of acceptable quality articles were tabulated in summary of evidence tables. The quality of the evidence for each question was rated according to the GRADE approach (Fig. 1) [3]. Based on this assessment, each subgroup proposed a statement and recommendation for each question. Recommendations were classified as strong or weak, in line with the GRADE methodology; if there was no evidence on a key question, or if it was of inadequate quality, no recommendation was made (Fig. 2) [3]. In a consensus meeting in Brussels in April 2016, the guidelines development group reviewed, modified, refined and approved the statements and recommendations. A summary of the guideline development process is presented in Fig. 3.

The guideline was presented in a session of the European Hernia Society Congress on June 8, 2016 in Rotterdam and each key question was evaluated in a consensus voting of congress participants. The results of the voting procedure are provided in Appendix III. The guideline manuscript was drafted in August 2016 and it was peer-reviewed by three external reviewers (one from Europe and two from the USA), who assessed its methodological soundness according to the AGREE II instrument.

Results

Introductory Question 1
What is the incidence of parastomal hernias?

Statement: The overall incidence of parastomal hernia is unknown, but is estimated to be over 30% by 12 months, 40% by 2 years and 50% or higher at longer duration of follow up.

The incidence of parastomal hernia varies widely in the literature, as it depends on the duration of follow up, the type of stoma, patient characteristics and the definition of occurrence. Two randomized controlled trials (RCTs) reported on incidences of 32% and 44% at a median follow up of 12 months [5,6]. Another 2 case series and a RCT reported on incidences between 30 and 46% at 29-36 months follow up [7-9]. However, it should be noted, that this evidence comes from studies of patients with colostomy and no robust evidence on the incidence of hernia in other types of stomas exists. An incidence of parastomal hernia (excluding stoma prolapse) of up to 58% has been reported by systematic reviews with a maximum follow up of 7 years [10-13].

Fig. 1 Criteria for assigning grade of evidence

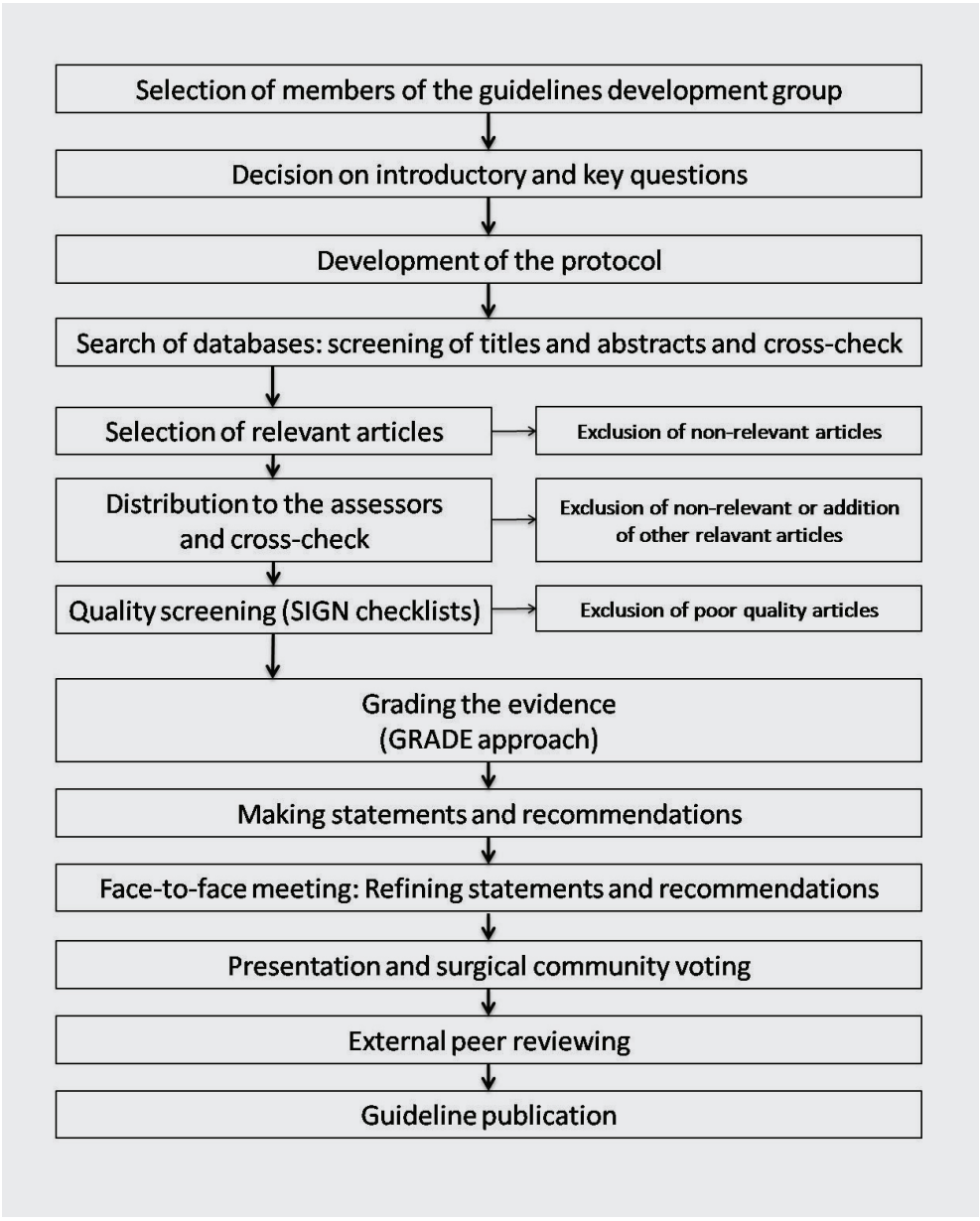
Underlying methodology	Quality rating	Definitions
Randomized trials: or double-upgraded observational studies.	High	Further research is very unlikely to change our confidence in the estimate of effect
Downgraded randomized trials; or upgraded observational studies.	Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Double-downgraded randomized trials; or observational studies.	Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Triple-downgraded randomized trials; or downgraded observational studies; or case series/case reports.	Very low	Any estimate of effect is very uncertain.

Criteria for assigning grade of evidence	
Type of evidence	Randomized trial = high Observational study = low Any other evidence = very low
Decrease* grade if	• Serious or very serious limitation to study quality • Important inconsistency • Some or major uncertainty about directness • Imprecise or sparse data • High probability of reporting bias
Increase grade if	• Strong evidence of association—significant relative risk of > 2 (< 0.5) based on consistent evidence from two or more observational studies, with no plausible confounders (+1) • Very strong evidence of association—significant relative risk of > 5 (< 0.2) based on direct evidence with no major threats to validity (+2) • Evidence of a dose response gradient (+1) • All plausible confounders would have reduced the effect (+1)
	* Each quality criterion can reduce the quality by one or, if very serious, by two levels.

Fig. 2 Criteria for assigning strength of recommendation

Strong recommendation	Based on the available evidence, if clinicians are very certain that benefits do, or do not, outweigh risks and burdens they will make a strong recommendation.
Weak recommendation	Based on the available evidence, if clinicians believe that benefits and risks and burdens are finely balanced, or appreciable uncertainty exists about the magnitude of benefits and risks, they must offer a weak recommendation.
No recommendation	If based on the literature research no evidence could be found, no recommendation can be made.

Fig. 3 of guidelines development summary



Introductory Question 2
Is there a difference in the incidence of parastomal hernia for colostomy, ileostomy or ileal conduit?

Statement: End colostomy is reported to be associated with a higher incidence of parastomal hernia, compared to loop colostomy and loop ileostomy. The incidence of parastomal hernia in the setting of ileal conduit or end ileostomy is unknown.

Direct comparative data between types of stoma do not exist. Matched cohort studies and multivariate analyses would provide information on the relative risk of parastomal hernia between different types of stoma; these would however require large sample sizes. An overview of the literature suggests that end colostomy is associated with the highest incidence of parastomal hernia. Loop ileostomy was associated with a parastomal hernia incidence of 16% at 4 months in a RCT, where diagnosis was established during surgery for continuity restoration [14]. A similar incidence was reported in a case series with a clinical diagnosis of parastomal hernia at a mean follow up of 9 years [15].

Introductory Question 3
Which classifications of parastomal hernias have been published and what is their use in the literature on parastomal hernias?

Statement: There are 5 classifications on parastomal hernias at the moment, including the European Hernia Society classification proposed in 2014. No classification has been subject to validation.
Recommendation: There is insufficient evidence to favour one classification over another. We suggest the use of the European Hernia Society classification for uniform research reporting.
Quality of evidence: ☑☐☐☐
Strength of recommendation: weak

The value of classifications of parastomal hernia lies on assessment of the risk of stoma complications, defining the indication for surgical intervention and uniform research reporting to allow comparability and synthesis of outcomes. Five classifications have been published to date. These are heterogeneous and they are based on clinical examination [16,17], perioperative assessment [18], or clinical imaging [19-21]. The use of these classifications has been very limited and they have not been validated to date.

The classification proposed by the EHS [21] shares some features with the one described

by Szczepkowski [17], and takes into account both the size of the defect and the presence of a concomitant incisional hernia. In view of the lack of validation, the guidelines development group proposes the use of the EHS classification, as it is the result of a multinational collaboration, reflecting the views and expectations of surgeons from several European countries. Furthermore, this classification provides an unambiguous definition of the different types of hernia and specifies the presence of a primary or recurrent parastomal hernia.

Endoscopic ultrasound (EUS) with 3D reconstruction has been recently proposed as a tool for classification of parastomal hernias. EUS was associated with a fair inter-observer and intra-observer reliability and may become a low cost method for assessment of parastomal hernias [22].

Key Question 1
What is the diagnostic accuracy of the clinical diagnosis of parastomal hernias versus a diagnosis by medical imaging?

Statement: The sensitivity of clinical examination against CT scan as reference study for the diagnosis of parastomal hernia ranges between 66% and 100% and the negative predictive value between 75% and 100%. However, CT scan seems to also result in false positive diagnoses. More studies are needed to clarify the clinical relevance of ultrasonography in the diagnosis of PSH.
Recommendation: Clinical examination in supine/erect position and using the Valsava maneuver is necessary for the diagnosis of parastomal hernia, whereas CT scan or ultrasonography may be performed in uncertain cases.
Quality of evidence: ☑☐☐☐
Strength of recommendation: weak

There is currently no gold standard examination for the detection of parastomal hernias. These are evident at clinical examination in a large proportion of patients, with reported sensitivity rates between 66% and 94%, whereas specificity rates are reported to be as high as 100%. Some cases of parastomal hernia are, however, not detected on clinical examination, with reported negative predictive values ranging from 63% to 96% [5,7,19]. Furthermore, clinical diagnosis of parastomal hernia has been considered challenging, as it is characterized by poor inter-observer reliability [23]. These estimations are based upon abdominal computed tomography scan (CT) as a reference study; however, even this examination may fail to detect cases in 7% of patients [24]. CT examination with the patient in the prone position seems to be associated with a strong interobserver reliability, whereas CT examination in the supine position may not be as reliable [25].

The clinical significance of parastomal hernias that are evident on CT but not on clinical

examination is unknown. Although there is no gold standard diagnostic method, CT scan has been the traditional imaging modality to confirm the diagnosis or obtain better characterization of parastomal hernia. The correlation between hernia rates diagnosed with clinical examination and by CT scan is poor [5,7,24]. There is also evidence suggesting that CT scan may also result in false positive diagnoses when surgical diagnosis is considered the reference diagnostic method [24], relevant data are, however, scarce.

Intra-stomal 3-D ultrasonography is a new imaging modality to confirm the diagnosis of parastomal hernia [22,23,25,26]. Dynamic ultrasound examination may be performed without the necessity of the patient lying in the supine position and without the use of radiation. More studies are needed before ultrasonography may be considered a routine imaging technique for the diagnosis of parastomal hernia, according to the currently available evidence. Furthermore, relevant experience may not be available in every institution; therefore, CT scan has, at this point in time, the predominant role in cases of diagnostic uncertainty. Nevertheless, the clinical value of the imaging diagnosis of parastomal hernias and their correlation with patient symptoms has been insufficiently investigated.

Key Question 2
Is there a place for watchful waiting in patients with a parastomal hernia?

Statement: There is no evidence on the comparative outcome of the benefit of watchful waiting versus surgery for patients with a parastomal hernia.
Recommendation: No recommendation can be made on the policy of watchful waiting for patients with a non-incarcerated parastomal hernia.
Quality of evidence: ☑☐☐☐
Strength of recommendation: weak

Watchful waiting for patients with parastomal hernias is a common practice, although relevant evidence is scarce. High recurrence rates following parastomal hernia repair and the lack of symptoms in a considerable proportion of patients make conservative approach an attractive option. Risks associated to watchful waiting, such as the risk of strangulation, the potential enlargement of the hernia and the development of comorbidities, which may increase the difficulty and risks of subsequent surgery, the increased incidence of perioperative complications following emergency surgery, as well as quality of life parameters, need to be taken into account when making clinical decisions. Although the size of the hernia orifice has been identified as an independent risk factor for postoperative complications in incisional hernia, such an association has not been investigated for parastomal hernias [28]. One relevant retro-

spective analysis of 16 patients with parastomal hernia was found in the literature, which was considered to be outdated and of insufficient quality [29]. In the absence of adequate evidence, no recommendation on the policy of watchful waiting could be made. Support garments may improve symptoms and could be of benefit with regard to the risk of hernia enlargement and strangulation. However, there is little evidence to support this hypothesis. Undoubtedly, strangulation of a parastomal hernia during a course of watchful waiting requires emergency surgery.

Key Question 3
Are there techniques for stoma creation without prophylactic mesh use that result in fewer parastomal hernias?

a. extraperitoneal versus transperitoneal stoma construction

Statement: There is insufficient evidence on the comparative risk of parastomal hernia development after construction of a stoma via the extraperitoneal or the transperitoneal route.
Recommendation: No recommendation can be made in preference of stoma construction through the extraperitoneal over the transperitoneal route.
Quality of evidence: ☑☐☐☐
Strength of recommendation: no

b. stoma construction at a lateral pararectus location versus a transrectus location

Statement: There is insufficient evidence on the comparative risk of parastomal hernia development after construction of the stoma at a lateral pararectus location or a transrectus location.
Recommendation: No recommendation can be made in preference of stoma construction at a lateral pararectus location over a transrectus location.
Quality of evidence: ☑☐☐☐
Strength of recommendation: no

c. size of the fascial aperture

Statement: There is insufficient evidence on the comparative risk of parastomal hernia development after construction of the stoma at a lateral pararectus location or a transrectus location.
Recommendation: No recommendation can be made in preference of stoma construction at a lateral pararectus location over a transrectus location.
Quality of evidence: ☑☐☐☐
Strength of recommendation: no

Specific operative techniques for stoma construction may result in decreased risk of parastomal hernia. Placing of the stoma through the extraperitoneal route has been hypothesized to reduce the risk of herniation [30]. A meta-analysis has synthesized the results of seven retrospective studies. The pooled estimate of treatment effect was in favor of the extraperitoneal route (odds ratio 0.41; 95% confidence interval, 0.23-0.73, p = 0.002). Again, the non-randomized design of the included studies limits our confidence on the reported results. The extraperitoneal route of stoma placement warrants further investigation.

Location of the stoma at a lateral pararectus versus a transrectus location has been also suggested to reduce the risk of parastomal hernia. Proponents of the first technique argue that the integrity of the rectus muscle and sheaths is preserved with minimization of the anterior abdominal wall disruptions and a consequent reduction of the risk of hernias at a lateral position of the stoma. A Cochrane systematic review encompassing nine retrospective studies of 761 patients has tested the hypothesis of a different risk for parastomal herniation following stoma construction at a transrectus or a pararectus location [31]. Although the risk of herniation and stoma prolapse was not statistically different, the low quality of the included studies challenges the internal validity of the pooled outcome. Recently, a pilot RCT failed to demonstrate significant treatment effects of either technique, it was however underpowered [14].

There is some evidence suggesting that the size of the aperture is associated with the risk of parastomal herniation. Logistic regression analyses of retrospective data from 108 patients, identified trephine size as an independent risk factor for parastomal herniation, although the selected cut-off value was not reported [32]. There was unanimous consensus among the guidelines development group that the size of the aperture should be as small as possible, but without challenging perfusion of the stoma.

Key Question 4
Does the use of a prophylactic mesh during stoma construction reduce the incidence of parastomal hernias?

Statements: High quality evidence supports the use of a prophylactic mesh during construction of a permanent end colostomy in elective surgery in reducing the incidence of parastomal hernia development.
Recommendation: It is recommended to use a prophylactic synthetic non-absorbable mesh when constructing an elective permanent end colostomy to reduce the parastomal hernia rate.
Quality of evidence: ☑☑☑☑
Strength of recommendation: strong

Recommendation: No recommendation to use a prophylactic mesh can be made for ileostomies or ileal conduit stomata, nor for the use of synthetic absorbable or biological meshes.
Quality of evidence: ☑☑☐☐
Strength of recommendation: no

High parastomal hernia rates prompted surgeons to use meshes upon stoma construction as a prophylactic measure. The same three randomized clinical trials published before 2012 [6,7,33] were analyzed in four meta-analyses [10,12,13,34]. Since then, another six RCTs have been published [5,24,35-39]. Most of the studies used the open surgical approach with a retromuscular mesh with a hole in the center of the prosthesis [6,7,24,33,37,38]. Three studies use a laparoscopic approach either by placing a keyhole mesh [5,35] or using a modified Sugarbaker technique [36]. In most studies a synthetic non-absorbable mesh [5-7,24,35,36,38] and in two studies a biological mesh [33,37] was used.

The magnitude of comparative treatment effects, the consistency of outcomes, the low comparative risk of adverse events and the low cost of synthetic meshes prompted the guidelines development group to unanimously support a strong recommendation.

It may be expected that a decrease in the risk of parastomal herniation will improve quality of life and reduce human and material resources associated to stoma care and surgery for hernia repair, thereby outweighing the required additional resources. Two cost-effectiveness studies were published suggesting that mesh prophylaxis may be a cost-effective strategy [40,41], although future research is expected to further address these issues. The use of funnel-shaped meshes in the context of parastomal hernia prevention is a further subject of research [42,43].

Most trials have applied open retromuscular position of a synthetic non-absorbable mesh in patients operated on for rectal cancer and subjected to end colostomy. No recommendation could be made with regard to the use of biological or synthetic absorbable meshes and on the application of prophylactic mesh for the construction of loop colostomies, ileostomies, or ileal conduits. Future trials are expected to address the clinical effectiveness of absorbable meshes and of mesh application in stomas other than end colostomy.

Key Question 5
Is a suture repair for elective parastomal hernia repair an option?

Statements: There is no high quality evidence on the comparative risk of recurrence followinga parastomal hernia repair with mesh, stoma relocation or suture repair. There is, however, evidence suggestive of a high risk of recurrence following suture repair.

There is insufficient evidence on the comparative risk of morbidity following mesh repair, stoma relocation or suture parastomal hernia repair. There is, however, evidence suggestive of a low rate of infectious complications for parastomal hernia repair with a synthetic mesh.
Recommendation: It is recommended not to perform a suture repair for elective parastomal hernia surgery because of a high risk of recurrence.
Quality of evidence: ☑☑☐☐
Strength of recommendation: strong

There are no high quality studies comparing different techniques of elective open parastomal hernia repair. In a retrospective observational study of 50 patients with recurrent parastomal hernia, in which stoma relocation was compared with suture repair, the authors have found similar complication rates between the two groups after a mean follow-up of 2 years 44. Same side relocation was associated with recurrence in 4 out of 5 patients, whereas contralateral side relocation was associated with recurrence in 7 out of 18 patients. Comparison of direct suture repair versus contralateral side relocation demonstrated a lower recurrence rate for the latter approach ($p = 0.021$). The validity of this study is limited by the source patient population, which had recurrent parastomal hernias, the larger proportion of patients with an ileostomy in the suture repair group, and the low power to detect potential pragmatic differences.

In a retrospective study comparing relocation versus suture repair with and without the use of mesh and including both primary and recurrent parastomal hernias, the authors have found significantly less recurrences in the stoma relocation group (11 of 25 versus 29 of 36, $p < 0.01$) [45]. However, no summative data on complications and effect sizes were provided. Hansson and colleagues performed a systematic review of case series, in which they reported on various techniques for parastomal hernia repair [46]. Applying logistic regression analyses, the authors have identified cohorts of studies on suture repair to be at higher risk for recurrence, compared with mesh repair ($p < 0.0001$). Furthermore, wound infection was higher in suture repair than in the other techniques (odds ratio 4.0, 95% confidence interval 1.7-9.5). Due to the considerable heterogeneity among and within studies with regard to operative techniques, mesh materials and patient characteristics, our confidence on these outcomes is limited. Available evidence, however, is suggestive of a high risk of recurrence following suture repair. The guidelines development group agreed that alternate techniques to suture repair of parastomal hernias should be strongly considered, although evidence to recommend a particular technique is inadequate. However, it recognizes that suture repair may pose less risks compared to mesh repair on specific patient groups, such as those subjected to surgery for strangulated parastomal hernia or in contaminated cases, although no relevant data exist to date. Without doubt, however, suture repair remains the technically simplest method of surgical management of parastomal hernia.

Key Question 6
Is a laparoscopic approach equivalent to an open approach for parastomal hernia mesh repair in elective surgery?

Statements: There is insufficient evidence on the risk of recurrence following laparoscopic versus open parastomal hernia repair with a mesh.
There is insufficient evidence on the morbidity following laparoscopic versus open parastomal hernia repair with a mesh.
Recommendation: No recommendation can be made in favor of laparoscopic or open parastomal hernia repair with a mesh in elective surgery.
Quality of evidence:☑☐☐☐
Strength of recommendation: no

Laparoscopic repair of parastomal hernia has emerged as an alternative to open repair. The keyhole technique involves placement of a mesh with a central hole or a slit around the bowel loop forming the stoma. In the laparoscopic modified Sugarbaker technique, the mesh covers the bowel loop, which lies in a side-to-side fashion onto the abdominal wall. The sandwich technique is a combination of the former two.

