Optimizing Inguinal Hernia Surgery

Wouter J. Bakker

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Optimizing Inguinal Hernia Surgery
PhD thesis, Utrecht University, the Netherlands

Printing of this thesis was financially supported by Applied Medical, Chipsoft, CoMedical BV, Diakademie, Dutch Hernia Society, Medilead, KNVB Sportmedisch Centrum, OviTex™ by GD Medical, Stichting Wetenschap Chirurgie Diakonessenhuis, Synappz Digital Healthcare, and UMC Utrecht Cancer Center.

ISBN 978-94-6423-352-0

Cover and layout Vera van Beek || www.proefschriftmaken.nl
Printing ProefschriftMaken || www.proefschriftmaken.nl

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Optimizing Inguinal Hernia Surgery

Het optimaliseren van liesbreukchirurgie
(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht,
op gezag van de rector magnificus, prof. dr. H.R.B.M. Kummeling,
ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen
op donderdag 30 september 2021 des middags te 12:15 uur

door

Wouter Jesse Bakker
geboren op 26 januari 1992
te Utrecht

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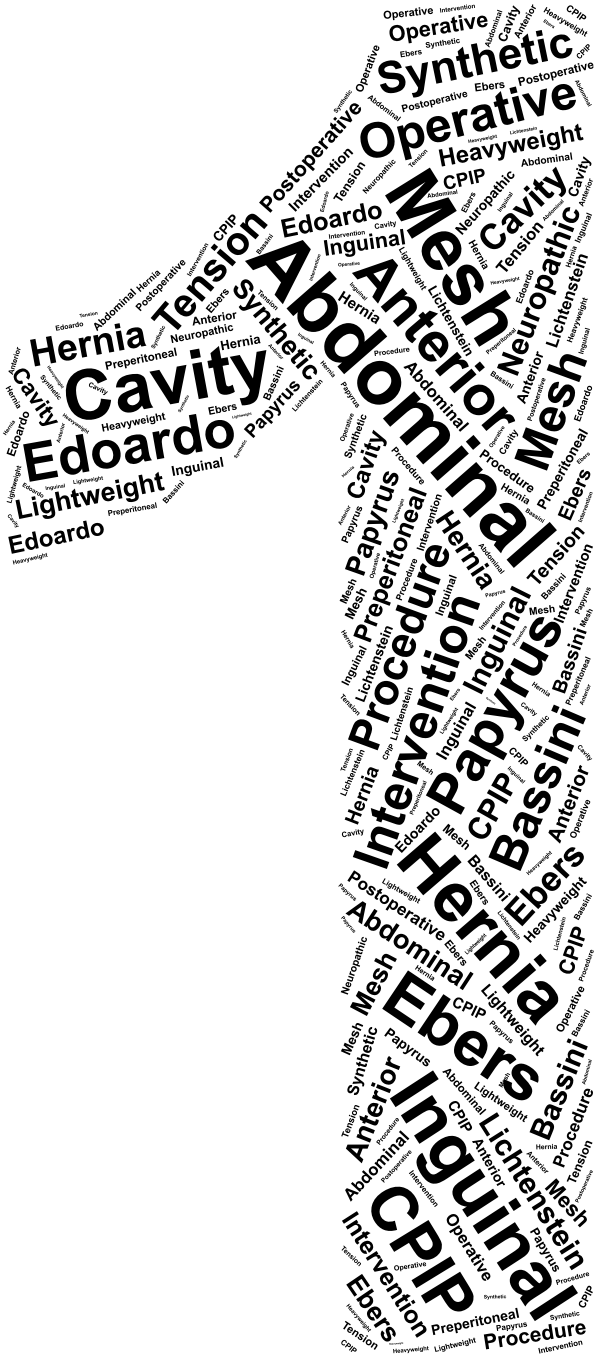
Abdominal
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Edoardo
Hernia
Inguinal
Mesh
Operative
Synthetic
Tension
Anterior
Bassini
CPIP
Ebers
Heavyweight
Intervention
Lightweight
Lichtenstein
Neuropathic
Papyrus
Postoperative
Preperitoneal
Procedure

General introduction and thesis outline

General introduction

An inguinal hernia is a protrusion of abdominal-cavity contents through a defect in the abdominal wall. An inguinal hernia can be classified as direct, medial to the inferior epigastric vessels; indirect, lateral to the inferior epigastric vessels and through the internal inguinal ring; or femoral, below the inguinal ligament and through the femoral canal (Figure 1). The lifetime occurrence of inguinal hernias is 27-43% in men and 3-6% in women.[1] An inguinal hernia repair is the most commonly performed elective surgical intervention worldwide with over 20 million procedures annually, and approximately 30.000 in the Netherlands.[1, 2] Therefore, optimizing inguinal hernia surgery is of far-reaching significance to surgeons and patients worldwide.

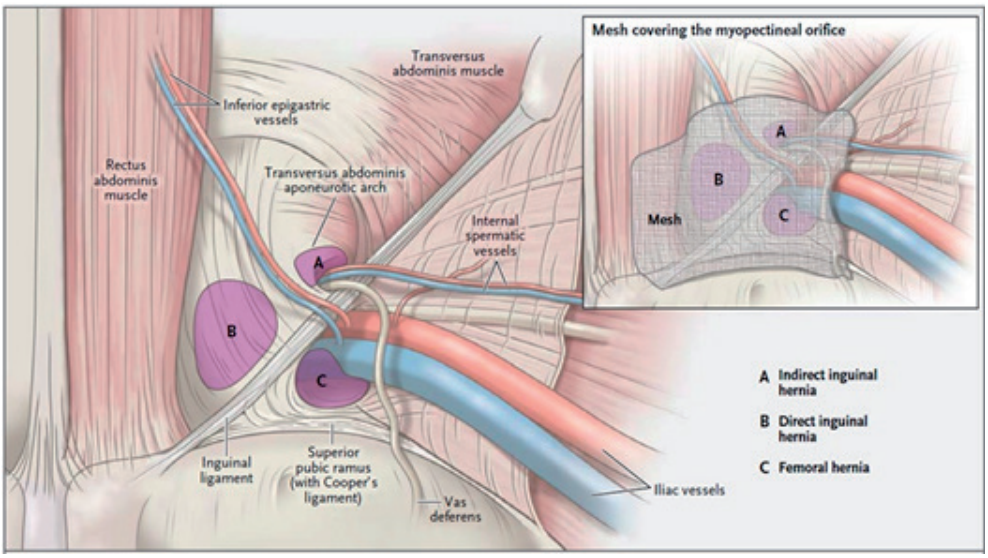

Figure 1 Classification of inguinal hernias

Reducing inguinal hernia recurrences

Inguinal hernia surgery reaches back to literature of the antiquity, as reported in the Ebers papyrus (1550 BC) by Greek and Egyptian surgeons.[3] Improvement of inguinal hernia repairs rapidly gained momentum when anatomy studies were performed during the sixteenth century.[4] As a result, inguinal hernia treatment went through many phases, from red-hot iron cauterization or instilling acidic chemicals for solid scar formation, to hernial sack ligation at the external inguinal ring, until in 1877 the German surgeon Vinzenz von Czerny performed the first operative procedure that narrowed the external ring of the inguinal canal (Czerny's suture).[5] Nevertheless, this reinforcement technique of the anterior wall resulted in high recurrence rates of about 100%. This led to a revelation in 1889 by the

surgeon Edoardo Bassini, which is still the basis for our present-day inguinal hernia repair: Reinforcement of the posterior wall of the inguinal canal and narrowing the internal inguinal ring.[6] With recurrence rates lowered to 10-30%, the surgical community now aimed to overcome the problem of tension on the suture line, which they were confronted with as the predominant cause of recurrences. In 1958 the concept of suturing the defect was abandoned by the American surgeon Usher with the introduction of synthetic mesh to cover the defect, thereby introducing a tension-free open anterior inguinal hernia repair.[7] In 1964 the American surgeon Lichtenstein developed a variant, reducing recurrences to 2-4%, which became the gold standard and still is the most frequently performed open repair technique for inguinal hernias (Figure 2).[8]

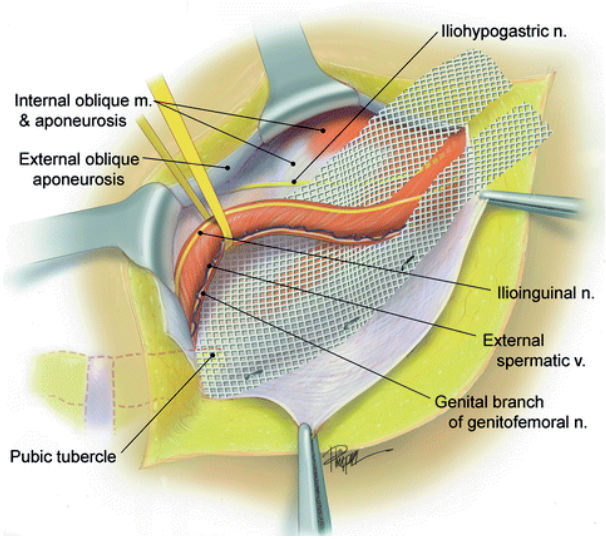

Figure 2 The Lichtenstein technique

Chronic postoperative inguinal pain

With the impressive decrease in recurrences, the most common disabling complication of inguinal hernia repairs shifted to chronic postoperative inguinal pain (CPIP) and mesh induced foreign body feeling.[9] CPIP is defined as inguinal pain lasting more than 3 months after surgery.[10, 11] The experienced CPIP or foreign body feeling can be due to neuropathic pain that derives from operative inguinal nerve injury, or nociceptive pain through a mesh-induced inflammatory response with subsequent formation of fibrosis.[12] The growing awareness of CPIP causes and anatomy of the groin enabled surgeons to decrease the incidence of CPIP in open anterior hernia repair by intraoperative identification and preservation of all three inguinal nerves (Figure 2).[13] Currently overall, clinically significant chronic pain is present in 10–12% of patients, and affects normal daily activities or work in 2-20% of patients, decreasing over time.[11, 14, 15]

Preperitoneal inguinal hernia repair

The next breakthrough in the history of inguinal hernia surgery was the introduction of laparo-endoscopic techniques with a posterior preperitoneal approach to the hernia defect.[16] The first endoscopic repair in the Netherlands was performed in 1991.[17] Laparo-endoscopic mesh repairs had persistent low recurrence rates and resulted in a faster postoperative recovery with reduced complications, shorter hospital stay, and faster return to daily activities, work and sports.[18, 19] Additionally, a reduction in chronic pain and foreign body feeling was accomplished by using a preperitoneal mesh that avoids direct contact with the inguinal nerves, compared to anterior repairs that place an intermuscular mesh adjacent to the inguinal nerves (Figure 2, 3). Two different laparo-endoscopic approaches are in widespread use: the totally extraperitoneal (TEP) and trans-abdominal preperitoneal (TAPP) inguinal hernia repair. In both, a mesh is inserted in the preperitoneal plane, however, the plane is accessed differently. When performing a TEP repair, an endoscopic totally preperitoneal approach is used, leaving the intra-abdominal cavity unopened. In TAPP repairs, a laparoscopy is performed and the mesh is placed in the preperitoneal plane after the peritoneum is opened from intra-abdominally. Studies comparing TAPP and TEP showed similar complication rates and the superior technique cannot be decided on, therefore the preferred technique is dependent on the education and experience of the surgeon.[11] A relatively long learning curve is described for the TEP repair.[20, 21]

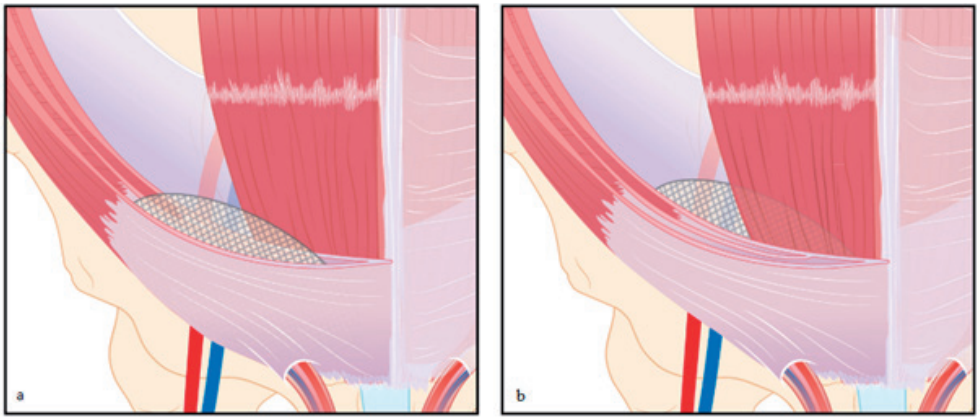

Figure 3 a = intermuscular mesh of Lichtenstein repair; b = preperitoneal mesh of laparo-endoscopic techniques

Lately, many different open preperitoneal mesh techniques have been developed as a result of commercial and technical considerations, e.g. the trans-inguinal preperitoneal repair (TIPP)[22], transrectus preperitoneal approach (TREPP)[23], the Onstep approach[24], the posterior Kugel technique[25], Wantz technique[26], Ugahary technique[27], and Rives' technique[28]. The TIPP, Rives, and Onstep techniques use an anterior dissection and open the inguinal canal to enter the preperitoneal space. The Kugel, TREPP, Ugahary, and Wantz techniques do not

enter the inguinal canal anteriorly and use an open repair with a posterior approach. Until now, these techniques should only be used in research settings, since there is no data to compare the individual approaches to each other and hence no recommendations can be made about the preferred technique.[11] However, from the limited available data open preperitoneal repairs are comparable to the Lichtenstein repair in terms of recurrences and possibly result in less postoperative pain and faster recovery.[11]

Mesh

The use of a prosthetic mesh has proven to be essential in inguinal hernia repair to decrease recurrences.[29, 30] However, a prosthetic mesh is a foreign body, which induces an inflammatory response resulting in fibrotic tissue formation that can be associated with CPIP, stiffness and the feeling of a foreign body, owing to inordinate tensile strength not proportionate to the flexibility of the local tissue.[31, 32] Traditionally, standard polypropylene mesh were used, however, as a result of the encountered mesh complications many different types of mesh with differing characteristics are presently commercially available. Currently no recommendations on the superior type of mesh can be made. A comparison of different mesh is difficult since many mechanical mesh properties (weight, pore size, elasticity, effective porosity, strength, and type of polymer from which the mesh is made) might influence the tissue reaction and clinical consequences of this reaction. Throughout literature mesh are most commonly grouped in lightweight mesh or heavyweight mesh. Lightweight mesh might improve flexibility owing to the decrease in bridging of collagen in scar formation and presumably the decrease in the inflammatory reaction owing to their elasticity, macroporosity, and the incorporation of less foreign material in the tissue when compared to heavyweight mesh.[33, 34] However, lightweight mesh raise concerns of higher recurrence rates.

Patient-tailored inguinal hernia surgery

Individual inguinal hernia repair techniques have varying advantages and disadvantages that should be tailored to hernia- and patient characteristics. In many specific patient populations the treatment strategy is evident. For example, female patients should receive laparo-endoscopic surgery to attain peroperative overview and adequately detect femoral hernias and patients with primary bilateral inguinal hernias can undergo simultaneous contralateral repair when operated on laparo-endoscopically. Furthermore, in elderly patients with (pulmonary) comorbidities an open procedure under local anesthetics should be considered, and in patients with recurrent inguinal hernias anterior and posterior surgical approaches should alternate. However, specific patient populations remain in whom the treatment strategy or work-up is inadequate or unclear.

Follow-up after inguinal hernia surgery

In our present-day society, with persistently increasing health care costs and restricted health care budgets, cost-efficiency is high on the agenda and optimization of inguinal hernia

surgery should no longer only focus on clinical outcomes. Follow-up after inguinal hernia surgery is performed with a patient-related purpose, for data registration for internal quality control and national- and international benchmarking, and in research settings. Consensus of regular follow-up (not in research settings) after inguinal hernia surgery is lacking. In the Netherlands there is substantial inter-hospital variability concerning the organization of follow-up after inguinal hernia surgery. Therefore, patients are unnecessarily burdened and surgeons and not time- and cost-efficient.

Specialized hernia centers

To further effectuate cost-efficiency and reduce complications, our present-day organization of healthcare encourages the centralization of care and the outsourcing of surgical procedures to specialized centers. Correspondingly, laparo-endoscopic inguinal hernia repair has favorable outcomes in specialized high-volume hernia centers.[35, 36] All studies described in this thesis were performed in a high-volume TEP hernia center in the Netherlands. In 2005 the Hernia Clinic of the Diakonessenhuis Utrecht/Zeist was founded and currently 5 inguinal hernia surgeons, that have completed the learning curve, perform approximately 1500 procedures annually. Research from our institution has contributed to the current national and international guidelines of inguinal hernia surgery. The aim of this thesis is to further optimize inguinal hernia patient care.

Thesis outline

Although inguinal hernia surgery has a rich scientific history, many questions regarding the optimal treatment of inguinal hernia patients remain unanswered. This thesis focuses on three key-aspects of present-day treatment of inguinal hernia patients. In **Part I** the current clinical practice with regard to the preferred type of mesh is discussed. In **Part II** the use of TEP repair for three specific patient populations is optimized: young inguinal hernia patients, athletes with inguinal disruption, and inguinal hernia patients in the work-up for a radical prostatectomy. **Part III** focusses on optimizing follow-up after inguinal hernia surgery.

A randomized controlled trial (RCT) compared the Ultrapro® lightweight mesh with the Prolene® heavyweight mesh in endoscopic TEP inguinal hernia repair for recurrences, chronic pain, foreign body feeling and quality of life (TULP-trial). At 3 months, 1 year and 2 years of follow-up beneficial results of using a lightweight mesh for endoscopic inguinal hernia surgery could not be established, and significantly more recurrences were seen in the lightweight mesh group. In **Chapter 3** the five-year follow-up results of this RCT are reported. **Chapter 2** and **Chapter 4** provide an update on the available RCTs comparing lightweight- and heavyweight mesh for, respectively, open inguinal hernia repair and laparo-endoscopic inguinal hernia repair, including the long-term results of the TULP-trial. The aim of the systematic reviews with meta-analyses is to provide a (definite) recommendation on using lightweight mesh or heavyweight mesh.

Known risk factors for CPIP after inguinal hernia surgery have long been young age, female gender, high preoperative pain level, early high postoperative pain, recurrent hernia, and open repair. However, *young age* remains undefined. Moreover, studies discussing young age as a risk factor for CPIP are based on open repair, and studies for endoscopic repair are barely available. Since endoscopic TEP inguinal hernia repair results in a significantly lower incidence of CPIP compared to open repair, it remains unclear if a young age is a risk factor for CPIP and a contra-indication for TEP repair. The aim of **Chapter 5** is to determine if young adults (18–30 years) are more prone to experience CPIP after TEP repair compared to adults of ≥31 years of age.

Many athletes suffer from chronic groin pain. When no clear pathology exists inguinal disruption might be present, defined as pain, predominantly in the groin area, either of insidious or acute onset, when no other obvious pathology explains the symptoms. In these patients a period of rest and/or physiotherapy is indicated, although if the results are insufficient a TEP repair that reinforces the posterior abdominal wall could be meaningful. **Chapter 6** aims to evaluate the effect of TEP repair in athletes with inguinal disruption, selected through a multidisciplinary, systematic work-up.

There is a demographic overlap of inguinal hernia patients and prostate cancer patients considering the lifetime occurrence and increasing frequency of diagnosis in the aging male. Previous laparo-endoscopic inguinal hernia mesh repairs might cause complications of subsequent radical prostatectomies due to adhesions and distortion of anatomic planes. In **Chapter 7** the experience of urological surgeons on the safety and feasibility of performing radical prostatectomies after laparo-endoscopic inguinal hernia mesh repair is assessed, and we discuss the role of surgeons regarding inguinal hernia patients that are in the work-up for a radical prostatectomy.

In **Chapter 8** patient satisfaction, and the methodology and purpose of follow-up after inguinal hernia surgery are evaluated. Follow-up can be performed by telephone instead of at the outpatient clinic, although this presents challenges for the assessment of recurrences in research settings or with the aim of data registration. In **Chapter 9** we describe our experience, and suggestions for enhancement, with a questionnaire that is designed and validated as a method of follow-up by telephone to detect recurrences. To overcome current monitoring limitations of inguinal hernia patients, follow-up can be performed by means of a smartphone and tablet application, which has incorporated preferred questionnaires. A smartphone application has the potential to substitute follow-up by phone or at the outpatient clinic, and to be nationally or internationally used for large-scale benchmarking and research. **Chapter 10** describes the protocol of the validation study of the promising and innovative Inguinal Hernia Application.

The studies of this thesis are summarized and discussed in **Chapter 11**. Furthermore, we discuss future perspectives for inguinal hernia surgery.

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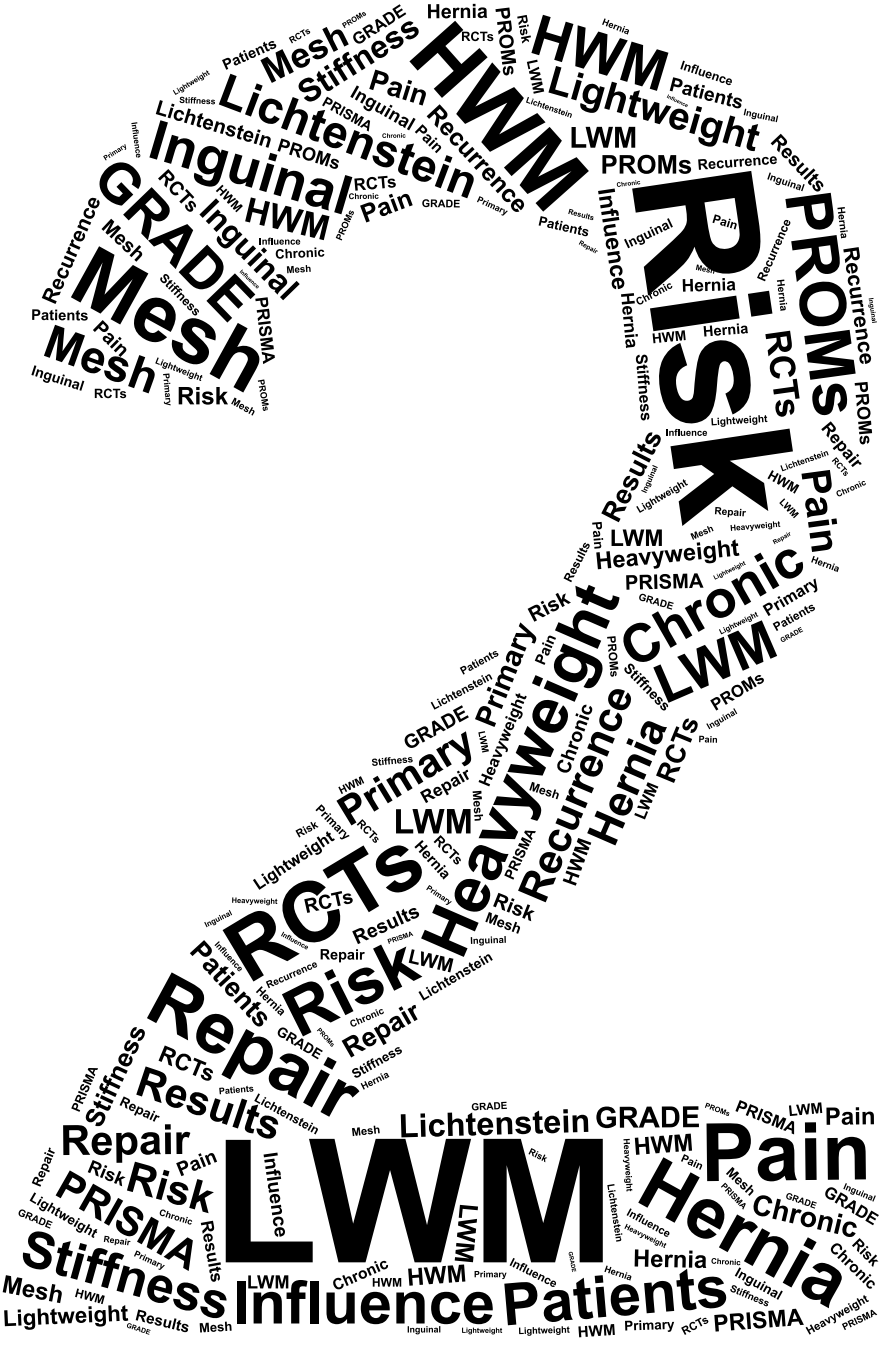
PART I

Part I

Optimizing the use of mesh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Patients
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Influence
Hernia
GRADE

Lightweight mesh is recommended in open inguinal (Lichtenstein) hernia repair: a systematic review and meta-analysis

WJ Bakker
TJ Aufenacker
JS Boschman
JPJ Burgmans

Surgery (2020) 167:581-589

Abstract

Background

The use of lightweight mesh (LWM) for inguinal hernia repair is probably preferable compared to heavyweight mesh (HWM). Nevertheless, surgeons do not use LWM routinely, possibly due to the higher price and lack of confidence in previous evidence syntheses. The aim of this systematic review and meta-analysis is to provide an update on the available randomized controlled trials (RCTs) and provide a recommendation on the use of LWM or HWM in open inguinal hernia repair.

Methods

A literature search was conducted in May 2019 in MEDLINE, Embase and the Cochrane library for RCTs comparing lightweight (≤50 g/m2) and heavyweight (>70 g/m2) mesh in patients undergoing open (Lichtenstein) surgery for uncomplicated inguinal hernias. Outcomes were recurrences (overall, after direct or indirect repair), chronic pain (analyzing any and severe pain) and foreign body feeling. The level of evidence was assessed using GRADE. Risk ratios (RR) and 95% confidence intervals (CI) were calculated by random effect meta-analyses.

Results

Twenty-one RCTs, encompassing 4,576 patients (LWM 2,257 versus HWM 2,319), were included. Follow-up ranged from 3 to 60 months. No difference between LWM and HWM was determined for recurrence rates (LWM 42/2,068 and HWM 34/2,132; RR 1.22; CI 0.76-1.96) or severe pain (LWM 14/1,517 and HWM 26/1,591; RR 0.73; CI 0.38-1.41). A significant reduction was seen for any pain after LWM (234/1,603) compared to HWM (322/1,683) (RR 0.78; CI 0.64-0.96) and foreign body feeling (LWM 130/1,053 and HWM 209/1,035; RR 0.64; CI 0.51-0.80).

Conclusion

LWM should be used in open (Lichtenstein) inguinal hernia repair.

Introduction

The Lichtenstein technique[1] with placement of a flat mesh is the most commonly performed open inguinal hernia repair.[2] The use of a prosthetic mesh has proven to be inevitable in inguinal hernia repair to reduce recurrences.[3,4] A prosthetic mesh is, however, a foreign body inducing an inflammatory response resulting in fibrotic tissue. This can be associated with stiffness and foreign body feeling, due to inordinate tensile strength not proportionate to the flexibility of the local tissue.[5] Moreover, in open inguinal hernia repair the surgical procedure, the mesh, the mesh induced scar tissue or the sutures may cause nerve irritation or damage to the inguinal nerves.[6-8]

An indecipherable number of commercially available mesh with differing characteristics are nowadays used. To compare different mesh, the weight, pore size, elasticity, effective porosity, strength and polymer type are all mechanical mesh properties that might influence tissue reaction and the clinical consequences of this reaction. From a pragmatic point of view, a comparison of mesh weight is most convenient and informative, as it has been the most researched characteristic. Lightweight mesh (LWM) might improve flexibility due to the reduction in collagen bridging in scar formation and presumably reduce the inflammatory reaction due to their elasticity, macro-porosity and the incorporation of less foreign material in the tissue when compared to heavyweight mesh (HWM).

Previous systematic reviews and meta-analyses summarizing the literature up until 2012 already showed the benefits of LWM on chronic pain and foreign body feeling and did not show higher recurrence rates.[9-11] Nevertheless, surgeons remain unconvinced and using LWM in the surgical community has not caught on, probably due to the higher price of LWM, the potential bias in previous meta-analyses and the remaining concerns of higher recurrence rates in large defects. Since the last systematic review on this topic, more than twice as many additional randomized controlled trials (RCTs) addressing the use of LWM versus HWM in patients undergoing open inguinal hernia repair have been published, demonstrating the ongoing urge to prove the safety and benefits of LWM and provide clear recommendations.

Therefore, the aim of this systematic review and meta-analysis is to provide an update on the available RCTs for the outcomes recurrences, chronic pain and foreign body feeling, and to provide a recommendation on the use of LWM or HWM in open inguinal hernia repair.

Methods

The systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[12] Details of the protocol for this systematic review were registered on PROSPERO (ID CRD42018100158).

Study selection

A literature search was conducted in May 2019, in MEDLINE, EMBASE and the Cochrane Library. The search was not limited by publication date or language. Studies needed to be published as full-length articles. The search strategy can be found in Supplemental Digital Content 1. All identified studies were transferred into EndNote (EndNote X8.2, Thomson Reuters, New-York) and subsequently into Rayyan (Qatar Computing Research Institute).[13] All duplicates were removed. Two independent reviewers (W.J.B. and J.S.B.) excluded non-relevant studies based on title and abstract and/or full-text screening. Any discrepancies were discussed between the 2 reviewers and the senior author (J.P.J.B). The reference lists of included RCTs were searched to identify additional studies that met the inclusion criteria. All RCTs that compared lightweight (≤50 g/m^2) and heavyweight (>70 g/m^2) mesh in patients undergoing open inguinal hernia repair (Lichtenstein) for uncomplicated inguinal hernias, using the same surgical technique in both groups, were included. Studies comparing either LWM or HWM to biological mesh were not included. The follow-up period had to be a minimum of 3 months and outcome parameters had to include either chronic pain or recurrences, or both. As elaborated on in the introduction, the weight of the mesh does not fully explain the properties of the mesh. Moreover, there is not one standardized weight definition for LWM or HWM. To achieve that most relevant mesh registered as lightweight or heavyweight were analyzed, cut-off points that are generally accepted of <50 g/m^2 for LWM and >70 g/m^2 for HWM were used.