There are no high quality studies comparing laparoscopic versus open parastomal hernia surgery. In a data analysis of more than 2000 patients from the American College of Surgeons – National Quality Improvement Program database, the authors have compared laparoscopic with open parastomal hernia repair after adjusting for age, gender, American Society of Anesthesiologists score, emergency designation of the operation, hernia type, and wound class [47]. They found that patients subjected to laparoscopy had approximately 60% lower odds of morbidity (odds ratio 0.42, 95% confidence interval 0.27-0.64) and operative time reduced by 13 minutes (mean difference -13.24, 95% confidence interval -24 to -3). The retrospective design and limitations associated to the database query do not allow for sufficient assessment of the comparative outcomes of laparoscopic versus open parastomal hernia repair. Pastor and colleagues retrospectively analyzed their data of a cohort of 25 patients and they did not find any difference in outcomes of interest in this underpowered study [48]. In the systematic review of case series by Hansson and colleagues, various techniques of parastomal hernia repair were reported [46]. The cumulative laparoscopic and open study populations consisted of more than 300 patients each. Applying logistic regression analyses, the authors have found laparoscopic parastomal hernia repair to be associated with lower odds of recurrence when compared to open suture repair, but to be equally effective to open intraperitoneal and open retromuscular repair. Furthermore, the odds of mesh infection and morbidity did not differ significantly between laparoscopic and open parastomal hernia repair. The evidence deriving from these data is limited, due to the considerable heterogeneity among and within studies. The heterogeneity of procedures and patient cohorts did not allow for drawing definite conclusions. Clinical decision making should depend on local

resources, patient preferences, surgical experience, and on specific patient conditions, such as co-morbidities, previous surgeries, intraperitoneal adhesions and the size of the hernia.

Key Question 7
Is there an optimal open parastomal hernia mesh repair technique?

Statements: There is insufficient evidence on the optimal technique for open parastomal hernia repair with regard to morbidity or recurrence.
Recommendation: No recommendation can be made in favour of any open parastomal hernia repair with mesh.
Quality of evidence:☑☐☐☐
Strength of recommendation: no

Parastomal hernia repairs using a mesh include the onlay (fixation onto the fascia of anterior rectus sheath and the aponeurosis of the external oblique muscle), the retromuscular (dorsally to the rectus muscle and anteriorly to the posterior rectus sheath) and the intraperitoneal (intra-abdominal fixation onto the peritoneum) techniques. There is a paucity of comparative evidence, although several case series and two systematic reviews have been published [46,49].

In the systematic review and synthesis of outcomes of open mesh repair by Hansson and colleagues, the onlay, retromuscular, Sugarbaker and keyhole techniques were associated with recurrence rates of 17.2% (95% confidence interval, 11.9% to 23.4%), 6.9% (95% confidence interval, 1.1%-17.2%), 11.6% (95% confidence interval, 6.4% to 18.0%) and 34.6% (95% confidence interval, 13.1% to 60.3%), respectively, with mesh infection rates not exceeding 2.6% [46]. Direct comparison of these pooled outcomes is not justified, due to the heterogeneity of patient characteristics, surgical techniques and mesh materials.

Key Question 8
Is there an optimal laparoscopic parastomal hernia mesh repair technique?

Statements: There is evidence favouring the use of a mesh without a hole in preference to a keyhole mesh for laparoscopic parastomal hernia repair in terms of recurrence.
There is insufficient evidence on the safest laparoscopic technique for parastomal hernia repair with regard to morbidity.
Recommendation: For laparoscopic parastomal hernia repair, a mesh without a hole is suggested in preference to a keyhole mesh.
Quality of evidence:☑☐☐☐
Strength of recommendation: weak

Techniques of laparoscopic parastomal hernia repair have not been comparatively evaluated to date. Relevant evidence derives from case series and small retrospective cohort studies, which have been synthesized by two systematic reviews. The meta-synthesis with logistic regression analyses by Hansson and colleagues suggests that the laparoscopic Sugarbaker technique is associated with a lower recurrence rate (pooled recurrence rate 11.6%, 95% confidence interval 6.4%-18.0%), compared to laparoscopic hernia repair using a keyhole mesh (pooled recurrence rate 34.6%, 95% confidence interval 13.1% to 60.3%; odds ratio for the comparison 2.3, 95% confidence interval 1.2-4.6) [46]. In another recent meta-analysis of case series, the pooled recurrence rates of the laparoscopic Sugarbaker technique and of the laparoscopic keyhole mesh repair were 10% (95% confidence interval 4% to 19%) and 28% (95% confidence interval 12% to 47%), respectively [50]. Perhaps the largest case series on the laparoscopic Sugarbaker technique reported a recurrence in four out of 61 patients at a mean follow up of 26 months [51]. Although available data suggest that the laparoscopic Sugarbaker technique may be associated with lower recurrence rates compared to the laparoscopic keyhole mesh repair, our confidence on these outcomes is limited, due to the retrospective study designs, heterogeneity in patient characteristics, definition of recurrence and types of stoma, both within and across studies. The sandwich technique, which may be considered a combination of the Sugarbaker and the keyhole technique, was associated with one recurrence in 47 parastomal hernia repairs in a prospective cohort study, at a median follow up of 20 months [52]. The hybrid parastomal endoscopic re-do (HyPER) technique combines open and laparoscopic repair using a funnel-shaped mesh. No recurrence was observed at 6-month follow up in a prospective study of 12 patients [53]. The latter two techniques have not been well established in the literature; comparative studies are awaited to assess their relative effectiveness. It should be noted, that most laparoscopic techniques require a level of expertise and may have a significant learning curve.

Key Question 9
Which meshes are the most effective?

Statements: There is insufficient evidence on the most effective mesh for parastomal hernia repair with regard to recurrence or morbidity.
There is no evidence supporting superiority of biological over synthetic meshes with regard to recurrence or morbidity.
Recommendation: No recommendation can be made on the use of specific mesh material for parastomal hernia repair.
Quality of evidence:☑☐☐☐
Strength of recommendation: No

There is a lack of comparative evidence on different meshes for parastomal hernia repair. Available data come from retrospective case series of patients subjected to parastomal hernia repair with polypropylene, expanded polytetrafluoroethylene (ePTFE), polyvinylidene fluoride (PVDF), polyester, or biological meshes. Evidence provided by retrospective case series suggests that biological meshes are associated with high recurrence rates (ranging between 16% and 90%) and may demonstrate some benefit in terms of mesh infection [54,55]. Current data are, however, of low quality and the guidelines development group could not make a relevant recommendation. Nevertheless, synthetic uncoated meshes are generally not considered for intraperitoneal use, due to the risk of adhesions, bowel erosion and stricture. A recent retrospective cohort study has demonstrated a significantly higher incidence of intestinal obstruction secondary to adhesions when using PVDF versus a composite coated polyester mesh (11.5% versus 0%, $p = 0.006$) [56].

Comments

This is the first international guideline focusing on parastomal hernias. The major limitation in making recommendations was related to the scarcity of evidence. This is associated with the fact that patients subjected to permanent stoma construction are few in an average tertiary care center and around 30-50% of those patients will present with parastomal hernia in the long term. It is imperative that future trials be based on power size calculations, in order to provide more precise treatment effect estimates. Multi-institutional design and adequate outcome reporting are essential for future studies to achieve this goal. This approach will allow performing subgroup analyses, which may reveal distinct effects in different patient populations (for example, terminal ileostomy in young patients with Crohn's disease versus terminal colostomy in older patients with colorectal malignancy). The available evidence was insufficient to allow for making distinct recommendations for specific patient subgroups. Clinical decision making should take into account patient characteristics and specific preferences, along with the present recommendations.

Another shortcoming was the retrospective study design of the majority of relevant studies. This is of specific importance for outcome assessment in patients with parastomal hernia, because attrition bias (due to loss at follow up) and detection bias (due to CT and magnetic resonance imaging examinations performed for indications other than diagnosing a parastomal hernia, such as postoperative cancer surveillance) limit our confidence on the true epidemiological and clinical outcome data.

As suggested by the GRADE methodology, this guideline was conservative in making recommendations based on experts' opinion in the absence of relevant research evidence. Our literature review and study assessment suggests that there is ample room for future research on several topics, including the use of classifications for parastomal hernias, the policy of

watchful waiting, specific techniques for stoma construction, the use of mesh for construction of end ileostomy, the use of mesh for parastomal hernia repair, and the application of laparoscopic surgery. There was no substantial evidence to support recommendations for these subjects. The results of the consensus conference presented in the appendix suggests that, although the scientific community agrees with the statement that relevant evidence is scarce, there is need for recommendations on numerous key subjects. Until new research output is available, clinical decision making on these subjects must rely on surgeons' discretion and knowledge, patient preference, and local resources. Management and treatment strategy options need to be adequately discussed with patients to assist them with making informed decisions and understanding as much as possible about the procedures they are agreeing to. An important feature of this guideline is the high level of consensus between the guidelines development group and the scientific community. The latter was represented by attendees of the 38th International Congress of the EHS, which are primarily hernia surgeons or general surgeons with a specific interest in hernia surgery. The views and preferences of a wide spectrum of European countries have been reflected in the consensus conference, resulting in wide agreement. This manuscript was assessed by three external reviewers using the AGREE II instrument. The outcome of this assessment is presented in Appendix IV.

Nevertheless, it should be noted that limitations might be imposed for several recommendations of these guidelines by local resources and healthcare policies. This is of specific importance in the context of social and economic circumstances, which vary across countries. It is recommended for national healthcare authorities to evaluate the capacity of healthcare resources to implement a policy of routine prophylactic mesh in end colostomies.

There are two parameters of these guidelines, which might have at least short-term direct financial implications. First is the policy of performing CT scan in uncertain cases of parastomal hernias. Particularly, the differential diagnosis between parastomal hernia and stoma prolapse may require CT imaging. Relevant financial implications are not expected to be significant, because the diagnosis of parastomal hernia is unclear in a minority of patients. Nevertheless, if the cost of such an approach is anticipated to be significant, ultrasonography examination is proposed. Second, the recommendation to routinely use a prophylactic mesh in the construction of end colostomy is also not expected to carry a significant financial burden, provided that conventional synthetic non-absorbable meshes are used exclusively for these very indications.

The impact of these guidelines on clinical practice is planned to be assessed through a web-based survey to be completed by members of the EHS, two years after publication of this manuscript. Partial or complete adherence to these guidelines by at least 70% of the participants will be considered suggestive of adequate implementation. Participants will be invited to submit comments and suggestions for the planned update of these guidelines. The results of this survey will be made publicly available. A two-year interval for repeated assessment is considered adequate to monitor the level of implementation.

An update of the guidelines is intended to take place in 2021, to be presented in the World Conference on Abdominal Wall Hernia Surgery. The rationale behind this intention is that the guidelines development group is not aware of planned or ongoing trials that would address major key points in the field of parastomal hernia surgery. The UK NIHR CIPHER Study will prospectively evaluate the surgical and patient risk factors for 4000 patients having stoma formation with a median follow up of three years. Patient recruitment for is planned to open in April 2017. This study will provide longitudinal epidemiological evidence on the incidence and prevalence of different types of stomas, examine the validity of the EHS classification, determine symptomatic questionnaires that will guide when to assess and treat parastomal hernias, quality of life follow up and health economic analyses among other. The methodology for the update of these guidelines is planned to be similar to the present guidelines, with the search strategy including articles published from February 2016 upwards. Further key topics, such as the assessment of risk factors of parastomal hernia and associated complications, the effects and risks of supportive girdles, and the role of abdominal exercise in the prevention of parastomal hernia will be addressed in this update.

Conclusion

The present guidelines provide an evidence-based approach to the diagnosis and management of parastomal hernias. There is a lack of evidence on several topics that are expected to be addressed by future trials. These will ideally be based on multicenter collaborations. The main feature of these guidelines is the recommendation to use a prophylactic mesh for end colostomies. Although there is robust evidence to support this policy, the clinical outcomes should be audited and reporting of adverse events is strongly suggested.

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Non-operative treatment as a strategy for patients with parastomal hernia: a multicentre, retrospective cohort study

CHAPTER 9

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Abstract

Aim: Parastomal hernia is the most common complication following stoma construction. Surgical treatment is usually chosen over non-operative treatment, but a clear rationale for the choice of management is often lacking. This study aims to investigate the reasons for non-operative treatment, cross-over rates, and postoperative complications.

Method: A multicentre, retrospective cohort study was conducted. Patients diagnosed with a parastomal hernia between January 2007 and December 2012 were included. Data on baseline characteristics, primary surgery and hernias were collected. For non-operative treatment, reasons for this treatment and cross-over rates were evaluated. For all patients undergoing surgery (surgical treatment and cross-overs), complication and recurrence rates were analysed.

Results: Of the 80 patients included, 42 (53%) were in the surgical treatment group and 38 (48%) in the non-operative treatment group. Median follow-up was 46 months (interquartile range, [24-72]). The reasons for non-operative treatment were absence of symptoms in 12 patients (32%), comorbidities in nine (24%), and patient preference in three (7.9%). In 14 patients (37%) reasons were not documented. Eight patients (21%) crossed over from non-operative treatment to surgical treatment, of which one needed emergency surgery. In 23 patients (55%), parastomal hernia recurred after original surgical treatment, of whom 21 (91%) underwent additional repair.

Conclusion: Parastomal hernia repair is associated with high recurrence and additional repair rates. Non-operative treatment has a relatively low cross-over and emergency surgery rate. Given these data, non-operative treatment might be a better choice for patients without complaints or with comorbidities.

Introduction

Parastomal hernia is the most common complication following stoma construction, especially after end colostomy.[1, 2] Incidence numbers depend on the type of stoma, with ileostomy resulting in 0-6.0% herniation and colostomy in 3.0-39% herniation.[2-4] Over 120,000 colostomies are created each year in the USA alone,[5] potentially resulting in 3,600-46,800 parastomal hernias.

Preventative strategies such as prophylactic mesh placement or extraperitoneal colostomy have lowered these numbers, but they remain high.[6-8]

Parastomal hernia commonly occurs within the first year after stoma formation, but the incidence increases over time.[1] Parastomal hernias can be asymptomatic. However, when parastomal hernias become symptomatic, complaints can be discomfort, pain, bowel obstruction, problems with stoma appliance handling, leakage, and incarceration.[3] The majority of patients with parastomal hernia are managed primarily by hospital stoma care nurses (SCN), who therefore play an important role in the provision of care for patients with parastomal hernia.[9] However, surgery remains the most common treatment of parastomal hernias. Surgical treatment can be performed open and laparoscopically and with or without mesh augmentation, but there is no consensus. Recent research has focused mainly on surgical repair with mesh augmentation.[10] However, mesh repair still results in recurrence rates of 6.9-17%.[11]

Apart from surgery, non-operative treatment potentially is an appropriate alternative. The obvious benefit of this strategy is the absence of the risk of complications and recurrence following surgical repair. On the other hand, the potential risk is emergency surgery for incarceration or strangulation, which is associated with higher complication rates than elective surgery.[12, 13]

For inguinal hernia treatment, the non-operative treatment strategy is generally accepted after being proven to be safe and cost effective.[14-16] More recently, Verhelst *et al*. found that non-operative treatment in patients with incisional hernia leads to a one-third cross-over rate with high rates of postoperative complications.[17] However, whether this strategy could be useful for parastomal hernia has not yet been properly investigated. Only one study from 1984 describes the possibility of non-operative treatment.[18]

This study by Cevese *et al*.[18] was characterized by a number of methodological flaws: only 27% of all patients having a colostomy were examined, a variety of different surgical approaches for creating the colostomy were included, and there was no definition of outcome. For these reasons, no robust conclusions could be drawn.

Therefore, the aim of this retrospective study was to identify the rationale for choosing non-operative treatment or surgical treatment for parastomal hernia and to compare outcomes of both strategies in terms of complications, hernia recurrences and cross-over rates.

Method

A multicentre, retrospective study was performed. The study was approved by the Institutional Review Boards of all participating hospitals. Informed consent was waived for participation in this study, because it was a retrospective review of the records. STROBE (Strengthening the Reporting of Observational studies in Epidemiology) recommendations for the reporting of observational studies were used for this study.[19]

All patients diagnosed with a parastomal hernia between January 2007 and December 2012 were included from the databases of the Erasmus University Medical Center Rotterdam, Academic Medical Center Amsterdam, Havenziekenhuis Rotterdam, and IJsselland Hospital Capelle aan den IJssel. Colostomies (end and loop), ileostomies (end and loop), and ileal conduits were included. The diagnosis of parastomal hernia could be made by the stoma care nurse or the surgeon and could be made clinically or radiologically. In all participating hospitals, experienced hernia surgeons were involved and both surgical treatment and non-operative treatment were treatment strategies used for parastomal hernia. Since no international guidelines exist on this topic, the decision to choose either treatment was made in agreement between surgeons and patients. Patients were divided into two groups based on initial treatment strategy chosen directly after diagnosis: surgical treatment (ST) and non-operative treatment (NT). Only patients who were diagnosed with parastomal hernia in an elective setting were included. Patients with first presentation of parastomal hernia in an emergency situation were excluded, since non-operative treatment is seldom a therapeutic option in these patients. Patient records and the electronic hospital database systems were reviewed. Patients were identified searching for DBC codes ('Diagnose Behandel Combinatie'; Diagnosis Related Groups (DRG's)) and ICD-9 codes (International Statistical Classification of Diseases and Related Health Problems). To minimize the risk of missing eligible patients, all codes for any abdominal wall hernia were searched for in the medical records of patients with a stoma.

Data collection

General patient characteristics, co-morbidities, medical history, American Society of Anesthesiologists (ASA) grade, and information regarding primary surgery were recorded. Symptoms at first presentation were categorized into groups: pain, appliance leakages, aesthetic complaints, and bowel obstruction. Parastomal hernia size (defect of the abdominal wall fascia, as measured with ultrasound or axial CT imaging) and the presence of a concomitant incisional hernia were noted in order to classify the parastomal hernias according to the European Hernia Society (EHS) classification (Class I; size <5cm without a concomitant incisional hernia, class II; size <5cm with a concomitant incisional hernia, class III; size >5cm without a concomitant incisional hernia, and class IV; size >5cm with a concomitant incisional hernia).[20]

For patients in the ST group and cross-over patients from the NT group, reasons for ST and type of repair were noted and postoperative complications (infection, postoperative ileus, perforation, obstruction) were scored. In general, patients visited stoma nurses or surgeons on a regular basis. Data on recurrence and, if needed, additional surgical repair were collected. For patients in NT group, the reason of NT (absence of symptoms, comorbidity, obesity, patient preference) was noted.

Statistical analysis

Statistical analyses were performed with the SPSS Software Package (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY). To test normal distribution of continuous variables, Levene's test for equality of variances was used. Continuous variables are presented as medians with interquartile ranges (IQRs) or as means with standard deviations (SDs), depending on the normality of data distribution. Categorical variables are presented as numbers with percentages (%). Differences between groups were compared using Mann-Whitney U test (continuous data) or Chi-squared test (categorical data). In case of small groups (n<5), Fisher's exact test was used. P-values <0.05 were considered statistically significant.

Results

A total of 80 patients were included from the hospital databases. Of these 80 patients, 42 patients (53%) were scheduled for surgical treatment (ST). Non-operative treatment (NT) was chosen in 38 patients (48%). Reasons for non-operative treatment were absence of symptoms in 12 patients (32%), comorbidities in nine (24%), and patient preference in three (7.9%). In 14 patients (37%) reasons were not documented. Eight patients (21%) of the 38 NT patients crossed over to ST. Of these eight patients, one patient had to undergo emergency surgery (2.63% of the total NT group). Median follow-up duration of all patients was 46 months (interquartile range [IQR] was [24-72]) and did not differ between the ST and NT group (respectively, 43.5 months [20.3-72.0] and 47.1 [28.5—96.2], p = 0.823).

Patient characteristics

Baseline characteristics of both groups are given in Table 1. The mean age in the ST group was 51±15 years and 63±12 in the NT group (p<0.001). There were less patients with COPD in the ST group than in the NT group (n=0 (0%) versus n=4 (11%), p=0.047). Ten patients (24%) in the ST group had their original operation for malignancy compared with 23 patients (62%) in the NT group (p<0.001). Consequently, more patients in the ST were operated for other reasons (n=16 (39%) versus n=5 (14%), p=0.020). All other characteristics (baseline characteristics, stoma types, and complications after primary surgery) were not statistically significantly different between the ST and NT groups.

Parastomal hernia characteristics

Parastomal hernia characteristics are listed in Table 2. The mean hernia size was 3.59±1.96 cm in the ST group and 3.43±1.37 cm in the NT group (p=0.762). Size details were not available for 18 patients (43%) of the ST group and 18 patients (47%) of the NT group because of the absence of ultrasound or CT images. There were less asymptomatic patients in the ST group compared with the NT group (n=1 (2.7%) versus n=9 (27%), p=0.005), but more patients with pain as their presenting symptom (n=24 (65%) versus n=6 (18%), p<0.001). Other symptoms were not significantly different. Presenting symptoms are presented in Table 2 and Figure 1. There was no difference between groups in the time between initial surgery and parastomal hernia diagnosis, or in EHS Classification.[20]

Type of hernia repair and complications after hernia repair

Table 3 shows the different types of procedures performed for hernia repair. The majority of patients (72%) underwent open mesh repair. For two patients (25%) in the NT cross-over group, no specified records were available on the type of procedure. This was the only significant difference between the two groups.

An overview of the surgical complications is listed in Table 4. There were no statistically significant differences between the two groups; complication rates were 45% for ST and 50% for NT cross-overs (p=1.000).

Figure 1: Parastomal hernia symptoms
The outer circle represents the non-operative treatment (NT) group, the inner circle represents the surgical treatment (ST) group.