Outcomes

The authors decided that chronic pain and recurrences were crucial outcome measures for decision-making. According to the International Association for the Study of Pain, chronic pain is defined as (inguinal) pain lasting a minimum of 3 months.[14] Any pain and severe pain (as defined by the authors of the RCTs) were assessed. Regarding recurrences, studies reporting any follow-up time-period after 3 months were assessed. Separate meta-analyses of the available data were performed to detect differences in recurrence rates between LWM and HWM after only indirect or only direct hernia repairs. Furthermore, the influence of the primary hernia defect size on recurrences for both mesh types was assessed. Foreign body feeling after a minimum of 3 months was regarded as the only clinically relevant secondary outcome parameter.

To analyze the influence of time to follow-up several sensitivity analyses were performed for chronic pain and foreign body feeling, therefore grouping the data in different follow-up periods of ≤6 months, ≤12 months, ≤24 months, ≥12 months and ≥24 months. For all outcomes separate sensitivity analyses were performed with only studies that used large pore (>1mm) LWM and without studies that had a high risk of bias, an inordinate loss to follow-up or with included recurrent inguinal hernias, the latter to correct for higher recurrence rates and a higher incidence of chronic pain after the repair of recurrent hernias.[15-17] To respect all available data and provide a complete insight, the shown forest plots presented the studies with their longest available follow-up and all studies included. If substantially different outcomes were seen after sensitivity analyses, the meta-analyses were presented in text.

Data extraction

The most important study characteristics and results were extracted from the original RCTs. Mesh characteristics were presented as described by the authors of the original studies. Interim analyses were excluded from the meta-analyses if longer follow-up data was available. Without exception, corresponding authors were contacted for additional information if no usable information for data pooling was published, so that bias relating to missing data could be avoided. For instance, when mean pain scores were published, authors were contacted to provide the number of patients with pain and the group sizes. If no response was given by the authors, or no requested additional data was available, the study was excluded from the meta-analysis of that particular outcome. In the subscript of the forest plots received unpublished data was denoted.

The quality of included studies was assessed using the Cochrane Handbook for Systematic Reviews of Interventions, version 5.1. Risk of bias was addressed by 2 independent reviewers (W.J.B. and J.S.B.) for method of randomization, concealment of allocation, blinding of patients, care providers and outcome assessors, selective outcome reporting (if available extracted from individual study protocols), loss to follow-up and violation of intention-to-treat analysis. Subsequently, the scoring system of Jadad et al. was used to assess the quality of the data.[18] A Jadad score under 3 was considered a high risk of bias. All reviewers agreed that blinding of care providers (operating surgeon) was impossible due to visible differences between lightweight and heavyweight mesh. Therefore, in the Jadad scoring system, the blinding of patients and outcome assessors was considered to be double blind. Loss to follow-up was considered a risk of bias when >15.0% were lost for follow-up <24 months, and when >20.0% were lost for follow-up >24 months. The level of evidence for each outcome was further evaluated using chapter 5 of the GRADE Handbook (Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group, Cochrane Collaboration).[19]

Statistical analysis

The estimate of the difference between both mesh was pooled using Review Manager, version 5.3 (Cochrane Collaboration, Copenhagen, Denmark). If pooling results was not possible, the results of the original study were described as reported by the authors. To correct for clinical diversity and methodological heterogeneity random effect meta-analyses were performed with risk ratios and 95% confidence intervals (CI) for binary outcomes using the Mantel-Haenszel method. Outcomes were considered statistically significant if the CI did not enclose 1. A forest plot was used for graphical display in which the boxes represent the risk ratios of the studies, the size of the box the weight of the study for the overall analysis, and the horizontal lines through the boxes the 95% CI. Heterogeneity was analyzed using chi-square tests, with significance set at $p<0.05$, and was quantified using I^2, with a maximum value of 30% identifying low heterogeneity.[19] Additionally, numbers needed to treat (NNT) with the CI for statistically significant outcomes were calculated for the comparison of LWM as the intervention and HWM as the control group, and presented as numbers needed to harm (NNH) if the outcome was a negative. A funnel plot of the selected studies for the meta-analyses was performed to determine possible publication bias.

Results

Twenty-six articles from 21 RCTs, encompassing 4 576 patients, were included in the systematic review. The LWM group contained 2,257 patients and the HWM group contained 2,319 patients. The range of follow-up was 3 to 60 months. In all studies Lichtenstein repairs were performed and no studies included femoral hernias. The study selection yielded no discrepancies between reviewers. The trial selection process is shown in the PRISMA flowchart (Figure 1).

The study characteristics and the baseline characteristics of patients from the included RCTs are presented in table 1. The specifications of the inguinal hernia repairs of the included RCTs are shown in table 2. The assessment of the individual study quality (risk of bias) is shown in table 3. All outcomes showed symmetric inverted funnel shapes (Supplemental Digital Content 2), thus publication bias was unlikely. Sensitivity analyses, in addition to those in table 4, of only studies with available follow-up data of ≤12 months and ≥24 months were performed but not shown, since they revealed no changes in significance and for most analyses few RCTs remained.

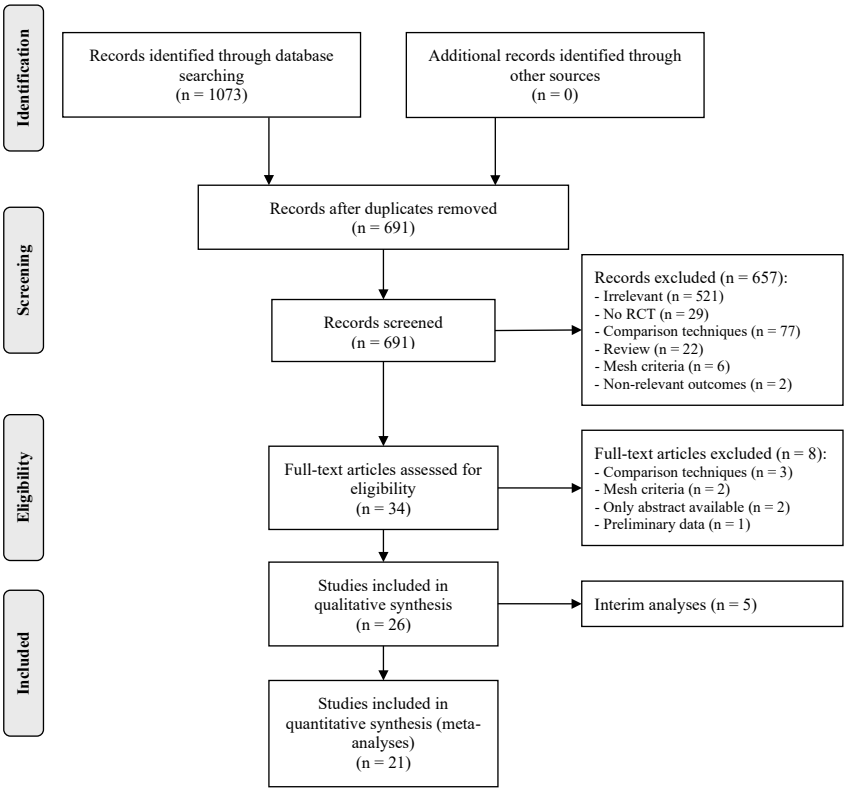

Figure 1 PRISMA Flow Diagram

Chronic Pain

Fourteen RCTs reported on the outcome 'any chronic pain'.[20-33] Thirteen studies reported 'severe chronic pain' results, although with varying definitions (Table 1).[20-30, 33, 34] Lee et al. (2017) and Carro et al. (2017) presented the mean score on a visual analogue scale (VAS) ± the standard deviation (SD), and did not respond with the required data for the meta-analyses.[35, 36] Both reported a non-significant difference between LWM and HWM (Lee et al. (2017): LWM 0.7 ± 1.1, HWM 0.8 ± 1.4, p=0.746; Carro et al. (2017): LWM 0.78 ± 1.37, HWM 0.75 ± 1.51, p=0.89).

The risk of any chronic pain was estimated to be significantly reduced by 22% when using a LWM (234 / 1,603 patients) compared to HWM (322 / 1,683 patients) (RR 0.78, 95% CI: 0.64 - 0.96) (Figure 2). There was low statistical heterogeneity (chi-square = 16.48, *df* = 13, P = 0.12, I^2 = 21%) among the RCTs. The NNT was 22 (95% CI: 14 – 51). The risk of severe chronic pain showed no significant difference (LWM 14 / 1,517 and HWM 26 / 1,591 patients, RR 0.73, 95% CI: 0.38 - 1.41) (Figure 3). There was low heterogeneity (chi-square = 3.22, *df* = 7, P = 0.86, I^2 = 0%). Sensitivity analyses revealed no significant changes for severe pain (Table

4). However, for any pain a variation in the upper limit of the CI was seen that either did or did not exceed 1. Especially, with increasing the length of follow-up significance fades.

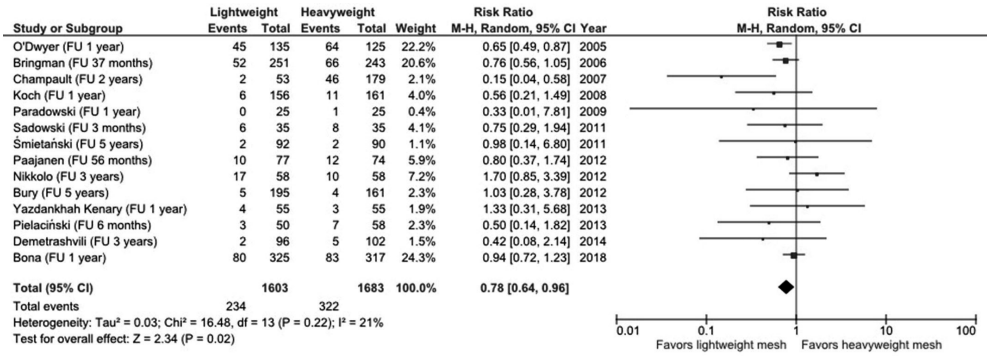

Figure 2 Pooled data from 14 RCTs regarding any chronic pain after the use of lightweight mesh versus heavyweight mesh in open inguinal hernia repair.

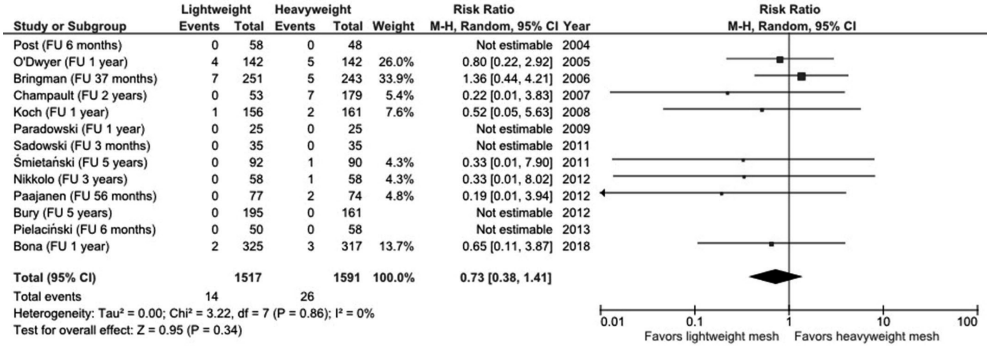

Figure 3 Pooled data from 13 RCTs regarding severe chronic pain after the use of lightweight mesh versus heavyweight mesh in open inguinal hernia repair.

Table 1 Study characteristics and baseline characteristics of patients from the included RCTs

Study	Country	Sample size, n (LWM:HWM)	Sex, % male	BMI, mean	Age, yrs (LWM:HWM)	Bilateral hernia, %	Recurrent hernia, %	Pain definition	Definition severe pain	FU, mos	Shortest FU, mos
Post (2004)[34]	Germany	64:53	92	NR	60:62	15.4	11.1	VAS	VAS > 5	6	6
Puccio (2005)[37]	Italy	15:15	92	26	59:54	0	0	VAS	N/A	12	12
O'Dwyer (2005)[20]	UK and Germany	162:159	97	26	55:57	NR	2.5	VAS	Modified SF-36	12	3
Bringman (2006)[21]	Sweden and Finland	296:294	100	NR	55:55	0	0	Questions	Use of analgesics	37	12
Champault (2007)[22]	France	58:215	97	NR	54	23	13	VAS	VAS > 5	24	24
Koch (2008)[23]	Sweden	156:161	100	25	56:57	0	0	VAS	Neuralgia	12	12
Paradowski (2009)[25]	Poland	25:25	100	NR	53:54	NR	0	VAS	VAS > 5	12	3
Śmietański (2011)[26]	Poland	101:99	98	25	55:58	0	0	VAS	Interferes with ADL	60	3
Sadowski (2011)[24]	USA	39:39	97	NR	54:56	0	23.1	VAS	Activity interference (IPQ)	3	3
Bury (2012)[29]	Poland	215:177	98	25	56:56	0	0	VAS	VAS > 3	60	3
Gundre (2012)[38]	India	35:35	NR	NR	NR	NR	0	VAS	N/A	60	60
Nikkolo (2012)[30]	Estonia	69:66	92	25	59:57	0	0	VAS	Use of analgesics	36	6
Canonico (2012)[39]	Italy	40:40	85	26	63:66	0	0	VAS	N/A	6	6
Paajanen (2013)[27]	Finland	104:101	93	23	58:61	1.8	9.8	VAS	Use of analgesics	56	12
Pielaciński (2013)[28]	Poland	73:76	100	NR	58:59	21	3.4	VAS	VAS > 6	6	3
Yazdankhah Kenary (2013)[31]	Iran	55:55	NR	NR	50:44	0	0	VAS	N/A	12	3
Demetrashvili (2014)[32]	Georgia	113:113	92	25	55:51	0	0	VAS	N/A	36	3
Carro (2017)[36]	Spain	58:58	91	NR	56	100	0	VAS	N/A	12	12
Lee (2017)[35]	Korea	25:25	100	24	64:64	0	0	VAS	N/A	4	3
Rutegård (2018)[40]	Sweden	194:197	100	25	59:58	0	0	Progress-scale	N/A	12	4
Bona (2018)[33]	Italy	411:397	95	25	59:61	6.6	0	VAS	No definition stated	12	6

BMI = Body Mass Index; FU = follow-up; NR = not reported; VAS = Visual Analogue Scale; N/A = not applicable.

Table 2 Specifications of inguinal hernia repairs of the included RCTs

Study	LWM, g/m²	Pore structure LWM	HWM, g/m²	Nerve handling objective	Local anesthetics	Surgeon, %	Residents, %	Operation time, min
Post (2004)[34]	Vypro (27-30)	Macroporous	Surgipro (100-110)	NR	38	18	82	73
Puccio (2005)[37]	Vypro (30)	Macroporous	Prolene (80)	NR	100	100	0	45
O'Dwyer (2005)[20]	Vypro II (32)	Macroporous	Atrium (85)	Not standardized	39	NR	NR	43
Bringman (2006)[21]	Vypro II (32)	Macroporous	Prolene (80)	Not standardized	11	100	0	52
Champault (2007)[22]	Glucamesh (50)	Microporous	Polypropylene (105)	NR	0	100	0	NR
Koch (2008)[23]	TiMesh (35)	Macroporous	Prolene (80)	NR	0	100	0	26
Paradowski (2009)[25]	Surgimesh WN (43)	Random	Surgipro (80)	NR	100	NR	NR	NR
Śmietański (2011)[26]	Surgimesh WN (38)	Random	Prolene (80)	Preserved	0	NR	NR	38
Sadowski (2011)[24]	Polyester (±40)	Macroporous	Polypropylene (80-100)	Not standardized	5	Mixed. No % presented.		83
Bury (2012)[29]	Ultrapro (35)	Macroporous	Prolene (80)	Not standardized	0	100	0	48
Gundre (2012)[38]	Polyethylene (35)	Unclear	Polypropylene	NR	NR	NR	NR	NR
Nikkolo (2012)[30]	Optilene (36)	Microporous	Premilene (82)	Preserved	2	61	39	51
Canonico (2012)[39]	Evolution P3EM (48)	Macroporous	Prolene (80)	Preserved	25	NR	NR	55
Paajanen (2013)[27]	Vypro II (50)	Macroporous	Premilene (82)	Not standardized	0	100	0	31
Pielaciński (2013)[28]	Polypropylene-polyglactin (35)	Macroporous	Polypropylene (100)	NR	0	Mixed. No % presented.		48
Yazdankhah Kenary (2013)[31]	Dynamesh (36)	Macroporous	Dynamesh (72)	NR	0	100	0	NR
Demetrashvili (2014)[32]	Ultrapro (28)	Macroporous	Prolene (82)	Preserved	78	100	0	60
Carro (2017)[36]	Polypropylene (43)	Macroporous	Unclear (105)	NR	0	100	0	NR
Lee (2017)[35]	Proflex (28)	Macroporous	Marlex (100)	NR	0	100	0	NR
Rutegård (2018)[40]	Ultrapro (28)	Macroporous	Polypropylene (90)	NR	100	100	0	NR
Bona (2018)[33]	Ultrapro (28)	Macroporous	Polypropylene (80-100)	NR	66	NR	NR	NR

NR = not reported; Macroporous = >1mm pore size.

Table 3 Risk of bias table for randomized controlled trials

Study	Describe method of randomization	Allocation concealment	Blinding of patients	Blinding of outcome assessors	Selective outcome reporting	Loss to FU, % / months	Violation of ITT?	Jadad score
Post (2004)[34]	Computer generated / Envelop	Yes	Yes	Yes	No	8.3 / 6	Unclear	4
Puccio (2005)[37]	Sealed envelopes	Unclear	No	No	Yes	Unclear	Unclear	1
O'Dwyer (2005)[20]	Computer generated	Yes	Yes	Yes	No	13.9 / 12	No	5
Bringman (2006)[21]	Computer generated	Yes	Yes	Yes	No	17.7 / 37	No	5
Champault (2007)[22]	Not reported	No	Unclear	Yes	No	15.0 / 24	Unclear	3
Koch (2008)[23]	Computer generated	Yes	Yes	Yes	No	5.4 / 12	Unclear	5
Paradowski (2009)[25]	Not reported	Unclear	Yes	Yes	No	2.0 / 12	Unclear	4
Śmietański (2011)[26]	Wichmann-Hill generator (modified by McLeod)	Yes	Yes	Yes	No	9.9 / 60	Unclear	5
Sadowski (2011)[24]	Not reported	Unclear	Yes	No	No	10.3 / 3	No	3
Bury (2012)[29]	Wichmann-Hill generator (modified by McLeod)	Yes	Unclear	Yes	No	9.2 / 60	No	4
Gundre (2012)[38]	Sealed envelopes	Unclear	Yes	No	Yes	Unclear	Unclear	2
Nikkolo (2012)[30]	Sealed envelopes	Yes	Unclear	Unclear	No	14.1 / 36	Unclear	2
Canonico (2012)[39]	Not reported	Unclear	Yes	Yes	Yes	Unclear	Unclear	3
Paajanen (2013)[27]	Sealed envelopes	Yes	Yes	Yes	No	26.3 / 56 *	Unclear	4
Pielaciński (2013)[28]	Not reported	Unclear	Unclear	Unclear	No	26.2 / 6 *	Unclear	2
Yazdankhah Kenary (2013)[31]	Computer generated	Yes	Yes	Yes	No	0.0 / 12	Unclear	5
Demetrashvili (2014)[32]	Simple random sampling	Yes	Yes	Yes	No	12.4 / 36	Unclear	4
Carro (2017)[36]	Random numbers table	Unclear	Yes	Unclear	No	13.4 / 12	Unclear	4
Lee (2017)[35]	Not reported	Unclear	Yes	Unclear	No	6.0 / 4	No	3
Rutegård (2018)[40]	Computer generated	Yes	No	Yes	No	7.2 / 12	Unclear	4
Bona (2018)[33]	Algorithm of Pocock and Simon.	Yes	Yes	No	Yes	20.5 / 12 *	No	4

FU = follow-up; * = inordinate loss to follow-up; ITT = intention to treat.

Recurrence

Twenty-one RCTs reported on the outcome recurrence (Figure 4).[20-40] The pooled analysis showed that the risk of a recurrence was not influenced when using LWM (42 / 2,068 patients) compared to HWM (34 / 2,132 patients) (RR 1.22, 95% CI: 0.76 - 1.96). There was low statistical heterogeneity among the RCTs (chi-square = 7.41, *df* = 13, P = 0.88, I^2 = 0%). Sensitivity analyses revealed no significant changes (Table 4).

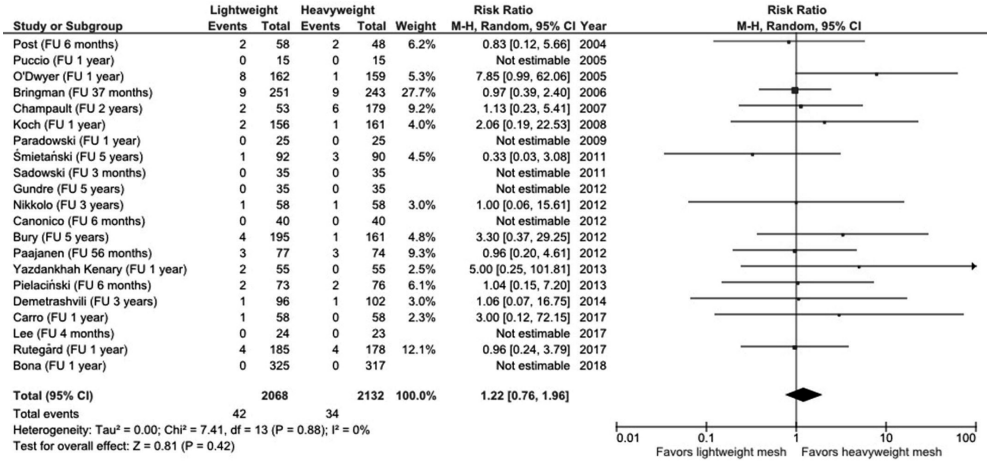

Figure 4 Pooled data from 21 RCTs regarding recurrences after the use of lightweight mesh versus heavyweight mesh in open inguinal hernia repair.

Recurrence after direct or indirect inguinal hernia repair

For these outcomes no studies reported their recurrence outcome with additional information suitable for meta-analyses. Nikkolo et al. (2012), Demetrashvili et al. (2014) and Rutegård et al. (2018) responded with the required data.[30, 32, 40] For the other studies that reported on the outcome recurrence attempts were made to contact the authors with no response.

The risk of a recurrence after a direct inguinal hernia repair was not statistically significantly influenced when a LWM was used (LWM 5 / 121 and HWM 2 / 109 patients, RR 2.03, 95% CI: 0.36 - 11.61) (Figure 5). Heterogeneity was low among the RCTs (chi-square = 1.05, df = 1, P = 0.30, I^2 = 5%). Also, the risk of a recurrence with a LWM after an indirect hernia repair showed a non-significant result (LWM 1 / 195 and HWM 4 / 208 patients, RR 0.43, 95% CI: 0.05 - 3.50) (Figure 6). There was low statistical heterogeneity among the RCTs (chi-square = 1.09, df = 1, P = 0.30, I^2 = 9%). Sensitivity analyses were not computable or influential, since only 1 study remained or the outcome was identical.

Table 4 Sensitivity analyses

	Longest FU and no studies excluded	Exclusion of high risk of bias studies	Exclusion of high risk of bias + inordinate loss to FU studies	Only studies with ≤6 months FU	Only studies with ≥12 months FU	Only studies with ≥24 months FU	Exclusion of studies with recurrence repairs	Only studies with large pore (>1mm) LWM
Any pain	0.78 (0.64-0.96)	0.77 (0.65-0.90)	0.68 (0.56-0.83)	0.90 (0.78-1.05)*	0.79 (0.63-1.00)*	0.78 (0.48-1.27)*	0.89 (0.74-1.07)*	0.78 (0.67-0.91)
Severe pain	0.73 (0.38-1.41)	0.75 (0.38-1.48)	0.84 (0.40-1.78)	0.64 (0.25-1.60)	0.73 (0.38-1.41)	0.75 (0.30-1.86)	0.85 (0.37-1.95)	0.85 (0.42-1.72)
Recurrences	1.22 (0.76-1.96)	1.24 (0.75-2.04)	1.27 (0.75-2.16)	N/A	N/A	N/A	1.15 (0.63-2.09)	1.33 (0.79-2.24)
Foreign body feeling	0.64 (0.51-0.80)	0.77 (0.62-0.96)	0.54 (0.38-0.78)	0.73 (0.56-0.93)	0.72 (0.52-1.00)*	0.66 (0.48-0.90)	0.79 (0.65-0.97)	0.62 (0.48-0.80)

Outcomes expressed as RR (95 % CI); FU = follow-up; N/A = not applicable; * = change in significance compared to all included studies

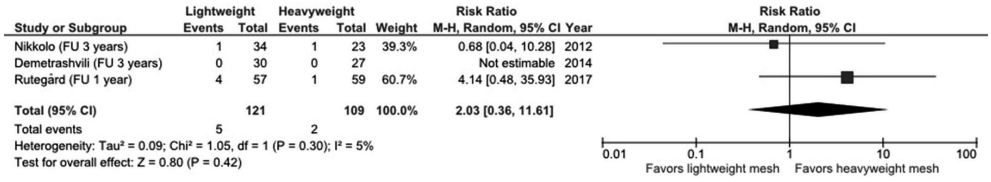

Figure 5 Pooled data from 3 RCTs regarding recurrences after only direct repairs comparing lightweight mesh versus heavyweight mesh in open inguinal hernia repair. For this outcome all data is unpublished and provided by the corresponding authors in response to the call for additional data.

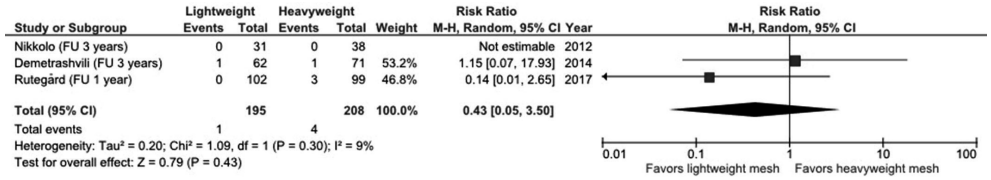

Figure 6 Pooled data from 3 RCTs regarding recurrences after only indirect repairs comparing lightweight mesh versus heavyweight mesh in open inguinal hernia repair. For this outcome all data is unpublished and provided by the corresponding authors in response to the call for additional data.

Influence of primary hernia defect size on recurrence

This outcome was ill-reported and no data required for meta-analysis was available. O'Dwyer et al. (2005) stated that the encountered recurrences were not related to the size of the defect measured during operation.[20] Nikkolo et al. (2012), Paajanen et al. (2012) and Demetrashvili et al. (2014) responded with additional information.[27, 30, 32] Nikkolo et al. (2012) found 1 LWM recurrence after a hernia defect repair of >3cm, and 1 HWM recurrence after a repair of 1.5-3 cm.[30] Paajanen et al. (2012) found all recurrences after small defects *(<1-2 cm)*.[27] Demetrashvili et al. (2014) found both indirect recurrences after large defects.[32]

Foreign Body Feeling

Twelve RCTs reported on the outcome foreign body feeling (Figure 7).[21, 23, 27, 28, 30-32, 34-37, 40] The risk of foreign body feeling was estimated to be significantly reduced by 36% when using a LWM (LWM 130 / 1,053 and HWM 209 / 1,035 patients, RR 0.64, 95% CI: 0.51 – 0.80). There was low heterogeneity among the RCTs (chi-square = 12.93, *df* = 11, P = 0.30, I^2 = 15%). The NNT was 13 (95% CI: 9 – 21). Sensitivity analyses revealed an outcome slightly less in favor of LWM for studies with ≥12 months follow-up (Table 4).

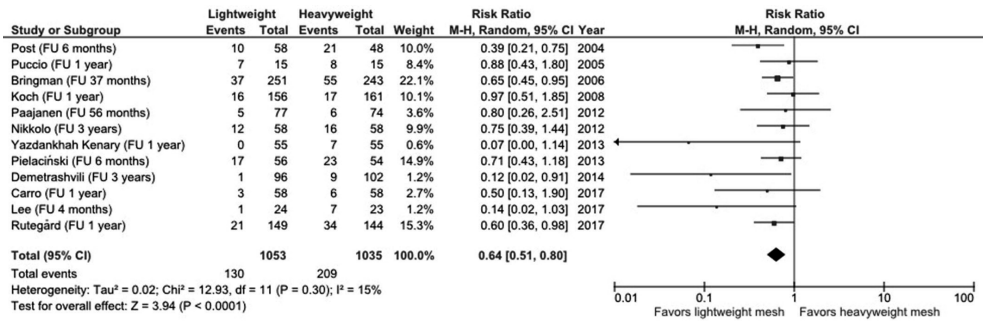

Figure 7 Pooled data from 12 RCTs regarding foreign body feeling after the use of lightweight mesh versus heavyweight mesh in open inguinal hernia repair.