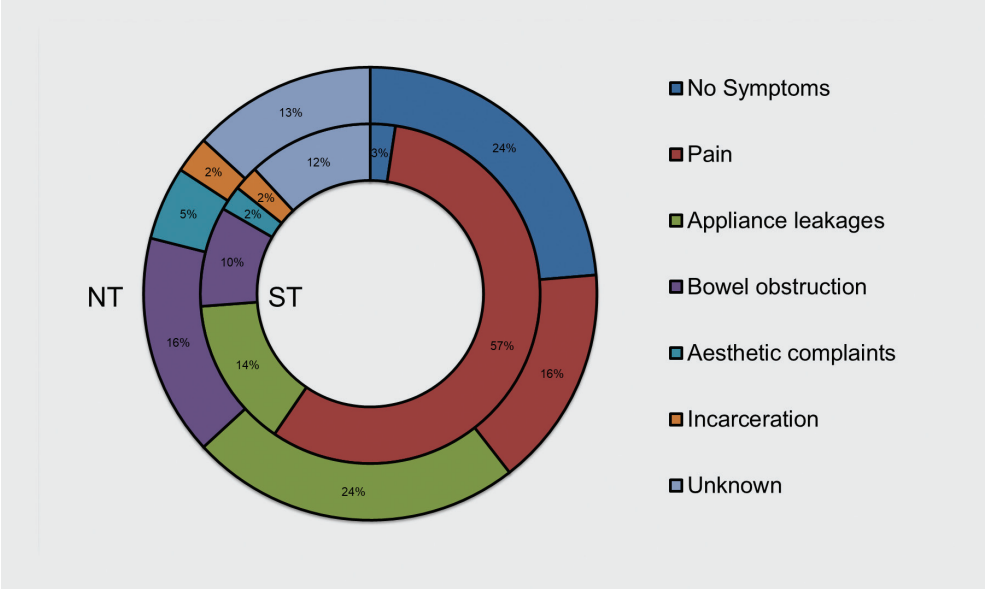

Table 1: Baseline patient characteristics

Characteristic	Surgical treatment (n=42)	Non-operative treatment (n=38)	P-value
Age (SD)	51 (15)	63 (12)	<0.001
Male (%)	17 (41)	22 (58)	0.179
BMI (SD)	27.65 (4.82)	26.02 (3.62)	0.101
Smoking (%)	10 (24)	7 (20)	0.786
COPD (%)	0 (0)	4 (11)	0.047
Corticosteroid use (%)	4 (9.5)	3 (7.9)	1.000
ASA Class (%)			0.169
I-II	37 (90)	20 (77)	
III-IV	4 (9.8)	6 (23)	
Indication of initial surgery (%)			
Malignancy	10 (24)	23 (62)	0.001
IBD	15 (37)	9 (24)	0.327
Other	16 (39)	5 (14)	0.020
Emergency surgery	11 (26)	10 (26)	1.000
ICU admission	6 (17)	7 (22)	0.760
Type of ostomy (%)			
End colostomy	23 (55)	26 (68)	0.254
Loop colostomy	2 (4.8)	0 (0)	0.495
End ileostomy	11 (26)	9 (24)	1.000
Loop ileostomy	2 (4.8)	1 (2.6)	1.000
Ileal conduit	4 (9.5)	2 (5.3)	0.678
Complications* (%)			
Surgical site infection	1 (2.9)	4 (12)	0.191
Abscess	2 (5.7)	5 (15)	0.259
Fistula	1 (2.9)	1 (3.0)	1.00
Ileus	4 (11)	2 (6.1)	0.675
Pneumonia	2 (5.6)	3 (9.1)	0.665
Other complications	7 (17)	4 (11)	
Follow-up time in months (IQR)	43.5 (20.3-72.0)	47.1 (28.5-96.2)	0.823

*Complications after initial surgery

SD, standard deviation; BMI, Body mass index; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; IBD, inflammatory bowel disease; ICU, intensive care unit; IQR, interquartile range

Parastomal hernia recurrence occurred in 48% of all operated patients: 23 (55%) in ST patients and in one (13%) NT cross-over patient (p=0.05). Recurrences lead to additional repair in 21 (50%) ST patients, but in none of the NT patients (p=0.015).

Emergency surgery was needed for incarceration of the parastomal hernia in three patients (7.1%) in the ST group and one patient (13%) in the NT group.

Table 2: Hernia characteristics

Characteristic	Surgical treatment (n=42)	Non-operative treatment (n=38)	P-value
Size in cm (SD)	3.59 (1.96)	3.43 (1.37)	0.762
EHS Classification (%)			
I	17 (71)	12 (60)	0.532
II	4 (17)	6 (30)	0.472
III	1 (4.2)	2 (10)	0.583
IV	2 (8.3)	0 (0)	0.493
Time to diagnosis in months (IQR)	16.69 (5.67-38.05)	15.49 (4.90-31.63)	0.907
Presenting symptoms (%)			
No symptoms	1 (2.7)	9 (27)	0.005
Pain	24 (65)	6 (18)	<0.001
Appliance leakages	6 (16)	9 (27)	0.382
Bowel obstruction	4 (11)	6 (18)	0.499
Aesthetic complaints	1 (2.7)	2 (6.1)	0.599
Incarceration	1 (1.4)	1 (1.4)	1.000

SD, standard deviation; EHS, European Hernia Society; IQR, interquartile range

Table 3: Type of parastomal hernia surgery

Type of repair	Surgical treatment (n=42)	Non-operative treatment* (n=8)	P-value
Open repair with mesh (%)	30 (72)	6 (75)	0.837
Open suture repair (%)	5 (12)	0 (0)	0.577
Restoration of continuity (%)	4 (9.5)	0 (0)	1.000
Stoma relocation (%)	3 (7.1)	0 (0)	1.000
Unknown (%)	0 (0.0)	2 (25)	0.023

*Cross-overs from non-operative treatment to surgical treatment

Table 4: Complications after hernia repair

Complication	Surgical treatment (n=42)	Non-operative treatment† (n=8)	P-value
Overall morbidity* (%)	19 (45)	4 (50)	1.000
SSI (%)	9 (21)	1 (13)	1.000
Seroma (%)	2 (4.8)	1 (13)	0.414
Obstruction (%)	2 (4.8)	0 (0)	1.000
Ileus (%)	3 (7.1)	1 (13)	0.514
Recurrence (%)	23 (55)	1 (13)	0.050
Additional repair (%)	21 (50)	0 (0)	0.015
Emergency surgery (%)	3 (7.1)	1 (13)	0.514
Follow-up time in months (IQR)	43.5 (20.3-72.0)	55.0 (34.5-74.0)	0.700

SSI, surgical site infection; IQR, interquartile range
*Number of patients with at least one complication.
†Cross-overs from non-operative treatment to surgical treatment

Discussion

In this retrospective study of 80 patients with a parastomal hernia, the main reason for choosing non-operative treatment (NT) over surgical treatment (ST) was absence of complaints (32%) and presence of comorbidities (24%). For 14 patients (37%), the reason for NT was not documented in the medical record. Although not documented, based on the baseline characteristics, it could be that the initial oncologic surgery was a reason for NT in some of these patients. During a median follow-up of 46 months, eight patients (21%) crossed over from NT to ST. Cross-over, however, did not result in higher rates of emergency surgery, postoperative complications, or recurrence rates.

To date, few published data exist on outcomes of NT for parastomal hernia. There is one study, from which no conclusions can be drawn because of its methodological flaws.[18] However, data on non-operative treatment for inguinal and incisional hernia are available.[14-17] The data on inguinal hernia suggest that non-operative treatment can be safe, whereas for incisional hernia, cross-over to surgical treatment was associated with higher rates (29% versus 17%) of postoperative complications.[17] Our study found higher postoperative complication rates in both groups (45% for ST and 50% for NT cross-overs). These figures are in accordance with literature data on parastomal hernia repair.[21]

Apart from complications, the cumulated recurrence rate of both groups was 48%. Similar rates (6.9%-69.4%) are found in the literature.[10] This demonstrates that parastomal hernia surgery still is not very successful. As long as these numbers remain this high, NT seems to be a feasible treatment option.

Limitations

The main limitation of this study is its retrospective design, which could potentially have introduced selection bias. Non-operative treatment strategy could have been chosen more often in patients with a worse general condition. This might be reflected in some of the baseline characteristics displayed in Table 1. However, it does not effect the results after hernia repair surgery in those patients that crossed over (Table 4).

It is possible that patients have visited other hospitals for surgical treatment (both elective and emergency surgery). Additionally, hernia characteristics and patients' complaints were not recorded systematically by surgeons or stoma nurses.

Secondly, we found a relatively small number of patients with parastomal hernia, given the study period and the number of participating hospitals. In our opinion, two possible explanations exist for this finding: 1) many patients with an asymptomatic parastomal hernia would not be referred to a hospital, and 2) many parastomal hernias would not be diagnosed or registered during regular follow-up for patients' underlying disease. For these reasons, we can conclude that any missed patients were more likely to be treated conservatively. Moreover, patients who have surgery are more likely to have been identified, because of that

documentation in the patient records. Therefore, the NT group might be larger and, consequently, cross-over rates might be lower than reported in this study. Finally, one important limitation in hernia research in general, is the lack of data on patient-reported outcomes, such as quality of life and body image. Although they were reported as reasons for treatment choice, no patient reported outcomes were available after surgery. Also, reasons for NT were missing in 37% of those cases. Therefore, the only outcome measures used to compare the two groups were parastomal hernia recurrence, postoperative complications, and emergency surgery rates.

To get more insight into the effects of different treatment options on patient reported outcomes, prospective studies or registries should include these as outcome measures. Widely used generic quality of life questionnaires might not be able to distinguish between the effect of the underlying disease and the parastomal hernia itself. Therefore, disease specific quality of life questionnaires concentrating on stoma specific symptoms should preferably be used. Recently, an attempt has been made to develop such a questionnaire, which might be useful for future research.[22] Furthermore, prospective research might be able to study more, possibly asymptomatic, patients with parastomal hernias, who are otherwise missed in retrospective reviews. Data from these future studies could support treatment recommendations for asymptomatic and symptomatic patients with a parastomal hernia.

In conclusion, despite the abovementioned limitations, this study is the first to provide insight into reasons, complications, and cross-over rates for non-operative treatment compared with surgical treatment in patients with parastomal hernias. Based on the results, non-operative treatment might be the better choice in patients without complaints or with comorbidities, since there is more potential for risks than benefit of surgical treatment in these patients.

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PART III TREATMENT OF COMPLEX HERNIAS

Long term results of open complex abdominal wall hernia repair with self-gripping mesh: A retrospective cohort study

CHAPTER 10

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Abstract

Background: In case of complex ventral hernias, Rives-Stoppa and component separation technique are considered as favourable treatment techniques. However, mesh-related complications like recurrence, infection and chronic pain are still a common problem after mesh repair. Previous studies have reported promising results of the use of a self-gripping mesh (ProGrip™) in incisional hernia repair. This study aimed to evaluate the long term results of this mesh for complex ventral hernia treatment.

Materials and Methods: Patients with complex ventral hernia undergoing repair between June 2012 and June 2015, using the ProGrip™-mesh in retromuscular position, were included. All patients visited the outpatient clinic to evaluate short term complications and recurrence. After at least one year, telephone interviews were conducted to evaluate long term results.

Results: A total of 46 patients (median age 59 years) were included. 40 patients (87%) were diagnosed with incisional hernia. Seven patients (18%) had incisional hernia combined with another hernia. Four patients (8.7%) had an umbilical hernia, one patient (2.2%) had an epigastric hernia and one patient (2.2%) had rectus diastasis. 39 patients completed follow-up. Median follow-up was 25 months (IQR: 19-35 months). 28 patients (72%) did not report any complaints. Nine patients reported pain (average VAS of 1.7). Two patients developed a recurrence requiring reoperation. One patient developed mesh infection requiring reoperation.

Conclusion: Long term results of the use of a self-gripping mesh for complex abdominal wall hernias show a low recurrence rate, even in complex hernia cases. This makes the mesh a good choice in this difficult patient group.

Introduction

Incisional hernia still is an important complication after abdominal surgery with incidence rates around 13-21% after midline laparotomy.[1] Because of these high incidence rates, incisional hernia repair remains a frequently performed surgical procedure. In the United States, around 350.000 ventral hernia repairs are performed each year.[2] Small hernias are usually repaired without many complications, but surgical repair of large hernias is associated with high morbidity rates and recurrence rates up to 17%.[3-6] When patients have a recurrent hernia or when patients have comorbidities (obesity, diabetes mellitus and chronic obstructive pulmonary disease), morbidity rates are higher and recurrence rates up to 34% are reported.[4, 5, 7]

The current treatment of choice for these large ventral hernias is surgical repair with mesh implantation. For this surgical repair, there is a great variation in surgical technique, mesh location and mesh types chosen.

For large ventral hernias, primary suture repair is usually not sufficient to allow tension free closure. Use of a technique to achieve abdominal wall advancement is often required in large defects to allow this tension-free mesh reinforced reconstruction of the abdominal wall, which is still considered to be the gold standard of hernia repair.[8-10]

The Rives-Stoppa technique and the (anterior) component separation technique (modified Ramirez technique) (both with retromuscular mesh placement) are commonly used techniques for repair of complex and large ventral hernias including incisional hernias. Both techniques seem to be beneficial compared to other techniques in terms of complications and recurrence rates.[11-13]

Retromuscular (also referred to as sublay) mesh placement for ventral hernia repair reduces the hernia recurrence rates to approximately 15%.[13-16] The downside of the use of mesh is the increase of complications like infections, seroma, fistulas and chronic pain.[11, 13, 17] Chronic pain in particular is thought to be caused by nerve entrapment or nerve irritation induced by sutures fixing the mesh. Also (intercostal) nerve entrapment might be a cause of muscular atrophy.

Because of the abovementioned mesh-related complications induced by sutures, a self-gripping mesh (Parietex™ ProGrip™, Medtronic, Trévoux, France) has been developed. This ProGrip™ mesh combines the properties of a well-known lightweight polyester mesh with a surface of absorbable, polylactic acid (PLA) microhooks for mesh fixation. Previous research has suggested a relation between acute or chronic postoperative pain and the use of sutures and this mesh might reduce this.[18] Clinical (randomized) studies of this mesh in inguinal hernia repair have shown promising results in terms of infection, chronic pain and recurrence rates.[19-24]

Recent literature about the use of this mesh for ventral hernia repair shows promising results.[25, 26] However, these studies only focus on short term results[25] or have a heterogene-

ous patient population with several different kinds of abdominal wall hernias, but not specifically complex ventral hernias.[26, 27]

The purpose of this study was to evaluate the long term results of complex ventral hernia repair with the ProGrip™ mesh after a follow up period of at least twelve months.

Material and methods

Patients

A retrospective, single-centre cohort study was performed between June 2012 and June 2015. This study's methods were partially described before.[25] All patients undergoing elective complex incisional ventral hernia repair at the 'Havenziekenhuis', a satellite hospital of the Erasmus University Medical Center Rotterdam, were included. This hospital has a high expertise in the field of complex ventral hernia repair. Hernias were diagnosed based on clinical examination at the outpatient clinic. In case of doubtful diagnosis, additional imaging (ultrasonography or computed tomography) was used to confirm the diagnosis. During the study period, hernia repair using the ProGrip™ mesh was the treatment of first choice for large incisional hernia in this hospital.

Data collection

The electronic hospital data system was used to collect the following characteristics: age, sex, Body Mass Index (BMI), smoking, Diabetes Mellitus (DM), other comorbidities, American Society of Anaesthesiologists score (ASA score), indication for repair, surgical technique used, defect size (cm), mesh size (cm*cm), duration of hospital admission, post-operative pain, adverse events, indication and duration of re-admissions, number of visits at the outpatient clinic, and duration of follow-up. Pain grade was based on analgesics use: mild (no use of analgesics), moderate (daily use of non-steroid anti-inflammatory drugs or weak opioids), or severe (daily opioid use). For all hernias, complexity was scored using criteria for defining complex abdominal wall hernia by Slater et al.[28] Any missing values were reported as unknown.

Surgical procedure

The original surgical procedures are described in more detail in the article describing the short-term results.[25]

Briefly, open Rives-Stoppa, modified Ramirez technique or a combination of both techniques was used in all patients.[14, 29] After excision of the hernia sac and (when needed) adhesiolysis, the mesh was placed in the retro-rectus (sublay) position with the self-gripping surface face down.

Follow up

All patients were invited to the outpatient clinic after two months to analyze postoperative complications or recurrences, and to evaluate pain or other complaints. After a minimum of twelve months, patients were interviewed by telephone. Suspected recurrence, pain (Visual Analogue Scale (VAS) score), and other complaints, and doctor's visits concerning the abdominal wall were questioned.

Statistical analysis

Statistical analysis was performed with the SPSS statistical software package (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Continuous variables are presented as medians with Inter Quartile Range (IQR) between brackets; categorical variables are presented as numbers with percentage between brackets.

Results

Patient characteristics

A total of 46 patients were included in the study. Patient characteristics are displayed in Table 1. The cohort consisted of 28 males (61%), and the median age was 59 years (IQR: 43.75-64.25 years). The median BMI was 27.20 kg/m2 (IQR: 24.72-29.40 kg/m2). At the time of repair sixteen patients (35%) reported smoking and five patients (11%) had DM in their medical history. Seven patients (15%) were ASA class I, 36 (78%) were class II and three patients (6.5%) were class III.

Table 1. Patient characteristics

Characteristic	N=46
Median age, years (IQR)	59 (43-63)
Male (%)	28 (61%)
Median BMI (IQR)	27.20 (24.51-29.40)
Smoking (%)	16 (35%)
Diabetes Mellitus (%)	5 (11%)
ASA class	
I	7 (15%)
II	36 (78%)
III	3 (6.5%)

IQR: Inter Quartile Range; BMI: Body Mass Index; ASA: American Society of Anesthesiologists

Hernia characteristics

The hernia characteristics are shown in Table 2. A total of 41 patients (89%) were diagnosed with an incisional hernia. Of these 41 patients, eight (17%) had an incisional hernia combined with another abdominal hernia (umbilical, parastomal or inguinal). Four patients (8.7%) had an umbilical hernia. Of these four patients, one (2.2%) had an umbilical hernia combined with an epigastric hernia. One patient (2.2%) had an epigastric hernia and one patient (2.2%) had rectus diastasis. Fourteen (30%) of all patients had a recurrence after previous hernia repair. All hernias were complex abdominal wall hernias according to the published criteria of a complex hernia.[28] Using these criteria, nine patients (20%) scored a minor severity score, 34 (74%) had a moderate severity score and three (6.5%) had a major severe complex abdominal wall hernia.

Symptomatic hernia was the reason for planned surgical repair in 34 patients (74%) and two (4.3%) patients because of hernia growth. One patient (2.2%) needed a reoperation because of a mesh infection after primary hernia repair elsewhere. One patient (2.2%) had hygienic problems due to a parastomal hernia, and one patient (2.2%) had signs of incarceration. For seven patients (15%) the specific reason for repair was not stated. All patients were operated electively under general anaesthesia.

Surgical procedure and hospital stay

The used surgical techniques are outlined in Table 3. In 30 patients (65%) a Rives-Stoppa procedure was performed, in twelve patients (26%) a component separation technique and in four patients (8.7%) a combination of both techniques. 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 one patients had two small serosa injuries sutured, and one patient had an additional repair of his inguinal hernia in the same setting. In 26 procedures (57%) the size of the mesh was 30*15 cm. In seventeen cases (37%) a smaller mesh of 20*15 cm was placed in order to gain a minimum overlap of 5 cm. In three cases (6.5%), other mesh sizes were used (one patient received a 20*15 cm mesh combined with a 30*15 cm mesh, one patient received a 30*20 cm, the mesh size of one patient was not documented). Acute postoperative pain was controlled with an epidural catheter. The median hospital stay was 5 days (IQR: 4.75-7 days).

Short term follow-up (three months)

The median follow-up was 15 weeks (IQR: 7-19 months) in which the median number of outpatient clinic visits was 3 (IQR: 2-4). None (0%) of the 46 patients had a recurrence during this period.

Three patients had adverse events during primary hospital admission. One patient had an extended hospital stay of 17 days because of postoperative ileus, which was treated conservatively; one suffered from postoperative angina pectoris, one patient had postopera-

tive pneumonia, and was successfully treated with antibiotics. Ten patients (21.7%) were diagnosed with a postoperative seroma. One was treated with an ultrasound-guided punction and nine patients were treated conservatively.

Five patients showed an adverse event during outpatient follow-up. One patient showed a hematoma which was treated conservatively. Four patients were readmitted to the hospital for various reasons. Two were readmitted for 11 days and 5 days respectively because of administering intravenous antibiotics for the treatment of wound infection. In one patient this infection resulted in a mesh infection, which was treated conservatively. The other two patients were readmitted for diagnostic imaging of late abdominal complaints and ileus, which could not be explained by the surgical intervention.

At the outpatient clinic 38 patients (82.6%) were without pain. Three patients (6.5%) had mild abdominal pain without use of analgesics; four patients (8.7%) used analgesics daily for moderate abdominal pain. One of the patients (2.2%) suffered from severe pain.

Table 2. Hernia characteristics

Hernia type	
Incisional only (%)	33 (72%)
Combination (%)	8 (17%)
Umbilical (%)	4 (8.7%)
Epigastric (%)	1 (2.2%)
Multiple defects (%)	15 (33%)
Recurrence after previous repair (%)	14 (30%)
Complex hernia severity class [28]	
Minor	9 (20%)
Moderate	34 (74%)
Major	3 (6.5%)
Defect size	
0 - 4.99 cm	12 (26%)
5 - 9.99 cm	16 (35%)
>10 cm	17 (37%)
Unknown*	1 (2.2%)

*Rectus diastasis

Long term follow up (one year or more)

Thirty-nine patients (85%) were included for long term follow up, seven patients were lost in follow up (15%). Five (11%) patients were unattainable, one patient (2.2%) was suffering from dementia and one patient (2.2%) was not willing to be included. Median follow up was 25 months (IQR: 19-35 months). Median number of doctors' visits concerning hernia complaints was 0 (IQR 0-2).

In total two patients (5.1%) had a recurrence. One of these patients had a pseudobursa and recurrence after 17 months requiring reoperation. The other patient had a recurrence after 19 months requiring reoperation.

One patient (2.6%) had a mesh infection after 4 months requiring mesh explantation and implantation of a biological mesh.

Thirty patients (77%) reported no pain. Nine patients (23%) reported pain complaints with a mean VAS score of 1.7 (range: 1-3).

None of the patients died during the follow up period.