Rating the quality of the evidence using GRADE[19]

The evidence originated from RCTs and its quality level therefore started at 'High'. We did not downgrade the outcomes for limitations in the methodological quality of the included RCTs (risk of bias), since removing the studies with a high risk of bias from the meta-analysis did not affect the outcomes and a sufficient number of studies remained. However, the quality of the evidence regarding severe pain and recurrences was downgraded with 1 level to 'moderate GRADE' for imprecision. A decision was made to downgrade the outcomes recurrences after direct and indirect repairs by 2 levels to 'low GRADE' for imprecision. Severe pain was further downgraded to 'low GRADE', for indirectness of evidence. The quality of the evidence regarding any pain and foreign body feeling was not downgraded, since there was no publication bias, inconsistency of results, indirectness of evidence, or imprecision.

Discussion

This systematic review and meta-analysis demonstrated that LWM should be used in open (Lichtenstein) inguinal hernia repair. Using LWM instead of HWM results in a 22% reduction of patients with chronic pain and a 36% reduction of patients with foreign body feeling. As recurrence rates are likely to be similar, the benefits for patients are undisputed and outweigh the (social) disadvantage of the higher price of LWM.

For any chronic groin pain and foreign body feeling the evidence explicitly favors the use of a LWM in open inguinal hernia repair. The level of evidence regarding any pain and foreign body feeling was 'high GRADE'. This means that we are confident that the true effect lies close to that of the estimate of the effect. Understanding chronic pain after inguinal hernia repair is complex, and more complicated than just the type of mesh used. Nevertheless,

we are confident the mesh type is of influence. By performing a meta-analysis of only RCTs, many other possible confounders were filtered out. The initial clinical concerns for using LWM were based on the evidently higher recurrence rate in the study of O'Dwyer et al.[20] The pooled data regarding recurrences of this review clearly shows these concerns to be unfounded, since only O'Dwyer et al. out of 21 RCTs found a nearly significant effect estimate favoring HWM.[20] A second issue raised could be a distinction between recurrences developing after small or large defects. Only 4 studies reported or responded for a total of 19 recurrences, resulting in an inconclusive outcome.[20, 27, 30, 32] A 2015 systematic review and meta-analysis of patient-related risk factors for recurrence found no influence of hernia defect size, with a risk ratio of 1.09 (CI 0.92-1.30) in favor of a HWM.[15] However, only 2 observational studies from the Swedish hernia database were included. Moreover, both were not specifically about open repairs.[41, 42] Another consideration would be a distinction between the use of LWM or HWM in direct or indirect hernia repairs. Only Nikkolo et al. (2012), Demetrashvili et al. (2014) and Rutegård et al. (2018) responded with data, which was insufficient to draw any firm conclusions.[30, 32, 40] No other trials reported on this topic or responded with suitable data. Regarding foreign body feeling, sensitivity analyses revealed an outcome slightly less in favor of LWM for studies with ≥12 months follow-up, however in the analyses of all other follow-up periods consistent significant effects were determined. Therefore a change over time in the determined reduction of foreign body feeling when using LWM is not expected.

The most recent systematic review with the same research question was done by Sajid et al. (2012), which included 9 RCTs conducted before May 2011.[20-23, 26, 34, 43-48] For current outcomes 1 study was irrelevant.[48] Moreover, multiple inaccuracies of data extractive mistakes and incorrectly included studies in the systematic review by Sajid et al. (2012) were corrected for in this review. Also the study of Puccio et al. (2005) and Paradowski et al. (2009) were missed.[25, 37] Although 12 new randomized trials were performed, resulting in 15 publications, the results of Sajid et al. (2012) were consistent with the results of this systematic review.[24, 25, 27-33, 35-40] They found no statistically significant higher recurrence risk when using a LWM. Using a LWM did reduce the risk of chronic groin pain and other groin symptoms. Moreover, in a comparable systematic review and meta-analysis by Śmietański et al. (2012), published around the same time as the review by Sajid et al. (2012), the same conclusions were drawn and a LWM for open inguinal hernia repair was advised.[11] They did, however, question the clinical relevance of their results, taking the higher price of a LWM into account, as well as the absence of a reduction in severe pain when a LWM was used. With significantly more studies pointing in the same direction for all outcomes the current evidence makes an even more compelling case. Moreover, it asks for contemplation why LWM should be more expensive when less material is used in the effective large pore mesh of comparable materials as HWM. The price of simple LWM nowadays already level with HWM, and it is to be expected other types should level in time.

One strength of the current systematic review and meta-analysis is that it reported new valuable information on crucial outcome measures for decision making in mesh choice for open inguinal hernia repair. Deliberately, less important outcomes for decision-making (early postoperative pain, perioperative complications, operation time) or outcomes that are subjective or easily influenced by prejudiced care providers and outcome assessors (seroma/hematoma formation or infection) were not analyzed. Unfortunately, patient reported outcome measures (PROMs) are not described in the studies and quality of life questionnaires, if used, are not uniform or suitable for data pooling. Data on these outcomes, that are nowadays more frequently used, could further enrich our understanding of the effect of mesh types on patients, however having more pain and foreign body feeling for years after surgery makes a negative influence on patient satisfaction very plausible. Moreover, adjustments were made to the current analyses for inaccuracies detected in previous systematic reviews and meta-analyses of comparable research questions. We are confident that our search query was well-built, partly because no additional relevant publications were found in the references of included studies.

Nevertheless, there were several limitations to this study. At the review level publication bias was unlikely. Statistical heterogeneity was low. However, at the study level the differences in in- and exclusion criteria (e.g., sex, age, hernia sizes, surgical expertise and bilateral/unilateral or recurrent inguinal hernias) between studies and/or the lack of baseline data made clinical heterogeneity logical. Moreover, some studies included small sample sizes without the performance of a power analysis. Potentially, those studies were underpowered for the recognition of small differences between groups. At the outcome level, the short durations of follow-up may have led to the underestimation of the long-term recurrence risk. Performing meta-analyses and additional sensitivity analyses compensated for these limitations to some extent. Lastly, there was no uniformity for the definitions of chronic pain (e.g., any pain, clinically relevant, severe) and foreign body feeling or for the measurement scales used between studies. The inguinal pain questionnaire (IPQ) can facilitate future RCTs with a uniform assessment for postherniorrhaphy pain.[49, 50]

The published RCTs, with an overall impressive sample size for comparing LWM and HWM, provided sufficient evidence to draw conclusions. Since the latest meta-analysis more than twice as many RCTs were performed that amplify our knowledge and confirm previous conclusions. This was needed because in the surgical community, despite the presented evidence, using LWM is not general practice. Moreover, sensitivity analyses were performed that address the possible reasons for doubt of using LWM amongst surgeons until now. Therefore, we feel confident to state that there is no need to undertake more randomized comparisons of LWM and HWM, however, maintaining prospective hernia registration

databases is advised. An important issue to resolve for future studies is the influence of direct or indirect repairs, and the hernia defect size on recurrences.

In conclusion, this systematic review and meta-analysis provided an update of published RCTs and reinforces and broadens the conclusions of previous systematic reviews. In open inguinal hernia repair the use of LWM reduces chronic pain and foreign body feeling. No difference in recurrence risk was established. Also, no change in recurrence rates was found when LWM and HWM were compared in respect to the hernia type (direct/indirect) or hernia size. The use of LWM in open inguinal hernia repairs is recommended.

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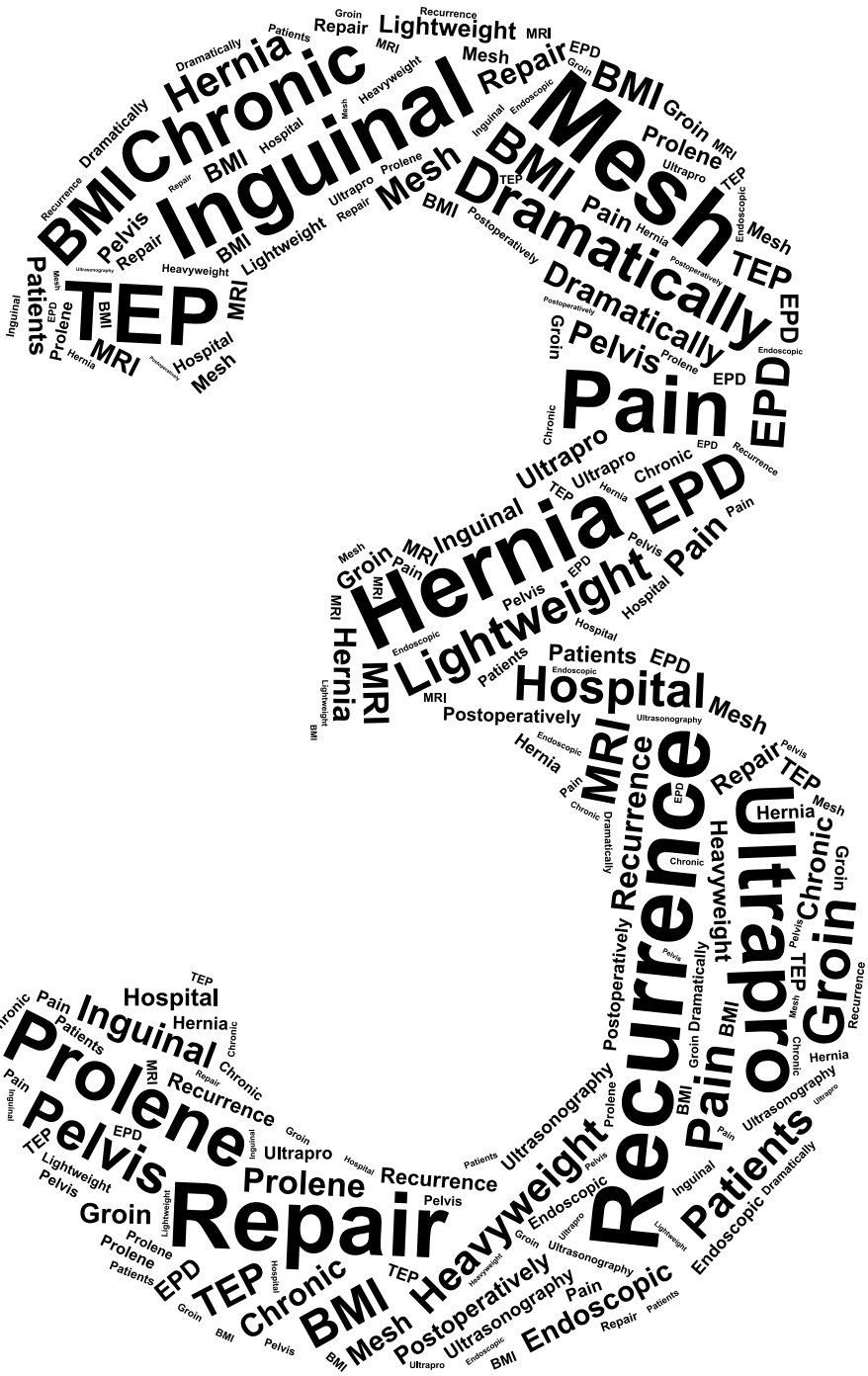
Mesh
Inguinal
Chronic
Hernia
Dramatically
Pain
EPD
TEP
Lightweight
Repair
BMI
Recurrence
Ultrapro
Groin
Heavyweight
Patients
Prolene
Pelvis
Hospital
MRI
Postoperatively
Endoscopic
Ultrasonography

Higher recurrence rate after endoscopic totally extraperitoneal (TEP) inguinal hernia repair with Ultrapro lightweight mesh:
5-year results of a randomized controlled trial (TULP-trial)

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Annals of Surgery (2018) 268:241-246

Abstract

Background

Recurrence is an important complication of inguinal hernia surgery. Higher recurrence rates of Ultrapro® lightweight meshes after TEP repair have been demonstrated, yet data regarding long-term follow-up are limited. The aim of this study was to determine inguinal hernia recurrence rates 5 years after endoscopic totally extraperitoneal (TEP) inguinal hernia repair when either lightweight or heavyweight mesh was used.

Methods

From 2010-2012, 950 male adult patients with primary unilateral hernias were randomized to TEP hernia repair with heavyweight (Prolene®) or lightweight (Ultrapro®) mesh. Five years postoperatively, the validated PINQ-PHONE telephone questionnaire was carried out. Participants with a positive questionnaire reply were scheduled for a clinical visit. A recurrence was defined as a clinically detectable bulge in the operated groin on physical examination.

Results

Data on development of recurrence could be obtained from 790 patients (83.2% 5-year follow up-rate). Four patients presented with a recurrence at the outpatient clinic between 2 and 5 years postoperatively. Thirty-five patients (4.6%) with a positive PINQ-PHONE reply (60.0 % lightweight vs 40.0% heavyweight) were physically examined at the outpatient clinic. In 2 patients (lightweight) a recurrence was detected. The total 5-year recurrence rate after TEP hernia repair was 2.4% (3.8% lightweight, 1.1% heavyweight, p=0.01). A significantly higher recurrence rate for lightweight mesh in primary direct hernias was found (p=0.003).

Conclusion

The overall recurrence rate 5 years after TEP inguinal hernia repair was low. Ultrapro® lightweight meshes showed higher recurrence rates than heavyweight meshes and are not recommended for endoscopic TEP inguinal hernia repair.

Background

Recurrence rates of inguinal hernia repair have dropped dramatically after the introduction of tension free mesh repair, which has become standard of care.[1-2] Also, endoscopic tension-free preperitoneal approaches have become increasingly popular, since these techniques yielded additional advantages such as faster recovery, lower recurrence rates, and a lower incidence of chronic pain compared to open techniques.[3-5]

When evaluating outcomes of inguinal hernia repair, chronic pain remains a significant problem. It is hypothesized that the mesh-induced inflammatory reaction with subsequent formation of fibrosis might play a substantial role in the occurrence of chronic pain.[6] Assuming the severity of the inflammatory response might correlate with the amount of mesh material and its pore sizes, lightweight meshes with larger pores have been developed.[7-8] In open anterior inguinal mesh repair, less pain and foreign body feeling were described when a lightweight mesh was used. [9] However, in endoscopic inguinal hernia repair, these benefits could not be shown and lack of consensus exists regarding the best mesh for endoscopic inguinal hernia repair.[10]

We performed a prospective double-blinded randomized controlled trial (TULP-trial) analyzing the outcomes of lightweight (Ultrapro®) versus heavyweight (Prolene®) mesh following endoscopic totally extraperitoneal (TEP) inguinal hernia repair in a hernia expertise center (Hernia Clinic Diakonessenhuis Zeist, the Netherlands) up to 2 years postoperatively. Use of lightweight mesh did not lead to less chronic postoperative pain.[11-12] However, outcomes of this trial demonstrated an increased incidence of recurrence when lightweight mesh was used. This finding was supported by the results of other studies.[13-15]

Up till now, few data are published with regard to long-term recurrence after TEP inguinal hernia repair with use of different mesh types.