Table 3. Surgical characteristics

Type of procedure	
Rives-Stoppa	30 (65%)
Modified Ramirez	12 (26%)
Combined technique	4 (8.7%)
Mesh size	
20*15 cm	17 (37%)
30*15 cm	26 (57%)
Other*	3 (6.5%)
Drain placement	41 (89%)

*One patient received a 20*15 cm combined with a 30*15 cm mesh, one patient received a 30*20 cm, the mesh size of one patient was not documented

Discussion

This retrospective cohort of 46 consecutive patients demonstrates promising results of the use of the self-gripping ProGrip™ mesh in complex ventral hernia repair, as only two of the patients (5.1%) in this study had a recurrence after a median follow-up of 25 months. This current study suggests that the use of the Parietex™ ProGrip™ mesh is a safe procedure with ten (22%) mesh related complications after short term follow up and three (7.7%) mesh

related complications after long term follow up.

In inguinal hernia repair, self-gripping meshes have already been proven to be feasible with low infection rates, less chronic pain and lower recurrence rates.[19-22]

A recent study has shown promising results in patients with simple incisional hernias with no recurrences after two years of follow up.[26] In the current study ventral hernias were all complex hernias regarding to the criteria of Slater et al.[28] These hernias are expected to increase the perioperative risks, complications and recurrence rates. Hence, the use of the ProGrip™ mesh has shown to be feasible even in these complex patients.[25]

Previous studies have demonstrated a wide variation of recurrence rates 0-30% for primary ventral hernia repair using mesh in retromuscular (sublay) position.[13-16] In this cohort, both recurrences were hernias with a hernia size greater than 10 cm. It has been described in literature that a greater hernia size is a risk factor for recurrence.[3] Also, one of the two patients had unilateral rectus muscle palsy, a highly possible cause of hernia development.
One of the possible limitations of this study is the retrospective nature of this study. However, all patients were interviewed to ask about their current complaints.

Secondly, this study comprises only 46 patients. This number however exceeds the studies published on this topic so far.[25, 26]
Taking these limitations into account, this study shows promising results after the use of a self-gripping mesh in retromuscular position with a low recurrence rate of 5.1%.

Conclusions

This study shows the promising use of the ProGrip™ mesh for complex ventral hernias. Because of the self-gripping surface of the mesh, sutures or tackers can be avoided. This makes the mesh easy and fast to use. Furthermore it decreases the chance on suture and tacker related complications (i.e. pain and discomfort). Ideally, prospective randomized studies should be conducted to further analyse the efficacy of the ProGrip™ mesh. However, complex ventral hernia surgery is an expert field requiring tailor made solutions. This makes larges randomized studies virtually impossible. Therefore, good prospective registration such as the EuraHS-format[30] should be performed to further investigate long term effects.

Ethical approval

The use of this mesh was standard procedure in the Havenziekenhuis, Rotterdam. The study was approved by the Institutional Review Boards.

Declaration of conflict of interest

The authors of this manuscript have no conflicts of interest to disclose.

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Complications and recurrence rates of patients with Ehlers-Danlos syndrome undergoing ventral hernioplasty – a case series

CHAPTER 11

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Abstract

Purpose: Ventral hernia repair is one of the most frequently performed surgical procedures, though recurrences are common. Recurrence can be caused by impaired collagen formation or maturation, hence patients with Ehlers-Danlos syndrome (EDS) are potentially at increased risk for hernia recurrence. EDS causes altered collagen metabolism, though little is known about the influence of EDS on ventral hernioplasty outcomes. This study aims to analyze these patients to report complication rates, recurrence rates, and, if possible, to give recommendations for surgical intervention.

Methods: A retrospective analysis between January 2000 and January 2017 was performed in a university hospital Belgium (UZ Ghent). Data on baseline characteristics, primary surgery, and hernias was extracted from patients' medical charts. Noted endpoints were postoperative complications and recurrences.

Results: Fourteen patients (50% males) were included. Ten (71%) had an incisional hernia and four (29%) a primary ventral hernia. Median age was 45 years (IQR 37.75-52.75), median BMI was 24.82 (IQR 22.43-26.87). Four patients (29%) smoked, one patient (7.1%) had diabetes mellitus, and five patients (36%) had an aneurysm of the abdominal aorta. All patients underwent elective open hernioplasty with mesh reinforcement. Three patients (21%) had a postoperative complication (two infections, one seroma). Recurrence rate was 7.1% (one patient).

Conclusions: This series describes 14 patients with a median follow-up of 50 months and a recurrence rate of 7.1%. The low recurrence rate could be explained by the use of large meshes that reinforce the entire midline to compensate for the reduced collagen strength in EDS patients.

Introduction

Incisional hernia formation is one of the most frequent complications after abdominal surgery with midline laparotomy, occurring in 11% to 20% of all laparotomies in the general population.[1] When patients have risk factors (obesity, smoking or abdominal aortic aneurysm), this rate can increase up to 35%.[2]

It is hypothesized that a disturbed balance between mature and immature collagen can be part of the underlying mechanism leading to incisional hernia formation. Klinge *et al*. explain recurrent hernia formation as a combined problem of biology and technique.[3] The human extracellular matrix consists of twenty different types of collagen, of which 95% is type I and III collagen.[4] Patients with recurrent ventral hernias have a decreased collagen I/III ratio. Collagen type I is mature, mechanically stable collagen, whereas collagen type III is immature, mechanically instable collagen.[3] Alongside the previously mentioned collagens it has been hypothesizes by Schumpelick *et al*. that tenascins, a family of glycoproteins, could be linked to hernia formation.[5] Given this mechanism, patients with an underlying connective tissue disease, such as Ehlers Danlos syndrome (EDS), can be at risk for a higher recurrence rate after both ventral and incisional hernia repair.[6,7,5] EDS was first described 1901 and the syndrome characterizes itself by a triad of skin hyperextensibility, joint hypermobility, and tissue fragility. Originally, EDS was divided into numbered subtypes. In 1998, the Villefranche classification scheme divided EDS into six subtypes, based on clinical features, biochemical and genetic findings, and mechanism of inherence: classic (type I and II), hypermobility (type III), vascular (type IV), kyphoscoliosis (type VI), arthrochalasia (type VIIA and VIIB), and dermatosparaxis (type VIIC).[8,9] Because of overlapping symptoms in these different subtypes, categorizing EDS is no easy task. Including all subtypes of EDS, the incidence is approximately one in 5000 people, of which the hypermobility subtype is most common.[8]

The recently published international classification of the Ehlers Danlos Syndrome describes the genetic basis for each type of EDS. The classical, vascular, and arthrochalasia types have been linked to either type I or type III collagen disorders. [4,1] The hypermobility type is linked to tenascin X alterations. Although not all types of EDS have been linked to a specific protein disorders, many surgeons fear a high recurrence rate following hernia repair in EDS patients because of similar collagen disorders associated with both EDS and hernia recurrence.[5-7]

EDS can potentially influence every part of the body where connective tissue is present. The literature on the relationship between EDS and hernia development is scarce and only includes a few case reports. Despite the lack of evidence, many surgeons believe that EDS may have a negative effect on the clinical outcome of ventral hernioplasty in terms of both higher postoperative complication and recurrence rates. The aim of this retrospective case series is to evaluate outcomes of ventral hernioplasty in patients with Ehlers-Danlos syndrome, the primary outcome is hernia recurrence and the secondary outcome is postoperative complications.

Methods

A retrospective analysis of hospital registries between January 2000 and January 2017 was performed in a large university hospital in Ghent, Belgium (Ghent University Hospital). Before commencement of the study, ethical approval and approval of the Institutional Review Boards was obtained. The hospital central registry was searched using either ICD-10/ICD-9-CM or Diagnosis Treatment Codes (DBC) for collagen disorder (Q79.6/756.83) and 'hernioplasty' (0303.123/0303.124). Any patient with a history of EDS (any type) and a ventral abdominal hernioplasty was eligible for inclusion in this study. Patients that registered an objection for participation in scientific research in their medical chart were excluded. Follow-up was obtained from patients' medical charts. All EDS patients were seen three weeks postoperatively, as well as every six months hereafter.

Data collection

The following data were extracted from patients medical charts: baseline characteristics (age, sex, body mass index (BMI), smoking, medical history and type of Ehlers-Danlos), information about the hernia (date of diagnosis, type of hernia, size, primary/recurrent hernia, complaints), details regarding the surgical procedure (date of operation, elective/emergency procedure, type of procedure, mesh type and size and drain placement), postoperative data (postoperative complications (seroma, hematoma, surgical site infection, other infection, mesh explantation, and recurrence)), and follow-up (duration, number of outpatient clinic visits, readmissions, reoperations, and complaints). Hernia characteristics were reported using the European Hernia Classification of the European Hernia Society (EHS).[11] All data was stored and analyzed in SPSS® for windows version 24, IBM corp. Armonk, NY, released 2013.

Results

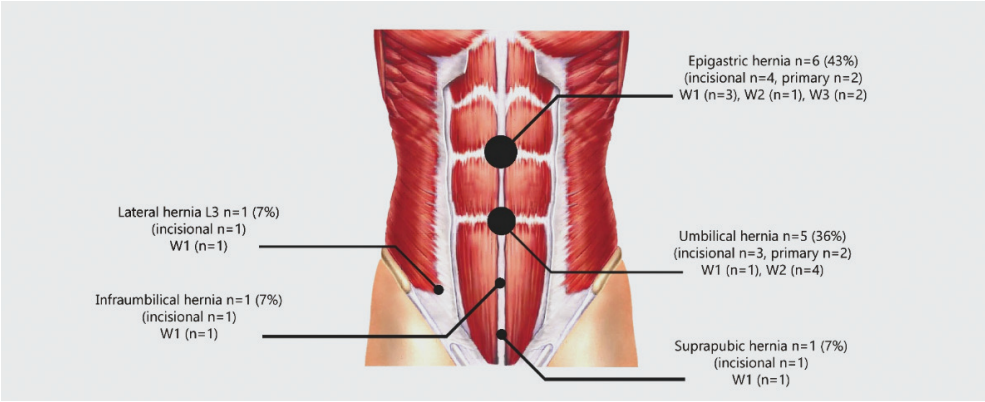
A total of 14 patients (seven males, seven females), with a median age of 45 years (range 24-60 years) were included with diagnosis dates between June 2009 and July 2016. Median BMI was 24.82 (IQR 22.43-26.87). Four patients smoked (29%), one patient (7.1%) had diabetes mellitus, and five patients (36%) had an aneurysm of the abdominal aorta. Ten patients (71%) were ASA Class II and three patients (21%) were ASA Class III.

Two patients (7.1%) had the classic type Ehlers-Danlos, six patients (43%) had the hypermobility type, and four patients (29%) had the vascular type. Patient baseline characteristics are shown in Table 1.

Hernia characteristics

Ten patients (71%) had an incisional hernia and four patients (29%) had a primary hernia (see Figure 1 for hernia characteristics). One of the incisional hernias was a recurrent hernia, previously treated with a Marlex® mesh. The median hernia length of the primary hernias was 2.5 cm (range 2.0-5.0 cm), and the median width was 2.0 cm (range 1.5-3.0 cm). The median

Figure 1 Hernia characteristics



hernia length of the incisional hernias was 5.0 cm (range 0.6-25 cm), and the median width was 3.5 cm (range 0.8-15 cm). None of the patients underwent any concomitant procedures, nor had they concomitant hernias in other locations.

Surgical characteristics

All hernia repair procedures were elective (see Table 2 for operation details). In all patients open surgery was performed, one procedure (a recurrent hernia repair) was planned as a laparoscopic procedure, but converted to an open procedure because of severe adhesions in the abdominal cavity. All patients received mesh reinforcement in either onlay (n=1, 7%), sublay (n=9, 64%), preperitoneal (n=3, 21%), or intraperitoneal (n=1, 7%) position. The onlay procedure was performed using an Adhesix® mesh, sublay repairs were performed with UltraPro® (n=7), Adhesix® (n=1), or Rebound® (n=1) mesh. Preperitoneal repairs were performed using the Ultrapro® (n=1, 33%), or Rebound® (n=2, 67%) mesh, and the intraperitoneal procedure was performed using a Dualmesh®. Average mesh size was 399 cm2 (range 63-900 cm2), with an average length of 23 cm (range 7.0-35 cm), and width of 16 cm (range 8.0-30 cm). All sublay repairs could be closed in the midline using the Rives-Stoppa technique without the need for additional procedures (component separation or other). Eleven patients (79%) received a drain at the end of the procedure.

Perioperative outcomes

No intra-operative complications were recorded. Postoperative complications occurred in three patients (21%) (Table 3). Mean hospital stay was 3.4 days (±1.04 days). One patient (7%) had a seroma and two patients (14%) had a surgical site infection. One of the patients with a surgical site infection had a BMI of 30.4 kg/m2, the other patient had a relatively large hernia (25*15cm). One of the patients with a surgical site infection required antibiotic treatment and was therefore classified as a Clavien-Dindo Grade II complication.[12] The

remaining two complications were Grade I. No other complications were recorded in the 30-day postoperative period.

Long term outcomes

Median follow-up after surgery was 50 months (IQR 18-82, range 6-152 months). Patients visited the outpatient clinic a mean of three times (range 1-4 times). During this follow-up period, recurrences were assessed using clinical examination (n=3, 29%), or clinical

Table 1 Patient characteristics

Patient characteristics	N = 14
Age at operation, years (IQR)	45 (38-53)
Male (%)	7 (50)
BMI, kg/m^2 (IQR)	24.82 (22.43-26.87)
Smoking (%)	4 (29)
Diabetes Mellitus (%)	1 (7.1)
Abdominal Aortic Aneurysm (%)	5 (36)
ASA Class (%)	
I	0 (0)
II	10 (71)
III	3 (21)
IV	0 (0)
Unknown (%)	1 (7.1)
Ehlers-Danlos type (%)	
Classic (type I and II)	2 (7.1)
Hypermobility (type III)	6 (43)
Vascular (type IV)	4 (29)
Kyphoscoliosis (type VI)	0 (0)
Arthrochalasia (type VIIA and B)	0 (0)
Dermatosparaxis (type VIIC)	0 (0)
Unknown (%)	2 (14)
Type of primary surgery (in case of incisional hernia, n=10)	
Gynecologic	2
Vascular	4
Gastric	3
Colorectal	1

IQR, interquartile range; BMI, body mass index; ASA, American Society of Anesthesiologists

examination combined with ultrasonography (n=10, 71%). One patient (7%) developed a hernia recurrence diagnosed by clinical examination. This patient was a 37-year-old female with EDS type III without relevant comorbidity or medical history (no diabetes, no aortic aneurysm, no smoking). The patient's BMI was 25.7. She presented with a primary umbilical hernia of 2 x 2 cm (EHS Primary Abdominal wall Hernia Class: Midline Epigastric Medium hernia). She underwent an elective open repair with a preperitoneal mesh placement (Rebound® 9 x 8 cm) in August 2009. The procedure was without any complication. She developed a clinical recurrence after approximately 24 months follow-up, which resulted in esthetic complaints. The patient did not seek medical attention for her recurrence until 89 months follow-up, as she does not wish to undergo reoperation for the recurrence. No readmissions were performed. During follow-up one patient died due to brain hemorrhage, unrelated to the hernioplasty procedure. For this patient, no long-term follow-up was available.

Discussion

This case series of 14 patients with Ehlers-Danlos syndrome (EDS) undergoing ventral hernia repair shows a 7.1% recurrence rate after a median follow-up period of 50 months. Current literature on ventral hernioplasty in EDS patients is scarce with only a hand full of case reports. Girotto *et al.* describes two patients with EDS and recurrent ventral abdominal wall hernias.[13] He treated these patients with a components separation technique and an onlay Marlex® mesh. Follow-up in this study is not described clearly. Fogel *et al.* describes a series of six ventral hernia repairs, of which two patients got a recurrent hernia, though important details regarding the surgical procedure and follow-up are not described as the focus of the article is on EDS and not on ventral hernia repair.

The current series is the first study that looks at patients with EDS as a specific risk group for developing hernia recurrence. Even though the detailed pathophysiology of incisional hernia formation is still illusive, many factors influence surgical wound healing and ultimately hernia formation.[14] One important factor is collagen synthesis and maturation. Given the well-established collagen impairment in EDS patients, a high recurrence rate in in this population was anticipated. However, the 7% recurrence rate after open mesh repair in this study is lower than the 12% found in literature in the general patient population after elective open ventral hernioplasty with mesh reinforcement, after a median follow-up of 59 months.[15] The low recurrence rate can potentially be explained by the large mesh size. The average mesh size in this series was 16 x 23 cm, for an average hernia size of 3 x 5 cm. The 'oversized' mesh ensured a large surface for tissue ingrowth, which could compensate for the reduced collagen quality. Additionally, all patients were known to be diagnosed with EDS preoperatively. This might lead to a higher awareness of the surgeon. More conservative choices could have been made and more attention to the suturing technique could have been given.

Table 3 Perioperative complications

Complication	N = 14
No complications (%)	11 (79)
Seroma (%)	1 (7.1)
Hematoma (%)	0 (0)
Surgical Site Infection (%)	2 (14)
Other infection (%)	0 (0)
Mesh explantation (%)	0 (0)
Other (%)	0 (0)

Table 2 Surgical characteristics

Characteristic	N = 14
Open procedure (%)	14* (100)
Emergency (%)	0 (0)
Mesh location (%)	
Onlay	1 (7.1)
Sublay/retromuscular	9 (64)
Preperitoneal	3 (21)
Intraperitoneal	1 (7.1)
Mesh type (%)	
Ultrapro	8 (57)
Dualmesh	1 (7.1)
Adhesix	2 (14)
Rebound	3 (21)
Mesh size	
Length, cm (range)	22.9 (7.2-35)
Width, cm (range)	15.8 (8-30)
Surface (length*width), cm^2 (range)	399 (63-900)
Drain placement (%)	11 (79)
Length of hospital stay, days (SD)	3.38 (1.04)

*One procedure started as a laparoscopic procedure, but was converted to an open procedure.
SD, standard deviation

These factors, however, are hard to objectify.

During the 17-year inclusion period of this consecutive case series only 14 patients were identified. There are several explanations for the relatively low number of EDS patients with ventral hernias. The most obvious one would be the low prevalence of EDS (1:5000). Another, more troubling, explanation would be identification failure of EDS in the outpatient hernia clinic. Since this case series is one of the first articles to discuss the potential influence of EDS on ventral hernia surgery outcomes, the problem may be underestimated or overlooked. Since EDS may be 'diagnosed' by one of many physicians either inside, or outside the hospital, central hospital registries may not always be up-to-date concerning the patient history. Hence the treating physician must actively acquire information regarding EDS symptoms, to not overlook the disease in the outpatient hernia clinic.

Limitations

A retrospective case series is methodologically unsuitable to determine the recurrence rate of ventral hernias in EDS patients accurately, hence the percentages reported in this series must be interpreted with caution. Furthermore, because of the small sample size, detailed analysis of the relations between different types of EDS and clinical outcomes could not be made. Additionally, only two of the fourteen patients (14%) had the classic EDS type. Although no in-depth analyses exist on the different subtypes of EDS and hernia recurrence, it could be hypothesized that the classic type would be more prone to recurrence than other types. This could partially explain the relatively low recurrence rate found in this study.

Finally, some patients had a relatively short follow-up period. This could potentially lead to an underreported recurrence rate.

Despite the abovementioned limitation, it is the authors' opinion that the following conclusions can be made based on the results of this article.

Recommendations for hernioplasty in EDS patients

- Establishing the diagnosis Ehlers-Danlos syndrome is the first step in providing tailored-care for this complex patient population. If the family history or physical examination suggests Ehlers-Danlos syndrome, further examination is advised before attempting ventral abdominal wall hernioplasty.
- Treat 'small' ventral abdominal wall hernias as if they were bigger. The patients described in this series presented with relatively 'small' ventral hernias, though they were treated with a large (oversized) mesh and an extensive repair (most often Rives-Stoppa) with reinforcement along the entire midline or previous incision. Using large meshes provides a large surface for tissue ingrowth, which could compensate for the collagen impairment in EDS patients.

Conclusion

Patients with EDS are prevalent in the ventral abdominal wall hernia population. Identifying these patients is the first step towards tailored care. This series describes 14 patients with a median follow-up of 50 months and a recurrence rate of 7.1% (one patient). The low recurrence rate observed in this series might be explained by the use of a large mesh and reinforcement of the entire midline to compensate for the reduced collagen strength in EDS.

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Declaration of conflict of interest

LK declares no conflict of interest directly related to the submitted work. EM declares no conflict of interest directly related to the submitted work. CR declares no conflict of interest directly related to the submitted work. NB declares no conflict of interest directly related to the submitted work. JL declares no conflict of interest directly related to the submitted work. FB declares no conflict of interest directly related to the submitted work.

Author contributions

LK designed the study, analyzed and interpreted data and wrote the report. EM designed the study, analyzed and interpreted data and wrote the report. CR collected and interpreted data and revised the report. NB designed the study, interpreted data and wrote the report. JL designed the study, interpreted data and wrote the report. FB designed the study, interpreted data and wrote the report.

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Submitted

A Post-Market, Prospective, Multi-Center, Single-Arm Clinical Investigation of Phasix™ Mesh for VHWG Grade 3 Midline Incisional Hernia Repair

CHAPTER 12

Abstract

Background: Incisional hernia is a frequent complication of midline laparotomy. The use of mesh in hernia repair has been reported to lead to fewer recurrences compared to primary repair. However, in Ventral Hernia Working Group (VHWG) Grade 3 hernia patients, whose hernia is potentially contaminated, synthetic mesh is prone to infection. There is a strong preference for resorbable biological mesh in contaminated fields, since it is more able to resist infection, and because it is fully resorbed, the chance of a foreign body reaction is reduced. However, when not crosslinked, biological resorbable mesh products tend to degrade too quickly to facilitate native cellular ingrowth. Phasix™ Mesh is a biosynthetic mesh with both the biocompatibility and resorbability of a biological mesh and the mechanical strength of a synthetic mesh. This multi-center single-arm study aims to collect data on safety and performance of Phasix™ Mesh in Grade 3 hernia patients.

Methods: A total of 85 VHWG Grade 3 hernia patients will be treated with Phasix™ Mesh in 15 sites across Europe. The primary outcome is Surgical Site Occurrence (SSO) including hematoma, seroma, infection, dehiscence and fistula formation (requiring intervention) through 3 months. Secondary outcomes include recurrence, infection and quality of life related outcomes after 24 months. Follow-up visits will be at drain removal (if drains were not placed, then on discharge or staple removal instead) and in the 1st month, 3rd month, 6th month, 12th month, 18th month and 24th month.

Conclusion: Based on evidence from this clinical study, Phasix™ Mesh may become a preferred treatment option in VHWG Grade 3 patients.

Trial Registration: The trial was registered on March 25, 2016 on clinicaltrials.gov: NCT02720042

Background

Incisional hernia (IH) is one of the most frequent complications after midline laparotomy, with incidences varying from 10% to 20%, and even higher percentages occur in high-risk groups [1, 2]. IH can lead to a high morbidity and reduces quality of life [3, 4]. Due to the high IH incidence rates, hernia repair surgery is one of the most frequently performed surgical procedures [5]. The aim of hernia surgery is to relieve symptoms, to prevent complications or to resolve acute complications.

There are several options for hernia repair, including primary suture repair, synthetic or biologic material placement, repair with relaxing incisions, component separation and use of musculofascial flaps, utilizing both open and laparoscopic approaches [6-8]. Synthetic mesh repair procedures, either open or laparoscopic, lead to fewer recurrences compared to primary repair; recurrences after mesh are 7.7% compared to 23.8% after primary closure [1, 3, 9, 10]. Improved outcomes are believed to be related to reduced tension on the fascial edges and sutures when mesh is used in hernia repair procedures. Despite reducing hernia recurrence rates, the use of synthetic mesh has been associated with complications in approximately 17% of patients. These complications include infection, pain, adhesions, fistulae and foreign body reactions including increased inflammation and/or connective tissue deposition [3, 11]. Especially complex and large abdominal wall defects continue to pose a challenge to surgeons, which are associated with recurrence rates of up to nearly 40% [12].
It can be stated that synthetic mesh is more prone to infection than primary closure, and this poses a problem in potentially contaminated hernias like Ventral Hernia Working Group (VHWG) Grade 3 hernias [13] (Figure 1). The success of the mesh repair is jeopardized by potential contamination due to complicating factors like previous wound infection, the presence of a stoma or violation of the gastro-intestinal tract.

The use of a biological tissue matrix has been advocated in (potentially) contaminated hernias, because of their ability to resist infection, milder inflammatory response and more orderly collagen deposition than non-resorbable, synthetic meshes [14-16]. Most often, biological meshes are derived from human, porcine or bovine dermis, and these materials have been processed to acellular sheets of collagen and elastin. The development of resorbable mesh products has faced challenges related to the rate of absorption with complications arising when the mesh product is resorbed too quickly. Rapid resorption does not support sufficient healing if structural reinforcement is diminished during the tissue repair period.

Therefore, some meshes contain chemicals to induce additional crosslinking in the graft. This slows down the degradation process, causing the mesh to retain its strength for a longer period of time[17]. However, crosslinking in the mesh reduces its biocompatibility; causing delayed cellular infiltration and neovascularization [17-19]. Ideally, a resorbable mesh should have a high ability to resist infections and retain its functional strength for a sufficient period of time to allow native cellular ingrowth tissue remodeling, maturation of collagen and gradual shift of

mechanical load.

Phasix™ Mesh is a commercially available biosynthetic mesh. It is a slowly resorbable mesh prepared from poly-4-hydroxybutrate which has been studied for use as a biomaterial for different medical applications due its strength and flexibility, biocompatibility and desirable degradation times [20-22]. Phasix™ Mesh is comparable in performance to traditional polypropylene mesh when using standard measures of mechanical strength (suture pullout, tear and ball burst strength) [23, 24]. Preclinical implantation studies indicate that Phasix™ Mesh retains approximately 70% of its original strength at 12 weeks [23]. Absorption of the mesh material will be essentially complete in 12-18 months [24]. Given the long-term strength retention observed in preclinical studies, it is anticipated that Phasix™ Mesh may result in low recurrence and complication rates with minimal pain and discomfort when used for hernia repair

.

Rationale

From a general perspective, the current literature still is rather void of evidence-based guidelines regarding optimal choice of mesh. Simple, uncontaminated hernias are usually treated with synthetic mesh; biologic meshes are mostly used in potentially contaminated hernias, since post-operative mesh infection is anticipated.

Until now, the use of Phasix™ Mesh was studied primarily in patients up to VHWG Grade 2 [25]. Based on the data gained from this clinical study, additional evidence may be provided with a view to optimal selection of hernia repair material in a population of higher risk. Based on the combination of the features of the Phasix™ Mesh proven in previous clinical and non-clinical investigations, and based on evidence from the clinical study as described in this protocol, Phasix™ Mesh may become a preferred treatment option in VHWG Grade 3 patients.

Methods

Objectives

The objective of this study is to collect additional data on safety and performance of Phasix™ Mesh in subjects requiring VHWG Grade 3 midline incisional hernia repair. Among others, Surgical Site Occurrence (SSO), hernia recurrence, pain, infection, reoperation and adverse events will be collected for subjects with a VHWG Grade 3 hernia meeting the study inclusion and exclusion criteria.

Design

The study has been designed as a post-market, prospective, single arm, multi-center, open-label study to collect data on performance and safety of Phasix™ Mesh in subjects with a VHWG Grade 3 midline hernia. This study will be conducted in 15 hospitals across Europe.

Participants

Subjects with a VHWG Grade 3 incisional hernia scheduled for hernia repair are eligible for this study and will be asked for informed consent at the outpatient clinic.

Inclusion criteria

All subjects who meet the following criteria listed below can be enrolled in the study:

- Age 18 years or older
- Diagnosis of an incisional midline hernia
- VHWG Grade 3 hernia
- Size of hernia >10 cm2, measured intraoperatively
- Elective retro-rectus hernia repair
- Signed informed consent

Exclusion criteria

All subjects who meet the following criteria must be excluded from study enrolment:

Regarding the subject:

- Body Mass Index (BMI) > 35 kg/m2
- Peritonitis
- Use or suspected future use of chemotherapeutic medication during any part of the study
- Known human immunodeficiency virus (HIV) infection
- Cirrhosis of the liver and/or ascites
- Pregnancy, plans to become pregnant during the study period or current breastfeeding
- Alcohol/substance abuse problem or a relapse within 12 months of the screening visit
- Involvement in another interventional clinical study in the last 30 days prior to inform consent signature
- Life expectancy of less than 2 years at the time of enrollment
- Known sensitivity to Phasix™ Mesh or component materials (subjects with known allergies to tetracycline hydrochloride or kanamycin sulfate)
- Any condition that, in the opinion of the investigator, would preclude the use of the study device or preclude the subject from completing the follow-up requirements

Regarding ventral hernia:

- More than 4 previous repairs of the hernia under observation
- The hernia repair requires more than a single piece of mesh
- Intact permanent mesh adjacent to the current hernia to be repaired

Regarding surgery:

- American Society of Anesthesiology class 4 or 5
- Surgical technique requires surgical bridge repair

- Complete removal of existing mesh from a prior hernia repair (in the same affected area) is not possible
- The hernia repair requires intraabdominal mesh placement

Study procedures

Screening

Subjects with a diagnosis of incisional midline hernia requiring surgical repair to close the defect who are presenting at the study site will be considered potential subjects for inclusion in this clinical study and should be pre-screened for study eligibility. If inclusion criteria are potentially met and no exclusion criteria are anticipated to be present at the time of pre-screening, the Investigator will invite the subject to participate in the study.

Informed Consent

Subjects will be asked to sign a written informed consent form. A copy of the informed consent will be provided to the subject.

Eligibility

Final eligibility will be determined intraoperatively. Subjects who fail to meet eligibility criteria should be considered screen failures and will be treated per hospital standard of care. Reason for screen failure will be documented.

Intervention

All subjects will undergo an open ventral repair of the hernia. All intraoperative inclusion and exclusion criteria will be verified.

Subjects will be administered perioperative antibiotics according to hospital protocol. Subjects will be prepared to undergo hernia repair with Phasix™ Mesh. The general instructions for the use of Phasix™ Mesh are supplied by the manufacturer.

Surgical technique

The surgical technique will require retro-rectus placement (onlay is allowed as an exception when retro-rectus placement cannot be achieved), using slowly resorbable sutures, with or without Component Separation Technique (CST). The peritoneum should remain posterior to the mesh upon completion of mesh placement. The mesh may be cut to shape or size desired for each specific application. The mesh is to be positioned so its edges extend beyond the margins of the defect by at least 5 cm. It is recommended that the mesh is fixated at approximately 5-6 cm intervals (6-12 absorbable sutures) around the periphery of the mesh. Defect closure must be confirmed. All skin incisions will be closed with staples/sutures and wounds will be dressed with sterile occlusive dressings.

Outcome parameters

Primary outcome

Primary outcome will be Surgical Site Occurrence (SSO) up to and including, the 3-month follow-up assessment. SSOs will be assessed by physical examination at each study visit through 3 months. SSO is defined as hematoma, seroma, surgical site infection, wound dehiscence, skin necrosis and fistula, all of which require intervention.

Secondary outcome

Secondary outcomes will be:

- Surgical Site Occurrence (SSO) after the 3-month follow-up assessment
- Surgical Site Infection (SSI)[26], is included in SSOs, but will also be analysed separately
- Hernia Recurrence rate (via physical exam, if uncertain via ultrasonography, CT or MRI)
- Pain at every follow-up point, measured with the Visual Analogue Scale (VAS)
- Device related adverse event incidence
- Rate of reoperation due to the index hernia repair
- Quality of Life assessments (Carolinas Comfort Scale™[27]a and EuroQol-5D (EQ-5D)[28])
- Surgical procedure time as measured from incision to closure (skin to skin)
- Return to work
- Length of hospital stay (day of index surgery until day of discharge, LOS)

To measure these outcomes, the following data will be gathered at different points in time, and saved in an electronic case report form:

Pre-operative data

- Demographic data (age, sex, race, ethnicity) and medical history
- Information regarding the inclusion and exclusion criteria
- Height and weight (calculated to a BMI)
- Length and width of hernia
- Wound assessment
  - o signs of infection
  - o status and location of potential previous mesh
  - o signs of necrosis
- Pain medication usage
- Pain (measured with VAS), discomfort (measured with Carolinas Comfort Scale™) and quality of life (measured with EQ-5D)

Peri-operative data

- Information regarding the inclusion and exclusion criteria
- Intra-operative evaluation of wound and abdomen
- Intra-operative assessment and description of hernia

- Intra-operative assessment of complications, e.g. enterotomy
- Surgical procedure
- Mesh details
- Fixation details
- Wound closure

Post-operative data

The following data will be collected at fixed follow-up visits, namely at drain removal (if applicable, otherwise at discharge or at staple removal), 1 month, 3 months, 6 months, 12 months, 18 months and 24 months (Table 1):

- Wound assessment
  - o signs of infection
  - o status and location of potential previous mesh
  - o signs of necrosis
- Hernia recurrence (diagnosed with physical exam, if uncertain via ultrasonography, or via CT/MRI)
- Adverse events
- Device failure/malfunction/defects
- Pain (measured with VAS)
- Discomfort (measured with Carolinas Comfort Scale™)
- Quality of life (measured with EQ-5D)

In addition, pain medication usage will be collected at 12 and 24 months follow-up.

Withdrawal/Early Termination

A subject is considered an Early Termination if discontinuation occurs after study treatment and before 24 months follow-up. The site will attempt to bring the subject back to the hospital to complete all Early Termination visit study procedures: Physical examination, Pain measured with VAS, Carolinas Comfort Scale™, EQ-5D and collect adverse events. Reason for subject discontinuation will be documented when possible.

Sample size consideration

The expected rate of SSO at 3 months is 37% based on historical data (ranging from 21-53%)[29-32]. With 75 subjects, the accuracy of the estimated SSO will be 11% (i.e. half of the width of the 95% confidence interval of the estimated rate of SSO is 11%). The study plans to enroll 85 subjects for follow-up. Anticipating on an attrition rate of about 10%, 75 subjects will be evaluable to assess the primary endpoint of Surgical Site Occurrence (SSO) at 3 months.

Statistical analysis

There will be a modified intention-to-treat population (mITT), which consists of the subjects

Table 1. Summary of procedures performed per visit.

Study Procedure	Screening and Baseline	Index Surgery	Drain Removal/ Discharge	1, 3, 6 and 18 Month Visit	12 and 24 Month Visit	Early Term
Describe study to potential subject	X					
Obtain informed consent	X					
Collect demographics and medical history	X					
Verify eligibility criteria	X	X				
Physical examination	X		X	X	X	X
Placement of device		X				
Pain Scale (VAS)	X		X	X	X	X
Carolinas Comfort Scale™	X			X	X	X
EQ-5D	X			X	X	X
Collect Adverse Events		X	X	X	X	X
Collect pain medications	X				X	

in whom Phasix™ Mesh has been implanted. The screen failures were not implanted, and therefore not used in the analysis. A per-protocol (PP) population may be created if there are subjects who have any major protocol deviations. However, all analyses will be primarily based on the mITT population.

Demographics and baseline characteristics will be summarized using the mITT population. Summary statistics for categorical variables will include frequency counts and percentages, and for continuous variables mean, standard deviation, minimum, median and maximum.
The primary endpoint is the SSO rate up to (including) 3 months (14 days) post device placement based on the mITT population. A 95% confidence interval will be reported for the SSO rate.

The SSO rate after 3 months, the hernia recurrence rates and surgical site infection rates until 1, 3, 6, 12, 18 and 24 months post device placement will be reported per visit along with their 95% confidence intervals based on the mITT population as secondary endpoints. Additionally, Kaplan-Meier analyses for the time from surgery to hernia recurrence and for the time from surgery to surgical site infection may be performed.

The secondary endpoints of VAS pain scale, Carolinas Comfort Scale™ and EQ-5D will be summarized based on the mITT population with mean, standard deviation, minimum, median and maximum presented by visit.

Device related adverse events will be tabulated by system organ class and preferred term. The number of subjects with a post procedure reoperation due to the index hernia repair will be presented by time intervals (until 1, 3, 6, 12, 18 and 24 months post device

placement), surgical procedure duration of the index procedure (calculated as time of skin closure complete minus time of first incision) and length of hospital stay will be summarized descriptively. The time to return to work will be tabulated using summary statistics as well.

Safety parameters, such as adverse events, device deficiencies (mechanical failure, malfunction or defects), physical examination and pain medication, will be summarized using the mITT population.

Subgroup analyses will be performed by sex, sites (sites with few treated subjects can be combined) and other factors of interest.

No missing value imputation methods will be applied in any of the aforementioned analyses.

Safety

In this study, Adverse Events (AE) are defined as any undesirable clinical event occurring in the abdominal wall or the abdominal space, as well as any other undesirable clinical events judged to be related to the study device or surgical procedure regardless of anatomical region, from time of implantation to end of study participation. Abnormal laboratory results are also to be considered as AEs if the results are accompanied by clinical signs or symptoms. The investigator will assess the relationship of an AE to the study device or procedure and categorize them as 'definitely', 'possibly' or 'not related'.

An adverse device effect (ADE) is an AE related to the use of the mesh product implanted (e.g. insufficient or inadequate implantation, installation, operation or malfunction of the Phasix™ Mesh).

Serious adverse events (SAE) are the events that meet the definition of serious in the ISO 14155:2011.

All events will be followed to satisfactory resolution or stabilization.

The investigator is responsible for the detection and documentation of events meeting the criteria and definition of AE, ADE or SAE. All SAEs and investigator-judged device related AEs that occur, must be reported to the sponsor within 24 hours of becoming aware of the event.

An independent safety monitoring committee will reassess safety of the study protocol and decide about potential adaptations if one of the following criteria are met:

- More than 4 device related SAEs within 3 months of Phasix™ Mesh implantation
- More than 1 device related recurrence within 3 months of Phasix™ Mesh implantation

The enrolment and treatment of new subjects are suspended until the impact of the study parameters (e.g. surgical technique, hernia size, mesh size, AE time-course) on the results is assessed. The follow-up for the subjects already treated continues.

Monitoring for accuracy and timely submission of data forms and compliance with the study protocol, meeting enrolment commitments and applicable regulations will take place by monitoring personnel.

Ethics

This study will be conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. The Medical Ethical Committee of the Erasmus Medical Center and the Institutional Review Board of every participating hospital have approved the protocol. Written informed consent will be obtained from all subjects. All study data will be recorded in electronic Case Report Forms provided to the investigational site. Site and subject numbers will be used to track subject information throughout the study.

Discussion

A major challenge in all hernia studies is the formulation of a clear definition on the severity or grade of the hernia. The difference between grade 3 and 4 hernias is not always clear, since the classification is more gradual than it seems. The definition for Grade 3 hernias used in this study is the same as the one of the Ventral Hernia Working Group in 2010, which excludes presence of infected mesh[13].

A discussion topic in this study is the absence of a control group. Because no standard treatment is recorded for VHWG Grade 3 hernias, comparing Phasix™ Mesh with synthetic mesh has been considered to be unethical, since the potential contamination of the hernia could cause complications when using a synthetic mesh . Comparing Phasix™ Mesh with just sutures (primary closure) would not be ethical either, due to the high recurrence rates associated with primary closure.

It was considered to compare Phasix™ Mesh with the treating surgeon's standard of care for VHWG Grade 3 hernias in each participating hospital. However, due to the lack of consensus on what standard of care for VHWG Grade 3 hernias is, this would lead to a very heterogenous control group. This justifies the single-arm design of the study.

Conclusion

This multicenter trial will collect additional data on safety and performance of Phasix™ Mesh in subjects with a VHWG Grade 3 midline hernia requiring surgical repair. Based on evidence from this clinical study, Phasix™ Mesh may become a preferred treatment option in VHWG Grade 3 patients.

List of abbreviations

Abbreviation	Definition
ADE	Adverse Device Effect
AE	Adverse Event
BMI	Body Mass Index
CCS	Carolina Comfort Scale
CST	Component Separation Technique
CT	Computed Tomography Scan
EQ-5D	EuroQol-5D
HIV	Human Immunodeficiency Virus
IH	Incisional Hernia
LOS	Length of hospital Stay
mITT	Modified Intention-to-treat
MRI	Magnetic Resonance Imaging
PP	Per Protocol
SAE	Serious Adverse Event
SSI	Surgical Site Infection
SSO	Surgical Site Occurence
TM	Trademark
VAS	Visual Analogue Scale
VHWG	Ventral Hernia Working Group

List of Declarations

Ethics Approval and consent to participate

This study will be conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. The Medical Ethical Committee of the Erasmus Medical Center and the Institutional Review Board of every participating hospital have approved the protocol. Written informed consent will be obtained from all subjects. All study data will be recorded in electronic Case Report Forms provided to the investigational site. Site and subject numbers will be used to track subject information throughout the study.

Consent for publication
Not applicable

Availability of data and material
This is a protocol, therefore no collected patient data was used. Not applicable
OR: The data that support the findings of this study are available from Bard Davol Inc. but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Bard Davol Inc.

Competing interests
The study was funded and reviewed by Bard Davol Inc. (the sponsor).

Funding
Bard Davol Inc (the sponsor) has designed and financially supported this trial, and will as well conduct interim analyses on the collected data.

Author's contributions
MMJvR and APJ were major contributors in data acquisition and writing the manuscript. TT, LNJ, TSdVR, GP, FK, MM, ACJW, FB, RHF, BD, GW, HLvW, FG, AK, GWMT and JFL acquired data, revised and approved the protocol. LFK was a major contributor in data acquisition, reviewing and approving the manuscript. JJ was a major contributor in designing, reviewing and approving the manuscript.

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Not Applicable.

Endnotes

a The CAROLINAS COMFORT SCALE™ questionnaire was created by and is licensed from the Division of Gastrointestinal and Minimally Invasive Surgery of Carolinas Medical Center, North Carolina

bReprinted from Surgery, 148(3), The Ventral Hernia Working Group, Incisional ventral hernias: Review of the literature and recommendations regarding the grading and technique of repair, 544-558, Copyright (2010), with permission from Elsevier.

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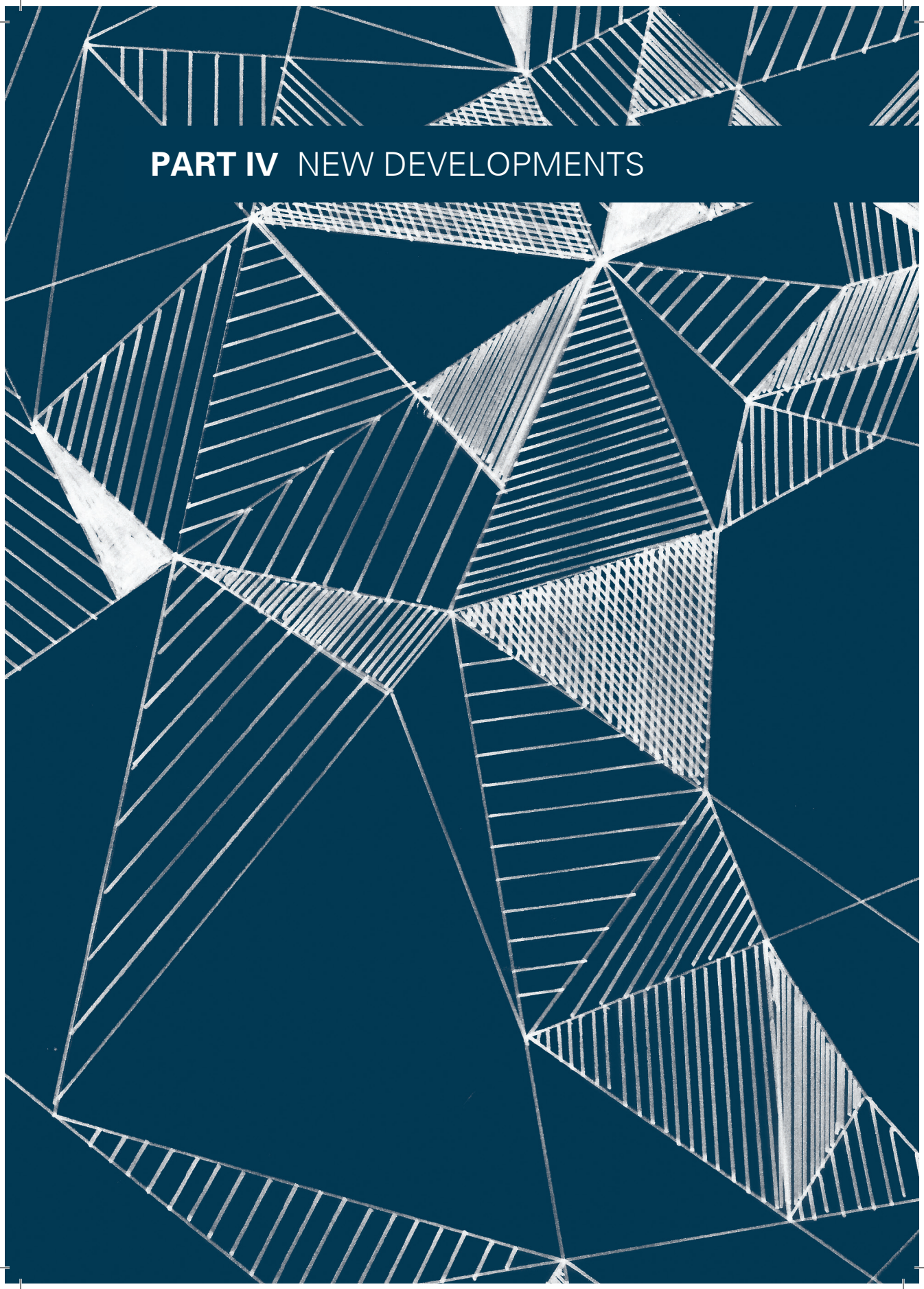
PART IV NEW DEVELOPMENTS



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The 'AbdoMAN': an artificial abdominal wall simulator for biomechanical studies on laparotomy closure techniques

CHAPTER 13

Abstract

Purpose: Incisional hernia remains a frequent complication after abdominal surgery associated with significant morbidity and high costs. Animal and clinical studies have exhibited some limitations.