The aim of the present study was to determine the recurrence rate 5 years after endoscopic TEP inguinal hernia repair when either a lightweight or heavyweight mesh was used.

Methods

Study Design

A 5-year follow-up of a previously performed double-blind randomized controlled trial (TULP-trial) comparing lightweight and heavyweight mesh in 950 patients that underwent TEP inguinal hernia repair was executed. The study protocol as well as the results up to 2 years have been published previously.[11,12,16] Patient enrollment commenced in March

2010 and ended in October 2012. The study was approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, the Netherlands) and the local ethics board of the hospital and was registered in the Dutch Trial Register (NTR identification number 2131).

Participants

Male patients over 18 years of age with primary, reducible, unilateral inguinal hernias and no contraindications for TEP hernia repair were eligible for inclusion. Exclusion criteria were collagen or connective tissue disorders and patients deemed unlikely to cooperate during follow-up (e.g. patients with language difficulties or without fixed address). Details about the recruitment process were published previously.[16]

Intervention

Participants were randomized to TEP hernia repair with use of either a heavyweight or a lightweight mesh. Randomization was performed in the operating room by computerized block randomization of eight. All patients were operated in one center by one of 4 surgeons with a minimum of 500 TEP procedures per surgeon. All TEP procedures were performed under general anesthesia, and the surgical technique and perioperative care were standardized in all patients. Operative details of the TEP technique have been described previously.[16,17] Fixation of the mesh was not routinely performed. The lightweight mesh was a polypropylene-poliglecaprone monofilament mesh (Ultrapro® Partially Absorbable Lightweight mesh, Johnson & Johnson company, Amersfoort, the Netherlands, dimensions: 10x15cm, pore size: 3-4mm, weight: 55 g/m^2 (28 g/m^2 after absorption of poliglecaprone)). The heavyweight mesh consisted of monofilament polypropylene (Prolene® Polypropylene Mesh, Johnson& Johnson, Amersfoort, the Netherlands, dimensions: 10x15cm, pore size: 0.8-1.2mm, weight: 80 g/m^2). Hernia types were intraoperatively classified according to the Nyhus classification and presence of a lipoma was recorded.[18] Intraoperative complications and operation time were registered. The type of mesh was not mentioned in the operation chart and unknown for the patient and surgeon performing the follow-up.

Outcomes

Follow-up took place in a standardized manner to a fixed schedule up to 2 years after operation. Pain, foreign-body feeling, quality of life and recurrences were assessed through questionnaires at different measuring points. Physical examination was performed at 6 weeks and 1 year and in case of any complaint at other measuring points. In addition, patients were stimulated to contact the hospital in case of any complaint at any moment.

The primary outcome of this 5-year analysis was the development of inguinal hernia recurrence. At 5 years postoperatively, we assessed all study subjects in the electronic patient documentation (EPD) to detect additional development of recurrences between our last point of follow-up (2 years) and 5 years. Afterwards, The PINQ-PHONE (Post-INguinal-

repair-Questionnaire by telePHONE) questionnaire was carried out in patients that had not developed a recurrence to our knowledge. The PINQ-PHONE is a validated questionnaire for detection of symptomatic and asymptomatic recurrences consisting of 4 elements; 3 questions and a do-it yourself Valsalva manoeuvre (*figure 1*).[19] This telephonic follow-up was performed by 5 independent researchers who were blinded for allocation of mesh type. For all participants a call attempt was made at least 3 times. In case of no response an e-mail was sent, inquiring whether and when we could contact the patient. Participants with a positive reply to one or more of the 4 elements of the questionnaire were scheduled for a visit to the outpatient clinic for physical examination performed by an experienced hernia surgeon. A recurrence was defined as a symptomatic or asymptomatic defect (bulge or weakness) in the abdominal wall of the operated groin with herniation of abdominal contents exacerbated by the Valsalva manoeuvre. In case of complaints without clear findings of an inguinal hernia on physical examination, imaging was offered (X-ray of the pelvis and/ or ultrasonography and/or MRI of the groin).

1. Do you have any symptoms at your operated groin?
2. Have you noticed anything at your operated groin?
3. Have you noticed something at the operated groin when coughing, sneezing or squeezing?
4. Could you please stand up and put your other hand flat in your operated groin. Now please put the phone down and put this hand to your mouth and blow. Do you feel something in your operated groin?

Figure 1 PINQ-PHONE questionnaire

For all recurrences, the initial hernia type, the type of recurrence and the time to recurrence and subsequent treatment were assessed. The date on which the patient re-attended the outpatient clinic and a recurrence was diagnosed was used as a surrogate for date of recurrence.

Statistical analysis

Analyses were performed using SPSS statistical software, version 24 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used for baseline data.

Absolute 5-year recurrence rates were analyzed on an intention to treat basis. The cumulative incidence of recurrence in both groups was assessed by Kaplan Meier analysis. The incidence of recurrence for lightweight and heavyweight mesh was compared by means of Chi-square analysis. Additional subgroup analyses based on hernia type with comparison

of recurrence rates of the two mesh types were performed. Binary logistic regression analysis was performed to correct for confounding factors on the risk of developing a recurrence, using the following variables: mesh type, body mass index (BMI), operation time, surgeon and hernia type. A p-value below 0.05 was considered statistically significant.

Results

Initially, 949 patients were successfully randomized to TEP hernia repair with lightweight or heavyweight mesh (*figure 2)*. At 5 years of follow-up, we were able to assess the presence of recurrence in 790 patients, who comprise 90.3% of the 2-year follow-up group and reflect a 83.2% five-year follow-up rate (*table 1).* We were not able to obtain information at 5 years of follow-up in 85 patients due to death, disease unrelated to the hernia repair, withdrawal or unresponsiveness.

Up to 2 years of follow-up, 17 participants developed a recurrence (13 lightweight, 4 heavyweight, p=0.03) (*table 2).* Between 2 and 5 years postoperatively, 4 additional recurrences were detected in the EPD (3 lightweight, 1 heavyweight) after 27, 39, 46 and 55 months, respectively.

The PINQ-PHONE questionnaire was carried out among a total of 769 patients (386 lightweight, 383 heavyweight). Fifty-two patients (6.8%, 31 lightweight, 21 heavyweight) scored positively on the PINQ-PHONE questionnaire and were eligible for assessment at the outpatient clinic. Of these positive respondents, 35 (21 lightweight, 14 heavyweight) were scheduled for an appointment for physical examination. Seventeen patients with a positive score were not seen at the outpatient clinic; 9 of these patients had already presented with complaints yet no recurrence could be detected, 4 were unwilling to undergo an assessment at the outpatient clinic, 1 patient could not be reached by telephone for the planning of an appointment, and in 3 patients the reason remained unclear.

In 2 of the 35 patients scheduled for assessment a recurrence was detected on physical examination. Of the patients where a recurrence could not be detected clinically, 4 patients experienced bothersome complaints and additional imaging was performed. No additional recurrences were detected and besides mild coxartrosis in one patient and oedema surrounding the abdominal muscles in another patients no abnormalities were found.

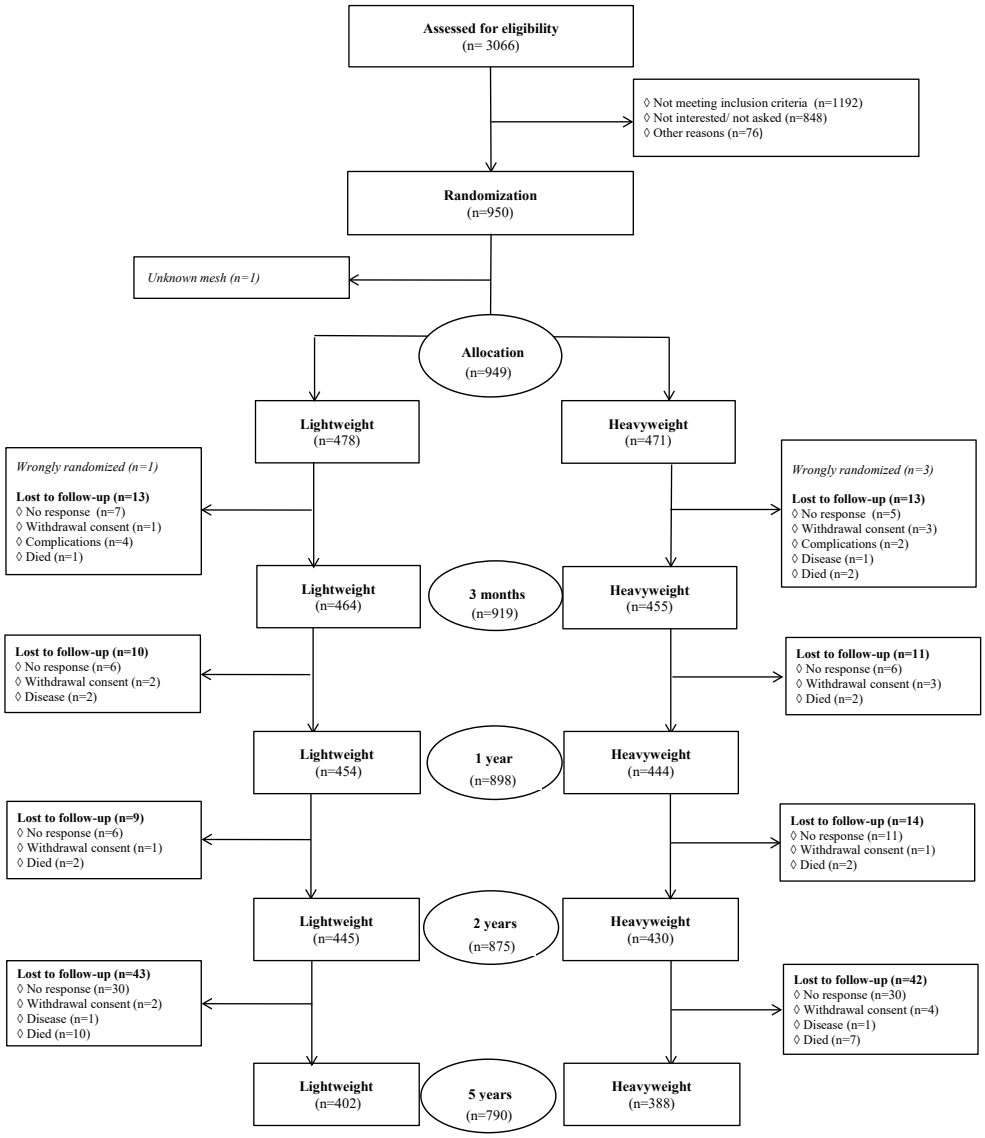

Figure 2 Flowchart

Both patients where a clinical recurrence was detected had been randomized to treatment with lightweight mesh. Since both patients were minimally symptomatic on clinical examination, no operative intervention was planned but they were instructed to contact the hospital in case of increasing complaints. One of these patients revisited the outpatient department after 3 months with a request for reoperation. In this patient, a Lichtenstein repair was performed.

Table 1 Baseline characteristics

	Lightweight (n=402)	**Heavyweight** (n=388)	***p-value***
Age (years), median (IQR)	55 (45-64)	56 (44-64)	0.78
BMI (kg/m^2), mean (SD)	24.9 (2.7)	24.8 (2.6)	0.44
Side, n (%)			
Left	186 (46)	160 (41)	
Right	216 (54)	228 (59)	
Hernia type, n (%)			0.60
Lateral	297 (74)	291 (75)	
Medial	102 (25)	95 (25)	
Femoral	3 (1)	1 (0)	
Surgeon, n (%)			0.32
1	123 (31)	113 (29)	
2	118 (29)	107 (28)	
3	47 (12)	55 (14)	
4	106 (26)	104 (27)	
5 resident	8 (2)	9 (2)	

IQR: interquartile range, BMI: body mass index, SD: standard deviation

Table 2 Recurrence rate at different time points

	Lightweight	**Heavyweight**	***p-value***
Recurrence, n (%)			
3 months	2 (0.4)	2 (0.4)	-
1 year	8 (1.7)	3 (0.6)	0.12
2 years	13 (2.7)	4 (0.8)	0.03
5 years	18 (3.8)	5 (1.1)	0.01

The total 5-year recurrence rate of our study population was 2.4% (n=23), 18 (3.8%) recurrences occurred in the lightweight mesh group and 5 (1.1 %) in the heavyweight mesh group (p=0.01) (*table 2, figure 3)*. The earliest recurrence developed 1 month after surgery and the last 2 recurrences were detected at the 5-year follow-up point (60 months). Hernias recurred after repair of 13 direct (1 heavyweight, 12 lightweight) and 10 indirect hernias (4 heavyweight, 6 lightweight). Subgroup analysis for the different primary hernia types demonstrated a significantly higher recurrence rate for lightweight mesh in primary direct hernias (p=0.003), yet for indirect hernias no significant difference in recurrence rate for the two mesh types could be found (p=0.545).

On multivariate analysis, the lightweight mesh remained associated with a higher 5-year recurrence rate (OR 3.86, 95% CI 1.41-10.61, p=0.009). Direct hernias were independently associated with development of recurrence (OR 3.93, 95% CI 1.66-9.32, p=0.002), whereas

indirect hernias decreased the chance on development of a recurrence (OR 0.27, 95% CI 0.11-0.63, p=0.003).

Of the 23 recurrences, 15 were reoperated (5 heavyweight, 10 lightweight). At reoperation, 6 direct hernias and 1 indirect hernia were found, whereas 3 recurrences were not further specified. In 5 cases only a lipoma instead of a true hernia recurrence was found. Three of these patients received a lightweight mesh and 2 received a heavyweight mesh. A significant higher recurrence rate for lightweight mesh remained when excluding the patients with only a lipoma from analysis (15 lightweight versus 3 heavyweight, p=0.004).