The purpose of this study was to develop an artificial human abdominal wall (AW) simulator in order to enable investigations on closure modalities. We hypothesized that a physical model of the human AW would give new insight on common used suture techniques representing a substantial complement or alternative to clinical and animal studies.

Methods: The 'AbdoMAN', was developed to simulate human AW biomechanics. The 'AbdoMAN' capacities include measurement and regulation of intra-abdominal pressure (IAP), generation of IAP peaks as a result of muscle contraction and measurements of AW strain patterns analysed with 3D image stereo correlation software. Intact synthetic samples were used to test repeatability. A laparotomy closure was then performed on five samples to analyze strain patterns.

Results: The 'AbdoMAN' was capable to simulate physiological conditions. AbdoMAN lateral muscles contract at 660 N, leading the IAP to increase up to 74.9 mmHg (range 65.3 – 88.3). Two strain criteria were used to assess test repeatability. A test with laparotomy closure demonstrated closure testing repeatability.

Conclusions: The 'AbdoMAN' reveals as a promising enabling tool for investigating AW surgery related biomechanics and could become an alternative to animal and clinical studies. 3D image correlation analysis should bring new insights on laparotomy closure research. The next step will consist in evaluating different closure modalities on synthetic, porcine and human AW.

Introduction

Incisional hernia is a common complication after abdominal surgery, especially after open surgery with a median laparotomy. Incidences of incisional hernia and burst abdomen after midline laparotomy range from 11 to 20% and 1 to 3% respectively and involve frequent reoperation.[1, 2] These complications occur even more often in high risk populations, like patients with comorbidities such as obesity, smoking or diabetes[1-3] and are associated with discomfort or pain, which result in a lower quality of life.[4] In the USA, over 300,000 hernia operations are performed annually, with estimated associated costs of $ 3.2 billion.[5] Mesh-based and suture-based repair of incisional hernia exhibits recurrence rate from 0.8 to 24% and from 12% to 67% respectively%.[6-8] Because most studies provide only short-term follow-up, these recurrence rates may be underestimated.

To prevent incisional hernia, laparotomy closure techniques have frequently been investigated in both experimental and clinical studies. Some of these showed that incisional hernia is an early complication after closure.[9] Several decades of research led to recommend continuous suture technique with small suture bites of 5 mm from the wound edge and an inter-stitch distance of 5 mm with slowly absorbable suture material as the most efficient closure technique compared to the commonly used large bites.[2, 10-15] The small bites suture technique still exhibits 13% incidence incisional hernia at one year.[15] Incisional hernias remain a clinical challenge. Both biological and biomechanical mechanisms that result in the occurrence of an incisional hernia remain globally unknown.

Therefore, further research should be conducted to develop and systematically investigate closure techniques and materials. Clinical studies will give the highest level of evidence but are expensive and in most cases not suitable to investigate new concepts. Preclinical experiments with cadaveric or animal specimens face several problems: the availability of human cadaveric tissue is limited and animal experiments tend to be more and more debated from an ethical standpoint. Moreover, the anatomy and physiology of animals is considerably different from the human ones. For example, the linea alba of a rat is relatively narrow and relatively much shorter compared to the human linea alba.[16] The pig abdominal wall (AW) is more comparable to the human AW, but still exhibits numerous anatomical differences.

Previous research has focused on linear tensile strength testing of sutured porcine AW.[12] Although this research provided important conclusions for further clinical investigation,[15] linear testing does not take into account the intra-abdominal pressure acting as well on the AW.

Moreover, linear testing features flat and not curved AW and therefore does not mimic the real physiology.

There is a strong need for a standardized way to compare different closure techniques and materials under physiological conditions. This device could be used to investigate pathophysiology and treatment of AW incisional hernia. A standardized artificial AW simulator could

also be used as a training device for mechanical evaluation.

The recent study published by Deerenberg et al.[15] clearly shows the impact of mechanical conditions of midline laparotomy closure on clinical outcomes.

The aim of this study was to develop a physical simulator to investigate the mechanical behavior of the AW under physiological conditions using 3D image stereo correlation and to demonstrate the possibility to describe the biomechanics of the AW after laparotomy closure. These experiments will provide a proof of concept of the 'AbdoMAN' device.

Methods

To simulate human AW biomechanics, the 'AbdoMAN' (Figure 1) was developed. The 'AbdoMAN' consists of several components which simulate the AW biomechanics. Two main factors had to be taken into account: the intra-abdominal pressure and the effect of AW muscle contractions.

Intra-abdominal pressure

Basal resting intra-abdominal pressure (IAP) varies between 2 and 17 mmHg under normal physiological circumstances,[17-19] but can increase up to 20 mmHg in patients suffering from ileus.[20] To simulate the abdominal contents, a 3.5 liter air-filled Vacufix® collecting bag (B. Braun, Melsungen, Germany) was used. This pillow was placed on a 3D-printed part, shaped like the AW geometry. A laparoscopic insufflator (Karl Storz, Schaffhausen, Switzerland) was used to regulate the basal pressure level in the pillow.

IAP was measured and recorded in the air pillow using a 0.35 bar pressure sensor (Measurement specialties, Hampton, VA, USA). As in the physiological human situation, the IAP was achieved by the combination of a basal IAP and IAP peaks caused by muscles contractions.

Abdominal wall muscle simulation

The external, internal oblique and transverse abdominal muscles are situated laterally of the rectus abdominal muscle and their fascias surround the rectus abdominal muscle joining together in the linea alba. These lateral muscles contribute in generating perpendicular force on the linea alba. Those forces can be summated into one force vector. This force can be split in a perpendicular force to the linea alba and a force in craniocaudal direction.[21]

Pneumatic actuators (type DMSP, Festo Technology Group, Hauppauge, NY, USA) were used to simulate the muscle contraction. These actuators have the capacity to mimic the contraction of antagonistic muscles. High-strength fibers provided a relation between raising the internal pressure which resulted in expansion in peripheral direction and decreasing its size in longitudinal direction. Three identical pneumatic actuators, activated synchronously,

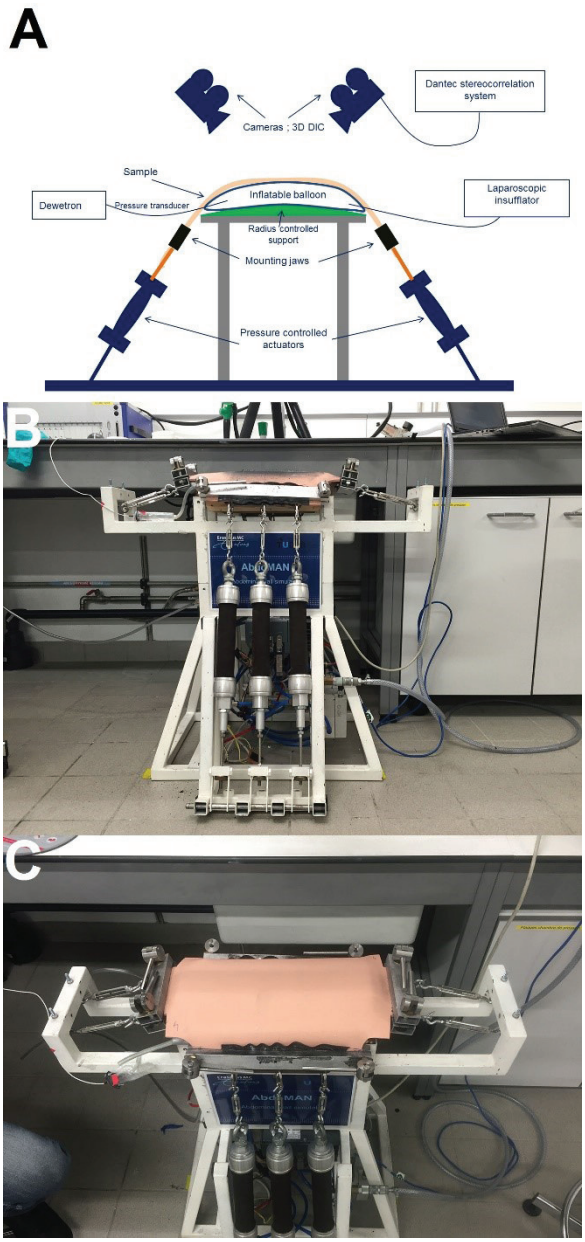


Figure 1: 'AbdoMAN' device

a. Schematic overview showing all different components
b. Side view showing three lateral muscle actuators connected to the mounted sample and the cranial/caudal jaws used to mount the sample
c. Top view showing an intact sample mounted on the 'AbdoMAN' using jaws on all four sides

were placed on both lateral sides, contracting simultaneously (Figure 1b).

The AW was fixed on the cranial and caudal sites to mimic the fixation of the rectus abdominis muscle to the rib cage and pubic bone (Figure 1c).

In the physiological situation, lateral muscles contraction causes a rise in IAP. During activities such as coughing or vomiting, IAP can increase up to 37-81 mmHg and 82 mmHg (with peaks of 255 mmHg) respectively.[18, 19] These rises were simulated with the pneumatic actuators and recorded using the pressure sensor connected to the air pillow. To create relevant IAP peaks, the physiological value of the contraction needs to be applied on a sample with material properties close to active human AW. The sample has to be placed on a relevant surrogate of the abdominal content.

Synthetic abdominal wall

In order to standardize testing, a custom made 5mm thick synthetic AW, especially made for this study, was used (Figure 2a). This synthetic material is made of a polyurethane matrix with two layers of elastane fibers (The Chamberlain Group, Great Barrington, USA). A small piece of each synthetic sheet was placed in a tensile testing machine (Instron, High Wycombe, England) to determine the stiffness in two directions (directions 1 (D1) and (D2). With the stiffness of these directions, the anisotropy ratio was calculated. This material has a comparable stiffness compared to the active human AW.[22]

Before sample mounting, 2 PTFE sheets were placed on the AbdoMAN to minimize any possible friction between the sample and the support. AW samples were mounted on the 'AbdoMAN' using clamps to attach the pressure actuators (Figure 2b). On the cranial and caudal sides, samples were clamped to ensure pretension.

3D image stereo correlation

To capture strain patterns in the artificial AW, 3D image stereo correlation system (Dantec Dynamics, Skovlunde, Denmark) was used. This system captures the 3D displacement and establishes the strain of the tested sample by using two cameras and dedicated software. Prior to the test, a black and white paint speckle was applied on the area of interest.

Experimental setup

Test setup repeatability

To investigate test reliability and repeatability, pressure and 3D image stereo correlation data were evaluated for a series of synthetic AW samples.

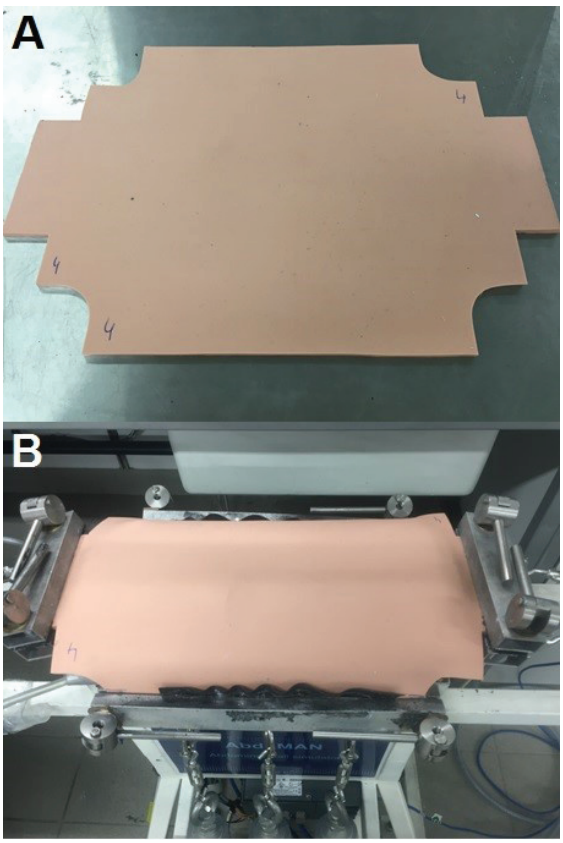
To simulate the physiological conditions, a test setup was chosen with standard IAP of 10 mmHg and to simulate coughing, actuator inner pressure, necessary to generate the lateral muscle force, was increased up to 3 000 mmHg during three cycles at 1 Hz frequency.

Midline closure repeatability

One of the purposes of this part of the experiment was to investigate the repeatability and the possibilities of visualizing the biomechanical effects of bite size and inter-suture distance using 3D image stereo correlation. A 15 cm median laparotomy was carried out on five synthetic AWs. The incision was closed using PDSII 1 sutures (Ethicon, Somerville, NJ, USA) and using a continuous 5x5 modality (5 mm distance between suture and incision, 5 mm distance between two sutures). The suture was knotted five times on both ends. After suturing, the sample was placed on the 'AbdoMAN' and cough tests were performed as described above. Strain patterns and incision distension at the moment of muscle contraction were measured using the 3D image stereo correlation system to test the reproducibility of sutured samples.

Video material is available as supplemental material online.

Figure 2: Abdominal wall samples



a. Shape of a sample prior to mounting

a. A mounted sample on the 'AbdoMAN' device with fixation in four directions

Results

Test setup repeatability

The stiffness of five synthetic samples was tested in a tensile machine in two directions (D1 and D2). A graph of the synthetic AW stiffness in both directions is shown in Figure 3. The mean Young's modulus of the stiffest direction of was 815 kPa (range 765-885 kPa; Figure 4a) and the mean anisotropic ratio was 1.26 (range 1.22 – 1.28).

After these tests, samples were mounted on the 'AbdoMAN'. The inner pressure of 3000 mmHg in each pneumatic actuator resulted in a muscle force of 660 Newton (N) (220 N per cylinder) on each lateral side. The length of the sample within the lateral jaws is 28.5 cm and his thickness is 5 mm. The force is applied on a cross-section of 14.25 cm2, which results in a stress of 0.46 MPa.

Fifteen tests were performed using five identical synthetic AWs. The mean IAP peak was 74.9 mmHg (range 65.3-88.3 mmHg; Figure 4b).

The displacement and strain fields were calculated after each test (Figure 5). Two criteria were defined to assess the repeatability of the test, the mean transversal strain over an area centered on the sample and the mean transversal strain over a transversal line (Figure 5b), which exhibited respectively 12.27% (range 11.38 – 12.75; Figure 4c) and 12.19% (range 11.38 – 12.75; Figure 4d) of strain.

Figure 3: Synthetic abdominal wall stiffness testing. Each sample was tested in two directions (D1 and D2).

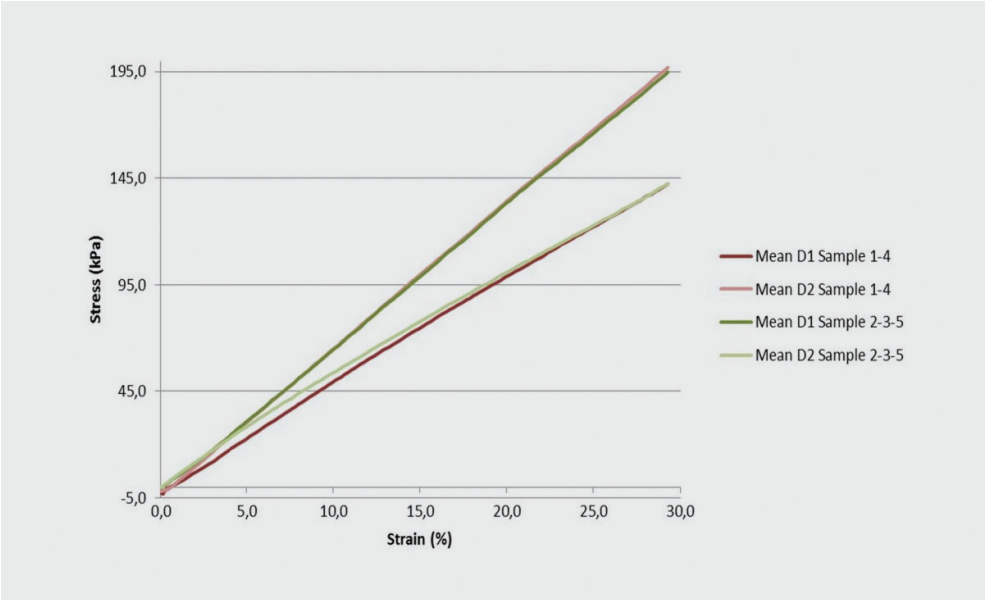
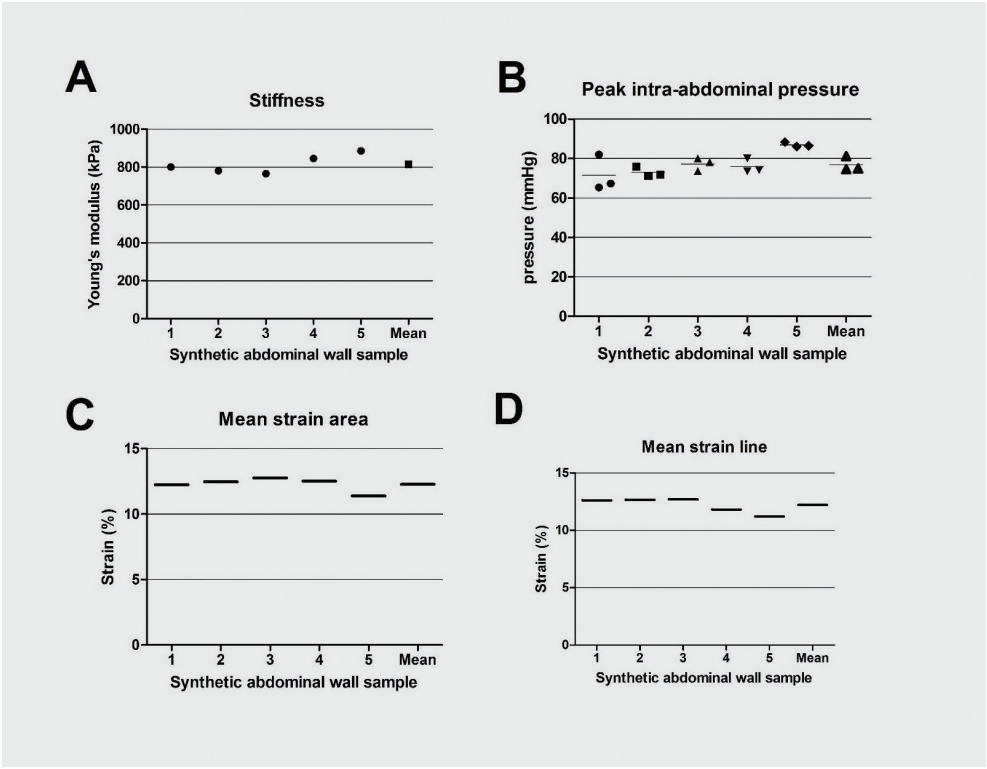
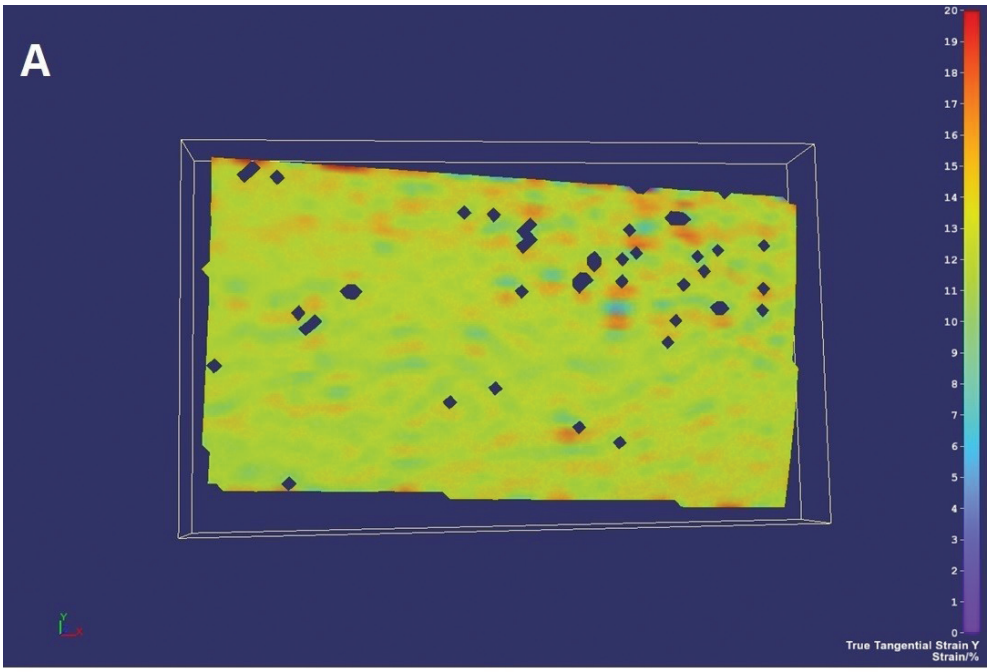


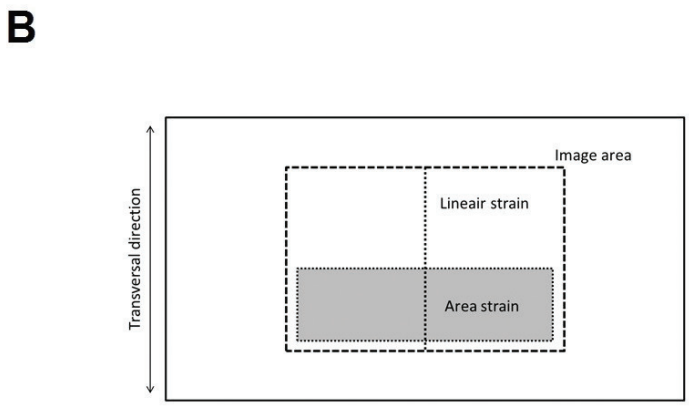
Figure 4: 'AbdoMAN' test setup repeatability results



a. synthetic abdominal wall stiffness determined by tensile machine testing of a small piece of each sample
a. peak intra-abdominal pressure during cough cycle of the samples mounted on the 'AbdoMAN'
a. mean strain over surface area of the samples mounted on the 'AbdoMAN'
a. mean strain over transversal line of the samples mounted on the 'AbdoMAN'

Figure 5: 3D stereo correlation criteria of intact samples





a. exemplary strain image of an intact synthetic abdominal wall sample at peak intra-abdominal pressure
a. schematic image of used strain analysis areas for 3D stereo correlation: linear strain in the muscle force direction and area strain of a larger surface area

Midline closure repeatability

Five incised samples were closed with a 5x5mm modality, resulting in a mean suture length to wound length ratio of 6.02 (range 5.88-6.17). No suture breaks were observed. Three comparison criteria between suture modalities were defined based on the analysis of the displacement and strain field of this configuration (Figure 6):

- Mean maximum strain around suture points. This area surrounds the place where the suture perforates the tissue. This area was used as an area of interest, because maximum force is brought upon this area. These strain areas are indicated in Figure 6a. The testing of five samples resulted in a mean value of 13.76% (range 11.7 – 15.1; Figure 7a).
- Peak-to-peak normalized strain profile through the suture points. Figure 6b shows the strain on a line, drawn along all points where the sutures perforated the tissue. As can be seen, the strain is the highest around the suture points and the lowest in the area between two suture points. The peak-to-peak normalized strain takes the mean variance between those two extremes. By doing so, attention is not only paid to the absolute value of the strain around the suture points, but also to the strain in relation to its surrounding tissue. The testing of five samples resulted in a mean value of 3.8% (range 1.3 - 6.7; Figure 7b).
- Maximum opening length of the incision. This was defined as the maximum distance between the two sides of the incision, measured during the peak of the muscle contraction (Figure 6c). The testing of five samples resulted in a mean value of 0.34mm (range 0.2 - 0.5; Figure 7c).

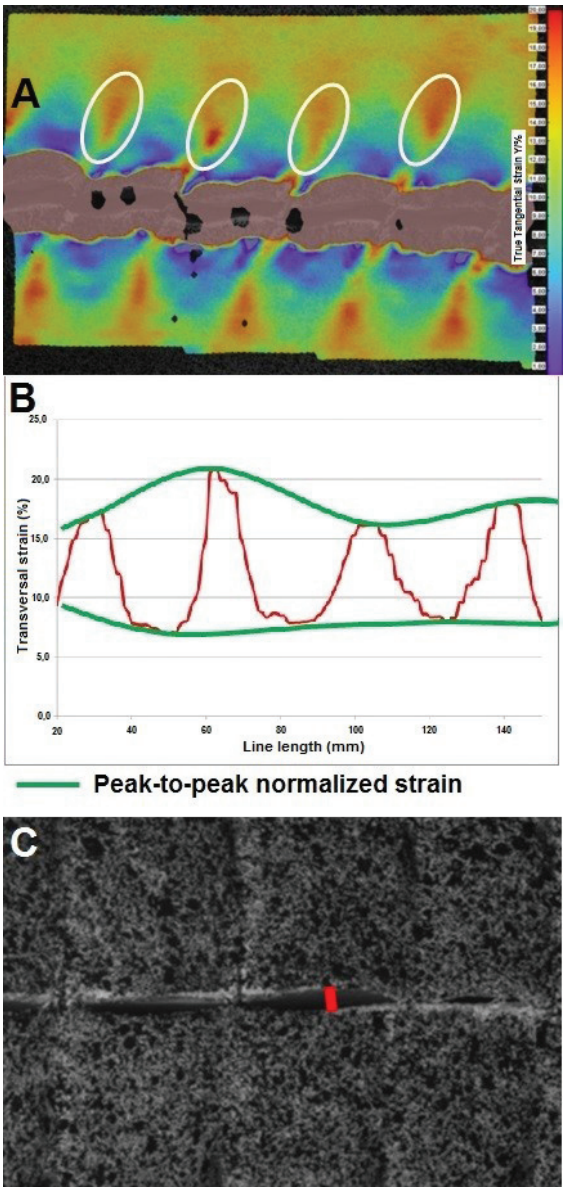
Discussion

The 'AbdoMAN' is the first human AW simulator that enables dynamic testing under physiological conditions. It combines both intra-abdominal pressure (IAP) and abdominal muscle activity.

The stiffness of the synthetic materials (765-885 kPa) is equivalent to an active human AW (600-1 000 kPa).[23] The found anisotropic rate of 1.22 – 1.28 is also in the same order of magnitude as that reported of human linea alba (1.47).[24] For coughing, the force applied by the pressure actuators, 660 N, and the resulting stress applied on the sample, 0.46 MPa, are within the range of the skeletal muscles stress (0.089 – 0.801 MPa).[18, 19, 25-27] Mean peak IAP was 74.9 mmHg (range 65.3 - 88.3 mmHg; Figure 3b) which is entirely in the physiological range of 37 - 81 mmHg during coughing.[18, 19]

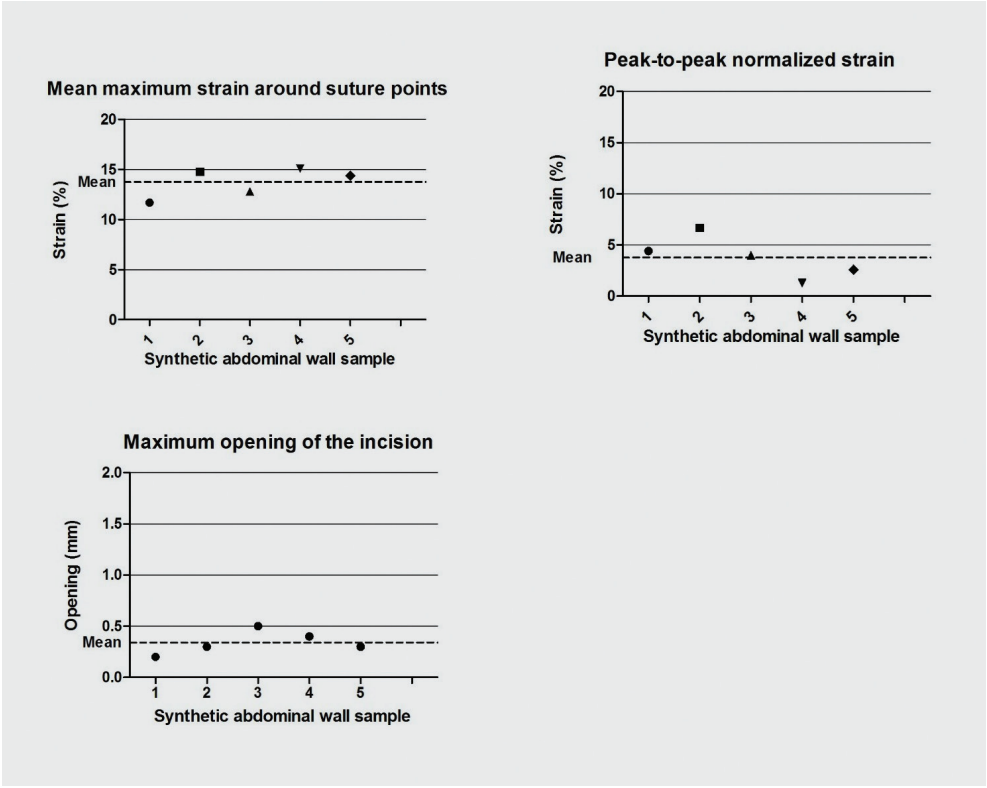
The use of 3D image stereo correlation in combination with a physiological biomechanical simulation model to analyze strain patterns and displacement in AW research was described before.[23, 28, 29] However, the combination with a dynamic simulation device has not been demonstrated yet, and provides insights in the biomechanics of the sutured AW.

Figure 6: 3D stereo correlation criteria of 5x5mm suture modality



a. Mean maximum strain around suture points. The areas are indicated in the white circles.
b. Peak-to-peak normalized strain profile through the suture points. Maximum and minimum peaks are indicated and connected with the green lines.
c. Maximum opening length of the incision. This is indicated with the red line.

Figure 7: Midline closure repeatability results



a. Mean maximum strain around suture points as indicated in Figure 6a
b. Peak-to-peak normalized strain profile through the suture points as indicated in Figure 6b
c. Maximum opening length of the incision as indicated in Figure 6c

The midline closure part demonstrates the possibility to visualize strain patterns around the incision and the suture points. Using a combination of the three criteria described previously, it might be possible to investigate different closure modalities and to find an optimal laparotomy closure modality from a biomechanical standpoint. The criteria used in this part show consistent test results when repeating test cycles with different samples. Therefore, they can be used to compare different suture modalities (i.e. bite sizes).
The next step in this research field will be the systematic testing of different midline closure modalities using both the 'AbdoMAN' and the 3D image stereo correlation system. In the future, human cadaveric AW or porcine AW could also be used with the 'AbdoMAN' device. For this purpose, additional experiments will be needed to check if the criteria used to compare modalities on synthetic AW will still be relevant using biological tissue.

When this next step has been completed, the 'AbdoMAN' can be used in experiments in which (cough) cycles are being repeated numerous times. This will reflect the physiologi-

cal situation in which incisional hernias develop over time after a longer period of repeated, intermitting stress.

When more will be known about strain and displacement data interpretation, the 'AbdoMAN' may be used for future research on finding new, ideal suture modalities. Moreover, different suture materials (such as elastic or barbed sutures) or mesh augmentation could be investigated using the 'AbdoMAN'. Even more challenging and interesting would be the creation and closure (with or without mesh) of AW defects to investigate different treatment modalities.

Finally, the 'AbdoMAN' could provide an easily accessible tool for training of laparotomy closure and hernia repair. For example, the effect of a suboptimal closure technique performed by a trainee could be directly evaluated.

To our opinion, the complete test setup can be reproduced at other sites, enabling standardized, simultaneous experiments or teaching settings throughout one (or more) countries.
The 'AbdoMAN' has limitations. It is not possible to simulate tissue healing, as it is a mechanical simulator.

One other limitation is the fact that in this setup, although the stiffness of the synthetic materials was set up to mimic active tissue, the AW does not reproduce the material properties changes driven by the contraction. This might result in different phenomena.
Also, the synthetic AW consists of two components to provide both the strength and flexibility needed to simulate the human AW features. This may react differently than the human linea alba, consisting only of connective tissue. The dimensions of the sample, comparable to a human AW, but five times thicker than a fascia,[30] the friction between the sample and the artificial abdominal cavity could as well be limitations.

Some variance was found in IAP and strain data, which might be explained by slight stiffness differences observed between synthetic abdominal walls.

Conclusion

The 'AbdoMAN' could become a promising alternative to or complement for animal and clinical studies on AW closure techniques. The device showed reliable and repeatable results. A first experiment to analyze laparotomy closure demonstrated the possible application of the 'AbdoMAN' device. Future research will evaluate different closure modalities on both synthetic and human or porcine AW to find out more about the underlying mechanisms that drive the biomechanics of laparotomy closure and incisional hernia repair.

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General discussion and future perspectives

CHAPTER 14

General discussion

This thesis provides an overview of the prevention, risk factors, and treatment of abdominal wall hernias. As stated many times in this thesis, the group of patients with an abdominal wall hernia is very heterogeneous. Great differences exist in etiology, risk factors, and treatment. In order to improve hernia surgery outcomes, it is of vital importance to understand these differences and to tailor treatment accordingly.

Prevention

In general, the majority of patients undergoing abdominal surgery will not develop an incisional hernia.[1] This is important to keep in mind when implementing preventative measures. For example, prophylactic mesh placement will reduce the hernia incidence rate from 30% to 11-17%,1 but this also implies that a large group of patients will receive a mesh without any benefits. The real challenge is represented by the identification of those patients being at risk for hernia development.

For parastomal hernias, this might be different; approximately 50% of all patients undergoing end colostomy will develop a parastomal hernia.[2-5] Given this high rate, preventive measures may have a greater beneficial effect. In this thesis it was found that extraperitoneal colostomy reduces the parastomal hernia incidence. The decrease in parastomal hernia rates suggests that other techniques might also be beneficial. The topic of parastomal hernia will only grow in relevance: with the rising life expectancy of patients undergoing major colorectal surgery requiring stoma formation, the incidence of parastomal hernia will probably rise as well.

Preoperative patient optimization

Many preoperative risk factors for postoperative complications and recurrence have been identified. Amongst those factors, several factors can be targeted prior to hernia repair surgery. In case of elective hernia surgery, timing of surgery should be depending on these factors. Based on the results described in this thesis, the main targets of this strategy are weight loss in obese patients and, if applicable, smoking cessation.

For patients with uncorrectable risk factors in patients with minimal symptoms, non-operative treatment (i.e. watchful waiting) could be considered. For inguinal6 and incisional hernia7 this has been studied before and, in this thesis, it has been studied for parastomal hernia. The outcomes of this strategy seem promising and justify further, more thorough analysis to see if these conclusions can be extrapolated to the whole parastomal hernia population.

Surgical techniques

For the treatment of abdominal wall hernias, several surgical techniques exist. The most commonly used techniques are suture closure with mesh augmentation, laparoscopic in-

traperitoneal onlay mesh (IPOM) procedure, the Rives-Stoppa technique8, the Ramirez technique9, and the more recently developed transverse abdominis release (TAR).[10] The population of hernia patients is very heterogeneous and should be approached likewise. When a treatment team can apply all different techniques, tailored hernia care can be delivered according to the patient's needs. Factors like the patient's anatomy, previous surgery, presence of any ostomy, and hernia location should be taken into account when choosing the optimal technique. Future research should look into the different surgical techniques in more detail to provide fundaments for decision making in the preoperative phase.

RCTs versus registries

In general, randomized controlled trials (RCTs) are considered to be the highest level of evidence (after systematic reviews or meta-analyses of RCTs) in medical research. Cohort studies are considered to be of lower evidence. However, this should depend on the research question asked. In abdominal wall hernia research, RCTs can only focus on hernia occurrence or recurrence. This is due to the sample size and follow-up period needed. In those studies, it is shown that mesh interventions are superior to non-mesh interventions. Mesh-related complications occur much later after surgery, but hernia RCTs do not have the statistical power to analyze these long-term complications. To enable research on these long-term effects, large cohort studies could be a better fit than an RCT. Several projects have now been started to allow this kind of long-term research and recently a first comparison of different hernia registries has been made.[11]

Dissemination

In this thesis, different statement and recommendations have been made on prevention and treatment. However, one of the biggest challenges is to communicate these recommendations to the surgeons who will actually make the difference. In the case of hernia surgery, this is, in many cases, not the hernia surgeon. Regarding hernia prevention, this will mainly be the vascular surgeon or the colorectal surgeon, depending on the type of index surgery. This is one of the real problems: new hernia knowledge (or even widely accepted hernia knowledge) will be disseminated during hernia meetings amongst hernia surgeons. During vascular or colorectal meetings, usually no presentations will be given on postoperative hernia development. This leads to a great delay in or even absence of knowledge transfer regarding hernia prevention. Therefore, a greater effort should be made by hernia scientists to disseminate their results to colleagues of different surgical specialties.

Future perspectives

Patient selection

Although recent studies on abdominal wall hernia prevention show impressive reduction of hernia occurrence,[1, 12-15] the rates remain unacceptably high. Preventive and therapeutic measures are effective for the whole patient population. However, over 70% of all patients will not develop a hernia, regardless of the measures taken. The real challenge is represented by accurate patient identification and selection to treat only those patients who will benefit from it.[16] By doing so, the balance between costs and benefits will shift in the right direction. First steps have been taken in this thesis to find risk factors for postoperative complications or recurrences. To further improve surgical outcomes, this direction should be taken in hernia research.

Patient selection does not consist of treatment selection only. Given the complexity of larger abdominal wall hernias, a different approach of the abdominal wall hernia surgery can be advocated. In parallel to oncological surgery, several steps could be taken.

First, abdominal wall hernia cases should be discussed in multidisciplinary teams including surgeons, internal doctors, dietitians, and physiotherapists. Together, these specialists can choose the right treatment and optimize the timing of surgical treatment.

Second, abdominal wall hernia care should be centralized. Higher volumes of complex abdominal wall hernia cases will increase the team's expertise and routine with this pathology. This underlines the multidisciplinary approach mentioned before. It is not only the surgeon, but the whole treatment team that has to be familiar with the specialized care. An example of this complex care is Chapter 11 in which a niche group of patients with Ehlers-Danlos and abdominal wall hernias was treated.

Finally, both point addressed above should lead to abdominal wall surgery as a subspecialty in surgery. Currently, surgeons of many different backgrounds perform abdominal wall hernia surgery. This does not have to change, but more formal recognition of the complexity of the topic will lead to a higher level of surgical care of abdominal wall hernia patients.

Classification of hernias

As mentioned in the introduction of this thesis, there is an enormous heterogeneity within the concept 'abdominal wall hernia'. To make fair comparisons and to evaluate treatment strategy, hernias have to be classified or subdivided. The biggest challenge of these kinds of classifications is the basis on which such classification should be made: it can be made on the hernia characteristics, the patient characteristics, or the surgical characteristics. In addition to these factors, the aim of the classification will also define it: is it a preoperative planning tool or is it based merely on postoperative outcomes such as postoperative complications or hernia recurrence?

In the past decade, amongst others, two widely used classifications have been developed:

the Ventral Hernia Working Group (VHWG) grading scale[17] and the EHS Classification.[18] More recently, Petro et al.[19] developed a new approach: as an analogy to the TNM staging system for malignancies, they developed their Ventral Hernia Staging System. One of the essentials of the TNM staging system is that is keeps evolving according to new clinical developments.[20, 21] Future research will demonstrate if this system is also applicable for hernia classification and hernia research.

Patient centered outcomes

The most important outcome measures in abdominal wall hernia research could be debated. Currently, most hernia research uses hernia occurrence or recurrence as their primary outcome measure. This is understandable, but it might not be the best outcome measure. Most patients do not present themselves with a complaint of a hernia, but with complaints like discomfort, pain, bulging, or bowel obstruction. Hernia research should use those kinds of patient reported outcomes measures (PROMs) as primary outcome measures. More recent studies include this kind of PROMs as outcomes, but most often, they are not considered as primary outcome and the studies are not powered to draw any conclusions on them. Because it would require far larger studies, prospective registries might be the solution for this topic.

Technical developments

Finally, new technical developments will also change abdominal hernia wall surgery. New physical simulation devices like the AbdoMAN will allow researchers and surgeons to test different techniques under similar circumstances. This may lead to a faster translation of theoretical ideas to practical treatment options. Until recently, translational research had to be performed in laboratory animals. This may change with the introduction of these kind of devices. This direction of research might even be extended with the addition of computer simulation models. Using data of physical experiments, preoperative and postoperative patient data might create prediction models that could support abdominal wall surgeons in their preoperative decision making.

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Summary
Nederlandse samenvatting
Contributors to this thesis
List of publications
PhD portfolio
Dankwoord
Curriculum vitae

Summary

This thesis addresses several aspects of abdominal wall hernia research.

Part I focuses on prevention and risk factors of incisional and parastomal hernias.

Chapter 2 reviewed the literature on incisional hernia prevention, focusing on laparotomy closure. Laparotomy closure should not be performed with mass closure, but with small bites (5 x 5 mm), continuous sutures. By doing so, the incisional hernia rate one year after surgery can be reduced from 20% to 11%. In high risk (i.e. obese patients or patients undergoing abdominal aortic aneurysm surgery), a prophylactic, onlay placed, polypropylene mesh should be advised.

In **Chapter 3** a systematic review was performed of literature reporting on different modalities of incisional hernia diagnosis. A total of fifteen studies, representing 2,986 patients, were included. Reported inter observer variation for CT-scan ranged from 11.2% to 69%. Reported disagreement between ultrasound and CT-scan ranged between 6.6% and 17%. Reported disagreement between physical examination and CT-scan ranged between 7.6% and 32%. Reported disagreement between physical examination and ultrasound ranged between 9% and 35%. Relative increase in incisional hernia prevalence compared to physical examination ranged from 0.92 to 1.8 for CT-scan and 1 to 2.4 for ultrasound. Given the wide ranges of all different modalities, no firm recommendation can be made on which modality to use. Moreover, it is of vital importance to report the number of patients diagnosed with a certain modality and the type of observer per modality.

In **Chapter 4** a systematic review and meta-analysis were performed of literature comparing extraperitoneal with transperitoneal colostomy for the prevention of parastomal hernia. Synthesis of the data of ten studies, comprising 1,048 patients, resulted in a reduction of parastomal hernia incidence from 17.8% to 6.3% and a reduction of stoma prolapse from 7.3% to 1.1%, without an increase of other stoma related complications like stoma necrosis.