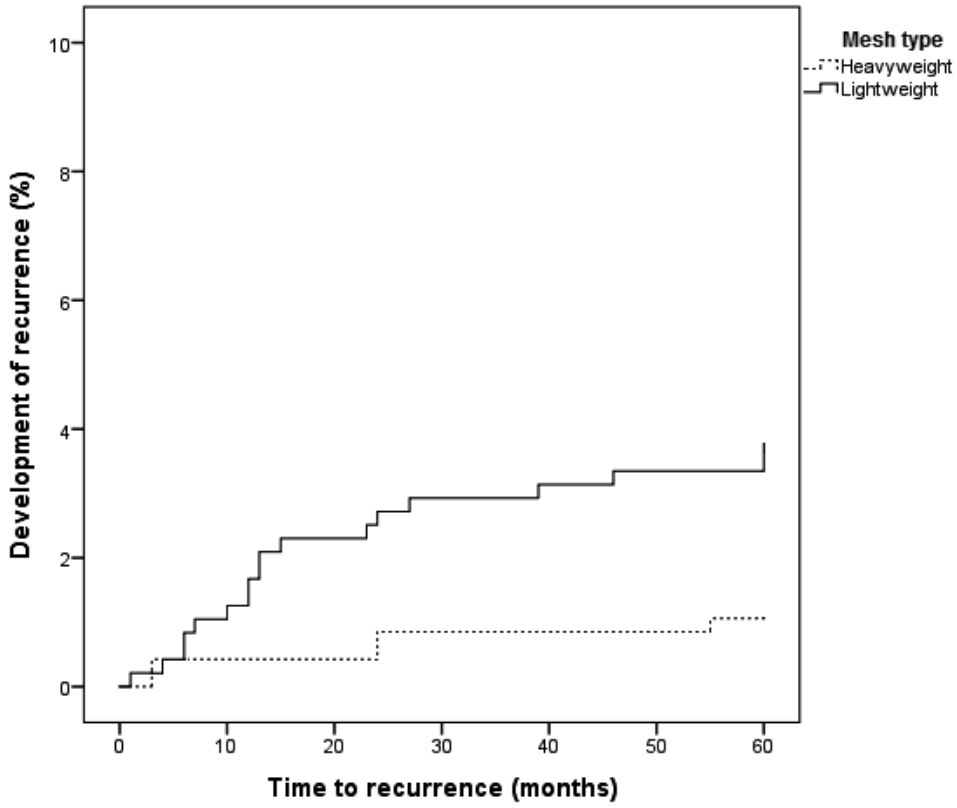

Figure 3 Cumulative incidence of recurrence after TEP for lightweight and heavyweight mesh

Discussion

The overall 5-year recurrence rate of 2.4% after TEP hernia repair was low, however a 3-4 times higher recurrence risk was observed for the patients that received a lightweight mesh. The majority of recurrences after insertion of lightweight mesh was found in patients with primary medial hernias.

It is plausible that recurrence rates are not only influenced by hernia type, repair method, mesh type and surgical expertise, but also by length and method of follow-up evaluation.[20] This is the first study to perform a long-term follow up of 5 years assessing recurrence using a validated telephone questionnaire in a large randomized sample of patients treated by TEP with either lightweight or heavyweight mesh.

The efficacy of mesh repair is based on strengthening weakened native tissue by scar tissue formation, formed by the inflammatory response induced by mesh material.[21-22] In our opinion, the use of Ultrapro® lightweight mesh has affected the recurrence rate in several ways. The intrinsic weakness of this mesh caused by the type and amount of the material and the partial absorption of the inserted material is likely to contribute to the recurrence rate. Also, since the amount of the implanted material is lower the inflammatory reaction might possibly be less intense, resulting in a decreased formation of fibrosis. Moreover, the type of collagen created in this fibrotic response when Ultrapro® mesh is used might be less organized and/or strong compared to the type of collagen formed after Prolene® mesh implantment. Taking these factors into account, less optimal fixation of lightweight meshes in the abdominal wall might have occurred, possibly explaining the observed higher recurrence rate in the lightweight group.

Less optimal fixation of lightweight meshes is disadvantageous for large defects, since these are more likely to recur.[14-15] Combined with the results of this study regarding primary hernia type, patients with large medial defects are at greatest risk of recurrence when lightweight mesh is used.

Higher recurrence rates for lightweight mesh used in TEP hernia surgery have also been described in previous studies. A randomized controlled trial conducted in 402 patients with bilateral groin hernias by Chowbey et al. demonstrated a recurrence rate of 1.3% for lightweight mesh (191 patients) versus a 0.2% recurrence rate for heavyweight mesh (211 patients) after 1 year of follow-up.[15] A retrospective data study of 1232 groin hernia repairs (861 heavyweight, 371 lightweight) performed by Akolekar et al. reported a higher number of recurrences for lightweight mesh as well; 4.3% of patients treated with lightweight mesh developed a recurrence after a median follow-up of 14.5 months, compared to 2.8% recurrences for heavyweight mesh after a median follow-up of 43 months.[14] Only

Langenbach et al. performed a randomized controlled trial with a long-term 5-year follow-up after endoscopic hernia surgery.[27] This study assessed recurrence rates in 180 patients that underwent TAPP hernia repair and were randomized into 3 groups (2 types of heavyweight and 1 lightweight mesh). A total recurrence rate of 2.3% without significant differences in recurrence rates between the groups was reported. However, since the overall recurrence rate after endoscopic inguinal hernia repair in experienced hands is low, the sample size of this study might have been too small to detect relevant differences between the different mesh types.

An important consideration for the interpretation of reported data on inguinal hernia recurrence is the difference between the true recurrence rate and the reoperation rate. The majority of studies describing recurrences after inguinal hernia repair report reoperation rates instead of recurrence rates. As not all recurrences are reoperated, reported results might therefore be an underestimation of their recurrence rates. Although we demonstrated a true recurrence rate of 2.4% in our population, only 1.6% of our study population was reoperated (2.1% lightweight, 1.1% heavyweight).

In the present study, most hernia recurrences occurred in the first 2 years after surgery. Of the 6 additional recurrences that were detected after 2 years of follow-up, 4 patients presented on their own initiative and only 2 recurrences were diagnosed after intensive and time-consuming assessment.

As pointed out earlier, most studies that compared lightweight and heavyweight mesh in endoscopic inguinal hernia repair did not perform a follow-up for more than 2 years. The study by Langenbach et al. reported a 5-year follow-up, however, the time point after surgery when recurrences were detected, was not mentioned.[27] In the study of Liem et al., where all participants received a polypropylene mesh, recurrences after TEP hernia repair were analyzed and reported at 2, 3 and 5 years after surgery.[28] As most recurrences occurred within 2 years postoperatively, these data are in line with the results of the present study. Confirmed by previous research, our results thus imply that only few additional recurrences will be detected when a routine long-term follow-up after 2 years is performed. Therefore, we would recommend not to implement a standard long-term follow-up more than 2 years after TEP inguinal hernia repair.

The strengths of this study are the performance of a long-term follow-up in a large randomized sample of patients with use of a validated questionnaire.
A possible limitation of this study is that not all patients in whom a 5-year follow-up was conducted were clinically assessed and therefore (asymptomatic) recurrences might have been missed. However, we deliberately decided on this telephonic follow-up, since we expected recurrence rates after TEP inguinal hernia repair to remain low and the evaluation

of our entire study population at the outpatient clinic would be a burden for both patients and doctors and would not likely yield many additional recurrences. The PINQ-PHONE questionnaire showed a sensitivity of 100% in its validation study, implying that recurrences can very reliably be excluded in patients with a negative reply on the questionnaire. [19] When evaluating patients with a positive reply at the outpatient clinic, we experienced only very mild or sometimes no complaints at all in the majority of patients, which implied that the PINQ-PHONE was able to detect even the slightest of complaints that were sometimes not even present anymore at the clinical visits. Therefore it is not very likely many additional recurrences would have been detected if all patients with a positive reply had been evaluated.

Since our center is a high-volume hernia clinic performing 1100 TEP inguinal hernia repairs annually, with all operating surgeons having extensive experience, the demonstrated recurrence rate might not entirely be attributable to all hospital settings where fewer TEP procedures are performed by less experienced surgeons. However, the fact that procedures were performed in a center with extensive experience makes the observed differences between the meshes even more reliable. This is also confirmed by the findings of the multivariate analysis, where lightweight mesh type was a significant predictor for development of a recurrence.

In conclusion, we have demonstrated a low recurrence rate of 2.4% 5 years after TEP inguinal hernia repair. The use of lightweight Ultrapro® mesh resulted in a recurrence rate of 3.8%, while only a 1.1% recurrence rate was seen after heavyweight mesh implantment. Patients with primary medial hernias were at greatest risk of developing a recurrence when lightweight mesh was used.

The results of this study strengthen our previous recommendation not to use lightweight Ultrapro® mesh in TEP inguinal hernia repair. Since the overall recurrence rate after endoscopic TEP inguinal hernia repair remained low and the majority of recurrences developed within 2 years after surgery, we would not recommend a standard long-term follow-up for detection of recurrences.

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Lightweight
Hernia
Mesh
Repair
Pain
HWM
LWM
TEP
TAPP
Results
Stiffness
Analysis
Complications
Chronic
Recurrence
Fixation
Lichtenstein
PRISMA
GRADE
RCTs
Heavyweight
Implanting
Symmetric

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GRADE
PRISMA

Heavyweight mesh is superior to lightweight mesh in laparo-endoscopic inguinal hernia repair:
a meta-analysis and trial sequential analysis of randomized controlled trials

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Annals of Surgery (2020) 273:890-899

Abstract

Objective

This meta-analysis and trial sequential analysis aims to provide an update on the available randomized controlled trials (RCTs) and recommendations on using lightweight mesh (LWM) or heavyweight mesh (HWM) in laparo-endoscopic inguinal hernia repair.

Background

LWM might reduce chronic pain through improved mesh flexibility and less fibrosis formation. However, in laparo-endoscopic repair chronic pain is already rare and LWM raise concerns of higher recurrence rates.

Methods

A literature search was conducted in May 2019 in MEDLINE, Embase and the Cochrane library for RCTs that compared lightweight (≤50g/m^2) and heavyweight (>70g/m^2) mesh in patients undergoing laparo-endoscopic surgery for uncomplicated inguinal hernias. Outcomes were recurrences, chronic pain and foreign body sensation. The level of evidence was assessed using GRADE. Risk ratios (RR) and 95% confidence intervals (CI) were calculated by random effect meta-analyses. Trial-sequential-analyses were subsequently performed.

Results

Twelve RCTs, encompassing 2,909 patients (LWM 1,490 *versus* HWM 1,419), were included. The follow-up range was 3-60 months. Using LWM increased the recurrence risk (LWM 32/1,571, HWM 13/1,508; RR 2.21; CI 1.14-4.31), especially in non-fixated mesh direct repairs (LWM 13/180, HWM 1/171; RR 7.27; CI 1.33-39.73) and/or large hernia defects. No difference was determined regarding any pain (LWM 123/1,362, HWM 127/1,277; RR 0.79; CI 0.52-1.20), severe pain (LWM 3/1,226, HWM 9/1,079; RR 0.38; CI 0.11-1.35), and foreign body sensation (LWM 100/1,074, HWM 103/913; RR 0.94; CI 0.73–1.20).

Conclusion

HWM should be used in laparo-endoscopic repairs of direct or large inguinal hernias to reduce recurrence rates. LWM provide no benefit in indirect hernias.

Introduction

The use of prosthetic mesh to ensure low recurrence rates is standard in inguinal hernia repair.[1, 2] Nonetheless, implanting a mesh can cause pain, stiffness and a foreign body sensation. To minimize these complications, different surgical techniques have been considered and investigated, and modifications to the mesh, such as using less material or making them partially absorbable have been introduced.

In experienced hands, laparo-endoscopic pre-peritoneal (TEP and TAPP) techniques are superior to open Lichtenstein repair in terms of postoperative pain, speed of recovery and chronic pain. In part, this improvement is due to avoidance of the surgical plane encompassing the inguinal nerves.[3] Today, many different types of mesh are commercially available, however no recommendations on the superior type of mesh can be made. Comparison of different types of mesh is challenging, since many mechanical mesh properties (weight, elasticity, pore size, effective porosity, polymer type and strength) can influence postoperative complaints. The weight of the mesh is the most widely investigated characteristic, therefore a comparison of lightweight mesh (LWM) to heavyweight mesh (HWM) is likely to be the most informative parameter. LWM has been shown to surpass HWM regarding chronic pain and foreign body sensation when used in open inguinal hernia repair, whilst the recurrence rate was unaffected.[4, 5] Considering that chronic pain in laparo-endoscopic repairs is already rare, determining differences in frequency of chronic pain between LWM and HWM has proven difficult. Thus, it is questionable whether the weight of the mesh influences pain results as in open repair. Moreover, there are concerns of higher recurrence rates when using LWM, especially for direct hernias or hernias with large defect sizes.

The latest systematic review and meta-analysis which summarizes the literature up to 2013 concluded that the use of LWM reduced the incidence of chronic groin pain and was not statistically associated with a difference in recurrences.[6, 7] This meta-analysis stated high quality randomized controlled trials (RCTs) with longer follow-up were needed to validate their findings. Moreover, no sensitivity analyses were performed that address possible reasons for doubt among surgeons, such as recurrences after direct or indirect repairs, the influence of the size of the hernia defect, or the influence of using fixation techniques on pain and recurrences. To date, surgeons remain unconvinced by the use of LWM, probably due to potential bias in previous meta-analyses, the higher price of LWM, the inconvenient handling and remaining concerns of an increased recurrence risk when using LWM.[6, 7]

Therefore, the aim of this systematic review and meta-analysis is to provide an update on the available RCTs for the outcomes recurrences, chronic pain and foreign body sensation, supplemented with the above mentioned sensitivity analyses. This study aims in turn to

provide a (definite) recommendation on the use of LWM or HWM in laparo-endoscopic inguinal hernia repair.

Methods

This systematic review and meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[8] The protocol of this systematic review was registered on PROSPERO (ID CRD42018100049).

Study selection

A literature search in EMBASE, MEDLINE and the Cochrane Library was conducted in May 2019. The search was not limited by language or publication date. Only studies that were published as full-length articles were included. The search strategy can be found in Supplemental Digital Content 1. All identified publications were transferred into EndNote (EndNote X8.2, Thomson Reuters, New-York) and subsequently into Rayyan (Qatar Computing Research Institute).[9] Duplicates were removed. Irrelevant publications based on title and abstract and/or full-text screening were excluded by 2 independent reviewers (W.J.B. and J.S.B.). Any discrepancies were discussed between the senior author (J.P.J.B.) and the 2 reviewers. Attempts were made to identify additional studies that met the inclusion criteria by searching the reference lists of included RCTs.

All RCTs that compared lightweight (≤50 g/m^2) and heavyweight (>70 g/m^2) mesh in patients undergoing laparo-endoscopic inguinal hernia repair (TEP or TAPP) for uncomplicated inguinal hernias, using the same surgical technique and fixation method in both groups, were included. Uncomplicated inguinal hernias were defined as inguinal hernias that were not incarcerated or strangulated. For LWM and HWM there are no standardized weight definitions. To ensure that the most relevant lightweight or heavyweight mesh were included, generally accepted cut-off points of >70 g/m^2 for HWM and <50 g/m^2 for LWM were set.[10-13] As elaborated on before, the mesh weight does not fully explain the mesh properties. Studies comparing biological mesh to either LWM or HWM were not included. Follow-up had to be a minimum of 3 months and outcome parameters had to include either recurrences or chronic pain, or both.