Part II consists of chapters reporting on the treatment of simple abdominal wall hernias.

In **Chapter 5** 4,565 patients from a registry-based, nationwide, prospective cohort with primary and incisional ventral hernias were compared regarding patient-, hernia-, surgical, and postoperative characteristics. Patients with primary and incisional hernias are often pooled in studies, but the data of this study clearly shows that this is not justified. Primary and incisional hernia patients were different for almost all characteristics analyzed. This supports the hypothesis that these are different entities. Therefore, these patient groups should not be pooled in future research.

In **Chapter 6** the European Hernia Society (EHS) classification for incisional hernias was

validated as a risk factor for postoperative complications in a registry-based, nationwide, prospective cohort of 2,191 patients. Incisional hernia repair was associated with 15% complications. After multivariable analysis, EHS width class, incarceration, open surgery, duration of surgery, Altemeier wound class, and therapeutic antibiotic treatment were independent risk factors for postoperative complications. Third recurrence and emergency surgery were associated with fewer complications. Given the found association, the EHS classification is useful to identify patients at risk for complications.

In **Chapter 7** the European Hernia Society (EHS) classification for primary ventral hernias was validated for postoperative complications in a registry-based, nationwide, prospective cohort of 2,374 patients. Primary ventral hernia repair was associated with 4.4% complications. After multivariable analysis, age, BMI, and duration of surgery were independent risk factors. The hernia diameter was no independent risk factor. Given these results, age and BMI should be used in the preoperative patient risk assessment.

Chapter 8 consists of the EHS guidelines on the prevention and treatment of parastomal hernias. For the conception of these guidelines, the AGREE II standards and methodology proposed by the GRADE working group were used. There was insufficient evidence regarding the route and location of stoma construction and the size of the aperture. The use of a prophylactic synthetic non-absorbable mesh upon construction of an end colostomy was strongly recommended. No such recommendation could be made for other types of stomata at present. It was strongly recommended to avoid performing a suture repair for elective parastomal hernia. So far, there is no sufficient comparative evidence on specific techniques, open or laparoscopic surgery, and specific mesh types. No recommendation could be made on watchful waiting as treatment strategy.

In **Chapter 9** watchful waiting was compared with surgery as a treatment strategy in 80 patients with a parastomal hernia. Parastomal hernia repair was associated with high recurrence and reoperation rates. Watchful waiting had a relatively low cross-over (eight patients: 25%) and emergency surgery rate (one patient: 3%).

Part III covers the treatment of complex abdominal wall hernias.

In **Chapter 10** a total of 46 patients with large, complex ventral hernias were operated using a self-gripping Parietex™ mesh (ProGrip™) placed in the retrorectus plane. After median follow-up of 25 months, two patients developed a recurrent hernia requiring reoperation. These results make this mesh a good choice for this difficult group of patients.

Chapter 11 describes a case series of 14 patients with Ehlers-Danlos syndrome who underwent ventral hernioplasty. All hernias were treated as larger hernias, considering the patients' syndrome. After a median follow-up of 50 months, one patient (7.1%) developed a recurrence. This low recurrence could be explained by the use of a relatively large mesh. The use of a large mesh might increase the midline reinforcement and thus compensate for the

reduced collagen strength.

Chapter 12 is a study protocol of a prospective study that looks at the use of a biosynthetic, slowly resorbable mesh in patients with Ventral Hernia Working Group Grade 3 hernias. In total, 85 patients will be included in the study. Fifteen hospitals across Europe will participate in the study. The primary outcome is Surgical Site Occurrence (SSO) including hematoma, seroma, infection, dehiscence and fistula formation (requiring intervention) through three months. It was hypothesized that a non-synthetic mesh could be beneficial in this group of patients.

Part IV describes new developments in abdominal wall hernia research.

In **Chapter 13** a completely new device, the AbdoMAN, is demonstrated. The AbdoMAN was developed to investigate laparotomy closure techniques. It was demonstrated that the AbdoMAN is capable of simulation normal human physiological circumstances. By doing so, it can be used to study suture techniques and mesh fixation techniques, also avoiding the use of laboratory animal research. In the future, it might be used for training purposes as well.

Nederlandse samenvatting

In dit proefschrift worden meerdere aspecten van het onderzoek naar buikwandhernia's belicht.

In **Deel I** ligt de nadruk op de preventie van en de risicofactoren op het ontwikkelen van littekenbreuken en parastomale hernia's.

Hoofstuk 2 geeft een overzicht van de literatuur over de preventie van littekenbreuken met de nadruk op het sluiten van de laparotomiewond. Dit sluiten moet niet gebeuren met de 'mass closure' techniek, maar met de 'small bites' (5 x 5 mm) techniek met voortlopende hechtingen. Door aldus te doen kan de incidentie van littekenbreuken na een mediane laparotomie verlaagd worden van 20% naar 11%. Voor hoogrisicopatiënten (patiënten met obesitas of patiënten, die een operatie ondergaan voor een aneurysma van de abdominale aorta) wordt aanbevolen om een profylactische polypropyleen mat te plaatsen, bij voorkeur in de onlay-positie.

In **Hoofdstuk 3** wordt een overzicht van de literatuur gegeven over de verschillende modaliteiten om een littekenbreuk te diagnosticeren. In totaal werden vijftien studies, met een totaal van 2986 patiënten, geïncludeerd. De inter-observer variatie voor CT-scans varieerde van 11.2 tot 69%. Verschillen tussen echo en CT-scan varieerden tussen 6.6% en 17%. Verschillen tussen lichamelijk onderzoek en CT-scan varieerden tussen 7.6% en 32%. Verschillen tussen lichamelijk onderzoek en echo varieerden tussen 9% en 35%. De relatieve toename in de prevalentie van littekenbreuken vergeleken met lichamelijk onderzoek varieerde van 0.92 tot 1.8 voor de CT-scan en van 1 tot 2.4 voor de echo. Gezien de grote variatie bij alle modaliteiten kunnen er geen harde conclusies worden getrokken over welke modaliteit het beste gebruikt kan worden. De resultaten benadrukken het belang van het rapporteren van de aantallen patiënten, die met een bepaalde modaliteit zijn onderzocht en door wat voor onderzoeker dit is gedaan.

Hoofdstuk 4 is een systematisch review en meta-analyse van studies, die het extraperitoneaal aanleggen van een eindstandig colostoma vergelijken met het transperitoneaal aanleggen van een eindstandig colostoma ter preventie van het optreden van parastomale hernia's. De samengevoegde data van deze studies leiden tot een reductie van de incidentie van parastomale hernia's van 17.8% naar 6.3%. De incidentie van stomaprolaps daalde van 7.3% naar 1.1%. Er was geen toename in het optreden van andere stomagerelateerde complicaties zoals stomanecrose.

Deel II gaat over de behandeling van eenvoudige buikwandhernia's.

Hoofdstuk 5 vergelijkt 4595 patiënten met primaire of littekenbreuken uit een nationaal,

prospectief registercohort. Patiënt- en herniakarakteristieken, operatieve data en postoperatieve uitkomsten werden vergeleken. De patiënten verschilden op bijna alle factoren, die werden onderzocht. Dit ondersteunt de hypothese dat primaire breuken en littekenbreuken verschillend zijn. Om deze reden moeten deze patiëntgroepen in toekomstige studies dan ook niet samengevoegd worden.

In **Hoofdstuk 6** wordt de classificatie van de European Hernia Society (EHS) gevalideerd als risicofactor voor het ontwikkelen van postoperatieve complicaties na een operatieve littekenbreukcorrectie. Hiervoor werden 2191 patiënten uit een nationaal, prospectief registercohort geanalyseerd. Littekenbreukcorrecties waren geassocieerd met 15% postoperatieve complicaties. Na multivariabele analyse bleven de EHS breedteklasse, incarceratie, open chirurgie, operatieduur, de Altemeier wondklasse en therapeutisch antibioticagebruik onafhankelijke risicofactoren voor postoperatieve complicaties. Een derde recidief en een spoedoperatie waren geassocieerd met minder complicaties. Gezien de gevonden associaties is de EHS classificatie en dan vooral de breedteklasse, bruikbaar om patiënten te identificeren, die een verhoogd risico hebben op postoperatieve complicaties.

In **Hoofdstuk 7** wordt de classificatie van de European Hernia Society (EHS) gevalideerd als risicofactor voor het ontwikkelen van postoperatieve complicaties na een operatieve correctie van primaire buikwandbreuken. Hiervoor werden 2374 patiënten uit een nationaal, prospectief registercohort geanalyseerd. Operatieve correctie van een primaire buikwandbreuk was geassocieerd met 4.4% complicaties. Na multivariabele analyse waren leeftijd, BMI en de operatieduur onafhankelijke risicofactoren voor het ontwikkelen van postoperatieve complicaties. De diameter van de breuk was geen risicofactor. Gezien deze resultaten moeten leeftijd en BMI van een patiënt meegenomen worden in de preoperatieve risicoinschatting.

In **Hoofdstuk 8** worden de EHS richtlijnen voor de preventie en behandeling van parastomale hernia's opgevoerd. Voor de totstandkoming van deze richtlijnen werden de AGREE II-standaarden en methodologie, zoals voorgesteld door de GRADE-werkgroep, gebruikt. Er is onvoldoende bewijs voor een specifieke techniek voor de constructie van het stoma en voor een bepaalde grootte van de opening in de buikwand. Het gebruik van een profylactische synthetische niet-absorbeerbare mesh bij een eindstandig colostoma wordt sterk aanbevolen. Deze aanbeveling kan niet voor andere types stomas worden gedaan. Het wordt sterk aanbevolen om het primair sluiten als behandelingstechniek te vermijden. Er is nog onvoldoende bewijs om specifieke technieken, open of laparoscopische benadering of type matten te kunnen vergelijken. Er kan geen aanbeveling worden gedaan over een 'watchful waiting' strategie.

In **Hoofdstuk 9** wordt 'watchful waiting' in een groep van 80 patiënten vergeleken met chirurgie als behandeling van een parastomale hernia. De chirurgische behandeling was geassocieerd met een hoog recidiefpercentage en veel heroperaties. 'Watchful waiting' leidde tot relatief weinig operaties (acht patiënten, 25%) en tot weinig spoedoperaties (één patiënt,

3%). 'Watchful waiting' is mogelijk een geschikte behandelingsoptie voor patiënten met weinig klachten of met comorbiditeit.

Deel III gaat over de behandeling van complexe buikwandhernia's.

In **Hoofdstuk 10** worden 46 patiënten met grote, complexe buikwandhernia's geopereerd met een 'self-gripping' Parietex™ mesh (ProGrip™). De mat werd in de retromusculaire positie geplaatst. Na een mediane follow-up van 25 maanden hadden twee patiënten een recidief hernia ontwikkeld die een heroperatie vereiste. Deze resultaten maken de self-gripping mesh een geschikte behandelingskeuze voor deze complexe patiëntengroep.

In **Hoofdstuk 11** worden 14 patiënten beschreven met het Ehlers-Danlos syndroom die geopereerd werden aan een primaire of littekenbreuk. Alle hernia's werden behandeld alsof het grotere hernia's waren. Na een mediane follow-up periode van 50 maanden ontwikkelde één patiënt (7.1%) een recidief. Het gebruik van een grotere mesh kan mogelijk dit lage recidiefpercentage verklaren. Een grotere mat leidt tot een toegenomen versterking van de linea alba, die de verminderde sterkte van het collageen compenseert.

Hoofdstuk 12 is een studieprotocol voor een prospectieve studie, waarin gekeken wordt naar het gebruik van een biosynthetische, langzaam oplosbare mesh in patiënten met een Ventral Hernia Working Group Graad 3-hernia. In totaal zullen 85 patiënten in vijftien ziekenhuizen door heel Europa worden geïncludeerd. Als primair eindpunt is 'Surgical Site Occurrence' (SSO) gedurende de eerste drie postoperatieve maanden gekozen. Hieronder vallen hematoom, seroom, infectie, dehiscentie en fistelvorming. De hypothese luidt dat een niet-synthetische mesh in deze patiëntengroen betere resultaten zal opleveren dan een synthetische mesh.

Deel IV gaat over nieuwe ontwikkelingen in hernia-onderzoek.

In **Hoofdstuk 13** wordt een geheel nieuw apparaat, de 'AbdoMAN' gedemonstreerd. De AbdoMAN is ontwikkeld om onderzoek te doen naar sluittechnieken van de mediane laparotomie. Dit apparaat blijkt in staat om de fysiologische omstandigheden van de humane buik na te bootsen. Hiermee kan zonder van proefdieren gebruik te hoeven maken onderzoek gedaan worden naar hechttechnieken of matfixatie. In de toekomst kan de AbdoMAN ook gebruikt worden voor opleidingsdoeleinden.

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A. Jänes, Sundsvall Hospital, Sundsvall, Sweden (Chapter 8)
J. Jeekel, Erasmus MC Rotterdam, the Netherlands (Chapters 1, 2, 4, 6, 9, 10, 12, 13)
L.N. Jorgensen (Chapter 12)
F. Köckerling, Charité Universitätsmedizin Berlin, Germany (Chapters 8, 12)
G.J. Kleinrensink, Erasmus MC Rotterdam, the Netherlands (Chapters 2-7, 9, 10, 13)
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J.R. Lambrecht, Innlandet Hospital Trust, Gjřvik, Norway (Chapter 8)
D.P.V. Lambrichts, Erasmus MC Rotterdam, the Netherlands (Chapter 9)
J.F. Lange, Erasmus MC Rotterdam, the Netherlands (Chapters 1-7, 9-13)
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C. Mariette, University Hospital of Lille, France (Chapter 8)
M. Miserez, UZ Leuven, Belgium (Chapters 8, 12)
E.H.H. Mommers, Maastricht University Medical Center, the Netherlands (Chapter 11)
A. Montgomery, Skĺne University Hospital, Malmö, Sweden (Chapter 8)
S. Morales-Conde, University Hospital Virgen del Rocío, Sevilla, Spain (Chapter 8)
F.E. Muysoms, Maria Middelares Hospital, Ghent, Belgium (Chapters 3 and 8)
C. Ordrenneau, Medtronic Trévoux, France (Chapter 13)
M. Prudhomme, CHU Nîmes, France (Chapter 8)
T. Rautio, Oulu University Hospital, Oulu, Finland (Chapter 8)
C. Robbens, UZ Gent, Belgium (Chapter 11)
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N.J. Smart, Royal Devon and Exeter Hospital, Exeter, UK (Chapter 8)
G.H.J. de Smet, Erasmus MC Rotterdam, the Netherlands (Chapter 4)
M. Śmietański, Medical University of Gdansk, Poland (Chapter 8)
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F. Turquier, Medtronic Trévoux, France (Chapter 13)
J. Verhelst, Ikazia Ziekenhuis Rotterdam, the Netherlands (Chapters 10 and 13)
T.S. de Vries Reilingh, Elkerliek Hospital Helmond, the Netherlands (Chapter 12)

List of publications

Kroese LF, Gillion JF, Jeekel J, Kleinrensink GJ, Lange JF. *A comparison of patient characteristics and postoperative complications of primary and incisional ventral hernias - a prospective cohort study of 4,565 patients.* International Journal of Surgery 2018

Kroese LF, Mommers EH, Robbens C, Bouvy ND, Lange JF, Berrevoet F. *Complications and recurrence rates of patients with Ehlers-Danlos undergoing ventral hernioplasty – a case series* Hernia 2018

Kroese LF, Gillion JF, Kleinrensink GJ, Lange JF. *The European Hernia Society Classification For Primary Abdominal Wall Hernias Is An Independent Predictor For Postoperative Complications After Incisional Hernia Repair, A Prospective Cohort Study Of 2,300 Patients* SURGERY 2018

Kroese LF, Sneiders D, Muysoms FE, Kleinrensink GJ, Lange JF. *Systematic review of different modalities to diagnose incisional hernias.* Hernia 2018

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Kroese LF, Van Eeghem KHA, Verhelst J, Jeekel J, Kleinrensink GJ, Lange JF. *Long term results of open complex abdominal wall hernia repair with a self-gripping mesh, a retrospective cohort study*. International Journal of Surgery 2017

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Vakalopoulos KA, Wu Z, **Kroese LF**, Jeekel J, Kleinrensink GJ, Dodou D, Lam KH, Lange JF. *Sutureless closure of colonic defects with tissue adhesives: an in-vivo study in the rat*. American Journal of Surgery 2016

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Boersema GS, Wu Z, **Kroese LF**, Vennix S, Bastiaansen-Jenniskens YM, van Neck JW, Lam KH, Kleinrensink GJ, Jeekel J, Lange JF. *Hyperbaric oxygen therapy improves colorectal anastomotic healing*. International Journal of Colorectal Disease 2016

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Kühlmann AYR, De Rooij A, **Kroese LF**, Van Dijk M, Hunink MGM, Jeekel J. *Perioperative music reduces anxiety and pain in adults: A systematic review and meta-analysis*. Submitted

Van Rooijen MMJ, Jairam AP, Tollens T, Jörgensen LN, De Vries Reilingh TS, Piessen G, Köckerling F, Miserez M, Windsor ACJ, Berrevoet F, Fortelny RH, Dousset B, Woeste G, Van Westreenen HL, Gossetti F, Lange JF, Tetteroo GWM, **Kroese LF**, Jeekel J. *A Post-Market, Prospective, Multi-Center, Single-Arm Clinical Investigation of PhasixTM Mesh for VHWG Grade 3 Midline Incisional Hernia Repair.* Submitted

Book chapters

Kroese LF, Lange JF, Jeekel J. *Hernia Prevention and the Importance of Laparotomy Closure*. In Hope W, Cobb W, Textbook of Hernia.

Kroese LF, Lange JF, Jeekel J. *Definitive closure, long-term results and management of ventral hernia*. In Coccolini, Ivatury, Sugrue and Ansaloni, Open Abdomen: A comprehensive practical manual.

PhD Portfolio Leonard Frederik Kroese MSc

Name PhD student: L.F. Kroese	**PhD period:** 2015-2018
Erasmus MC department: Surgery	**Promotors:** prof.dr. G.J. Kleinrensink and prof.dr. J.F. Lange
	Supervisor: prof.dr. J. Jeekel

1. PhD training	**Year**	**Workload**	
		Hours	**ECTS**
General courses			
Biomedical English Writing and Communication	2017		3
Scientific Integrity	2017		0.3
Specific courses			
Laboratory animal science (Artikel 9)	2016		3
(Inter)national conferences			
Wetenschapsdag AAV Erasmus MC	2015	8	1
Najaarsdag NVvH	2015	8	1
Wetenschapsdag Heelkunde Erasmus MC	2015	8	1
NVvH Chirurgendagen (oral presentation)	2016		1
European Society for Surgical Research (oral presentation)	2016		1
European Hernia Society (oral presentation)	2016		1
Najaarsdag NVvH	2016		1
Wetenschapsdag Heelkunde Erasmus MC	2017		1
Controversies in Hernia Surgery (2 oral presentations)	2017		2
American Hernia Society (oral and poster presentation)	2017		2
NVvH Chirurgendagen (oral presentation)	2017		1
European Hernia Society (oral presentation)	2017		1
MESH Congress (oral presentation)	2017		1
Hernia Prevention	2017		1
Other			
Organising committee EHS Congress 2016	2016		3
Member of the committee developing 'European Hernia Society Guidelines on Prevention and Treatment of Parastomal Hernias'	2016		2

2. Teaching	**Year**	**Workload**	
		Hours	**ECTS**
Lecturing			
Teaching anatomy to medical students	2015-2016	10	0,5
Supervising Master's theses			
Machteld van Rooijen	2017		1
Dimitri Sneiders	2017		1
Other			
Resuscitation exams Faculty of Medicine, Erasmus MC	2016-2017		1
TOTAL			**30,8**

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Voor de totstandkoming van dit proefschrift ben ik vele mensen dank verschuldigd. In het bijzonder wil ik de volgende mensen bedanken:

Mijn promotor, professor Kleinrensink: sinds de periode in het snijzaalteam was er altijd wel wat te beleven, of het nou ging om het bestellen van nieuwe afvalbakken of de audities voor het NSO. Toen ik de draai maar niet te pakken kreeg met de studie was jij het die op een bepaald moment mailde: "Het is misschien een idee om een keer bij te praten, rustig op mijn kamer met de beroemde Colombiaanse espresso." Hierna is het één grote stijgende lijn gebleken. Dat ik onderzoek zou komen doen bij de REPAIR was onvermijdelijk en ik heb er geen seconde spijt van gehad.

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Lieve Myrthe, het is zo geweldig om samen met jou te zijn. Ik heb nu al zin in wat er allemaal nog gaat komen.

Curriculum vitae

Leonard Kroese was born in Utrecht on April 14th 1986. He grew up in Leusden and graduated from the Stedelijk Gymnasium Johan van Oldenbarnevelt (VWO Gymnasium) in Amersfoort. After this, he commenced his medical training at the Erasmus University Rotterdam. During his school and study period, Leonard was an active participant as a violinist during multiple chamber music and orchestra projects, including the International Orlando Festival, Nederlands Studenten Kamerorkest (Nesko) and Nederlands Studentenorkest (NSO). Leonard was a board member of the NSO for the period of one year in 2010.

During his activities in the student team at the Anatomy Department of the Erasmus MC, Leonard joined the REPAIR Research Group (supervisors: prof.dr. J. Jeekel, prof.dr. J. Lange, prof.dr. G.J. Kleinrensink, and dr. A. Menon). He finished his elective research project with this group.

Following his clinical rotations, he obtained his medical degree in April 2015. Directly after his graduation, Leonard started as a PhD-candidate with the REPAIR Research Group. In 2016, he was part of the organising committee of the European Hernia Society Congress in Rotterdam. For his research projects, he collaborated with both private and public parties from the Netherlands, Belgium, and France. Research from this period has led to this thesis. Since September 2017, Leonard is working as a resident not in training (ANIOS) at the Department of Surgery of the Maasstad Hospital (Rotterdam) under supervision of drs. R.A. Klaassen.

He will start his surgical training on the 1st of July in the Reinier de Graaf Hospital (Delft) under supervision of dr. M. R. de Vries.