Outcomes

The authors decided that crucial outcome parameters for decision-making were chronic pain and recurrences. Chronic pain was defined as (inguinal) pain lasting a minimum of 3 months in accordance with the International Association for the Study of Pain.[14] Any pain and severe pain (the latter, as defined in the included RCTs) were assessed. Regarding recurrences, trials reporting follow-up of more than 3 months were assessed. Separate meta-analyses

of the available data for direct or indirect hernia repairs only were performed to detect recurrence rate differences between LWM and HWM. Furthermore, the influence of the primary hernia defect size on recurrences for both mesh types was determined. Moreover, possible variances in recurrence rates were assessed by first including RCTs that did not use fixation techniques and, subsequently including only the studies that did use fixation techniques. Foreign body sensation after a minimum of 3 months was considered to be the only clinically relevant secondary outcome parameter.

Data extraction

The most important study characteristics and results were extracted from the original RCTs by 2 independent reviewers (W.J.B. and J.S.B.). The characteristics of the mesh were presented as originally described by the authors of the studies. Interim analyses were excluded from the meta-analyses if longer follow-up data was available. For pain and foreign body sensation outcomes the number of patients were entered into the meta-analysis. With regard to recurrence outcomes in case of included bilateral repairs, the number of meshes were entered into the meta-analysis if retrievable. Without exception, the corresponding authors of the RCTs were contacted for additional specific information for data pooling if no usable results were published, so that bias related to missing data could be reduced. For instance, if only mean pain scores were available, authors were contacted to provide the group sizes and the number of patients with pain. A study was excluded from the meta-analysis of that particular outcome if no requested supplementary data was available, or no response was received. Received unpublished data was denoted in the subscript of the forest plots.

The Cochrane Handbook for Systematic Reviews of Interventions, version 5.1, was used to address the quality of the trials included. The risk of bias was assessed by 2 independent reviewers (W.J.B. and J.S.B.) for blinding of patients, care providers and outcome assessors, concealment of allocation, methods of randomization, selective outcome reporting (if available, extracted from individual study protocols), violation of intention-to-treat analysis and loss to follow-up. The scoring system of Jadad et al. was used to address the quality of the data.[15] A Jadad score under 3 (out of 5) was considered a high risk of bias. All reviewers agreed that the blinding of care providers (operating surgeon) was unmanageable due to the visible and handling differences between LWM and HWM. Therefore, the blinding of patients and outcome assessors was considered double blind in the Jadad scoring system. Loss to follow-up was considered a risk of bias when more than 15.0% was lost to follow-up in less than 24 months and more than 20.0% lost to follow-up after 24 months. For each outcome the level of evidence was further evaluated using chapter 5 of the GRADE Handbook (Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group, Cochrane Collaboration).[16]

Statistical analysis

The estimated difference between LWM and HWM was pooled using Review Manager (Version 5.3, Cochrane Collaboration, Copenhagen, Denmark). If pooling data was not possible, the results of the trial were described in text as reported by the authors. Random effect meta-analyses for binary outcomes with risk ratios (RR) and 95% confidence intervals (CI) were performed using the Mantel-Haenszel method to correct for methodological heterogeneity and clinical diversity. Outcomes were considered statistically significant if the 95% CI did not include 1. Forest plots were used for graphical display in which the squares represent the RR of the trials, the size of the square represents the weight of the trial in the overall analysis, and the horizontal lines through the squares represent the 95% CI. Heterogeneity was evaluated using chi-square tests, with $p<0.05$ set as significant, and was quantified using I^2, identifying low heterogeneity with a maximum percentage of 30%.[16] Numbers needed to treat (NNT) were calculated for the comparison of LWM as the intervention and HWM as the control group, and presented as numbers needed to harm (NNH) if the outcome was a negative. The 95% CI of the NNT/NNH were presented for statistically significant outcomes. Funnel plots were assessed to evaluate possible publication bias in the meta-analyses.

Several sensitivity analyses were executed to analyze the influence of the length of follow-up for chronic pain and foreign body sensation, therefore grouping the relevant data in follow-up periods of ≤6 months, ≤12 months, ≤24 months, ≥12 months and ≥24 months. For the outcome any pain, data of patients with the combination of a recurrence and pain was extracted from the RCTs and adjusted for in the meta-analysis. Separate sensitivity analyses for all outcomes were performed with only studies that included use of LWM with large pores (>1mm), and with studies excluded that had an inordinate loss to follow-up, a high risk of bias, or included repairs of recurrent inguinal hernias, the latter to correct for a higher incidence of chronic pain and higher recurrence rates in repairs of recurrent hernias.[17-19] Also, we investigated the effect of including only studies with only TEP repairs, and subsequently with only TAPP repairs. To provide a complete insight and respect all available data, the forest plots showed all available studies with their longest available follow-up. If substantial differences in outcomes were seen after sensitivity analyses, the results of the meta-analyses were outlined in text.

Furthermore, we performed a trial sequential analysis (TSA) to determine the required information size estimation with an adjusted threshold for statistical significance (trial sequential monitoring boundaries (TSMB)) in the cumulative meta-analysis to assess the conclusiveness and reliability of the available evidence.[20-22] We performed the analyses using the program Trial Sequential Analysis Viewer – version 0.9.5.10 Beta.[23] The TSA was performed with a two-sided α of 0.05 and a β of 0.20 (power 80%). Using the diversity (D^2) adjusted required information size (DARIS), the meta-analysis was changed from a random-effect model into a fixed-effect model.[21] A sensitivity analysis with a D^2 of 25% was performed if a

D^2 of <25% was encountered.[20] The DARIS for each outcome was established with relative risk reductions based on the intervention effect of the low-bias trials (LBT) that were included in the meta-analysis to detect if the overall established outcomes in the meta-analyses were of firm evidence, and additionally, based on an *a priori* intervention effect of 20% (AP20%).[22]

Results

Fifteen articles from 12 RCTs, encompassing 2,909 patients, were included in the systematic review. The LWM group contained 1,490 patients and the HWM group contained 1,419 patients. The range of follow-up was 3-60 months. The study selection yielded no discrepancies between reviewers. The trial selection process is shown in the PRISMA flowchart (Figure 1).

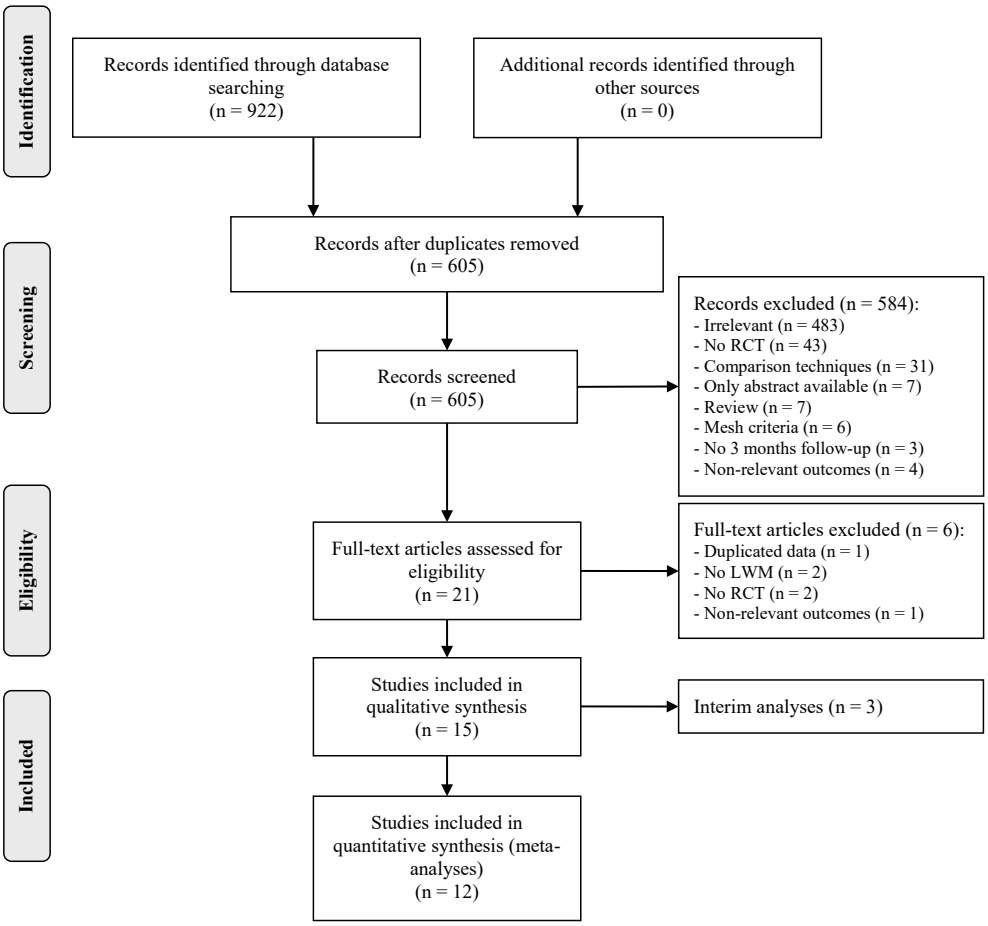

Figure 1 PRISMA Flow Diagram

The study characteristics and the baseline characteristics of patients from the included RCTs are presented in table 1a. The specifications of the inguinal hernia repairs in the included RCTs are shown in table 1b. The assessment of the individual study quality (risk of bias) is shown in table 1c. All outcomes showed symmetric inverted funnel shapes (see funnel plots, Supplemental Digital Content 2), making any publication bias unlikely. All outcomes of the sensitivity analyses and TSA are found in table 2. The TSA graphs can be found in Supplemental Digital Content 3. Sensitivity analyses of studies with a follow-up period of ≤12 months, ≤24 months, ≥12 months and a Jadad score over 3 only were performed but not shown in table 2, since they revealed no changes in significance and for most analyses few RCTs remained.

Chronic Pain – any pain, and severe pain

Eight RCTs reported on the outcome chronic pain.[24-31] Agarwal et al. (2009), Prakash et al. (2016) and Kalra et al. (2017) presented the mean score on the Visual Analogue Scale (VAS) ± the standard deviation (SD), however they did respond to the request for the additional data required for meta-analysis.[32-34] Eight of these 11 studies reported severe pain results, albeit with varying definitions (Table 1a).[18, 24, 26-29, 32-34]

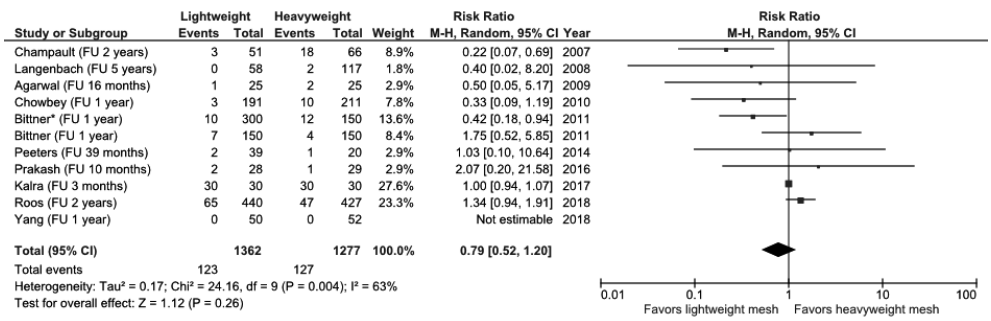

Figure 2 Pooled data from 11 RCTs regarding any chronic pain after the use of lightweight mesh versus heavyweight mesh in laparo-endoscopic inguinal hernia repair. Agarwal et al. (2009), Prakash et al. (2016) and Kalra et al. (2017) represent unpublished data.

Table 1 Study and baseline characteristics, specifications of performed inguinal hernia repair, and risk of bias for the included RCTs.

Study	Champault (2007)	Langenbach (2008)	Agarwal (2009)	Chowbey (2010)	Bittner (2011)	Bittner (2011)*	Peeters (2014)	Prakash (2016)	Kalra (2017)	Wong (2017)	Roos (2018)	Yang (2018)
1a *Study characteristics and baseline characteristics of patients from the included RCTs*												
Sample size, n LWM:HWM	57:80	58:117	25:25	382:422*	150:150	300:150	52:27*	89:86*	30:30	43:42	478:471	50:52
Sex, % male	97	100	100	91	88	89	100	NR	95	96	100	100
BMI, mean	NR	25	NR	NR	25	25	24	25	NR	NR	25	NR
Age, yrs LWM:HWM	54	62:63	62	53:53	54:52	59:57	43:34	55:55	40:44	62:58	55:56	47:45
Bilateral hernia, %	23	0	100	100	0	0	37	34	0	32	0	0
Recurrent hernia, %	13	0	NR	0	12	5	0	0	0	0	0	0
Pain measurement	VAS	VAS	VAS	VAS	VAS	VAS	VAS	VAS	VAS	VAS	VAS	Questions
Definition severe pain	VAS > 5	N/A	VAS > 5	Interferes with ADL	Use of analgesics	Use of analgesics	Cunningham scale	N/A	VAS > 4	N/A	VAS > 7	N/A
Shortest available FU (mos)	24	24	3	3	6	6	12	3	3	20	3	12
1b *Specifications of inguinal hernia repair of included RCTs*												
Technique	TEP	TAPP	TEP	TEP	TAPP	TAPP	TEP	TEP/TAPP	TAPP	TEP	TEP	TAPP
LWM, g/m²	Glucamesh (50)	PP-polyglactin (35)	PP	Ultrapro (28)	TiMesh (16)	Ultrapro (28) & TiMesh (35)	Vypro II (30) & TiMesh (35)	Prolene soft (30-45)	Ultrapro (28)	Ultrapro (28)	Ultrapro (28)	TiMesh (35)
Pore structure LWM	Microporous	Macroporous	Macroporous	Macroporous	Macroporous	Macroporous	Macroporous	Macroporous	Macroporous	Macroporous	Macroporous	Macroporous
HWM, g/m²	PP (105)	Double- (108) & multi-filament (116) PP	PP	Prolene (105)	Prolene (90)	Prolene (90)	Marlex (95)	3D max large (80-85)	3D max (80-100)	Parietex (116)	Prolene (80)	SPMM-66
Mesh fixation	None	Medial and lateral to epigastric vessels; and fascia transversalis (direct hernias) fixed on Cooper's ligament	None	At 2 points on Cooper's ligament using Protack	Sutured HWM at 2 points; medial and lateral to epigastric vessels	Fibrin glue	Mesh + fascia transversalis with a tacker (Protack) on Cooper's ligament in large direct hernias	None	3 Absorbable tackers; 1 on Cooper's ligament, 2 on anterior abdominal wall	None	None	None
Surgeon, %	100	100	100	100	43	52-60	100	NR	NR	100	>99	NR
Residents, %	0	0	0	0	57	40-48	0	NR	NR	0	<1	NR
1c *Risk of bias table*												
Method of randomisation	NR	Sealed envelopes	Sealed envelopes	Computer generated	Computer generated	Computer generated	Computer generated	Computer generated	Sealed envelopes	Sealed envelopes	Computer generated	Computer generated
Allocation concealment	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Blinding of patients	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear
Blinded outcome assessors	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	No	Unclear	Yes	Yes	Unclear
Selective outcome reporting	No	No	No	No	No	No	No	No	No	No	No	Yes
Loss to FU, % / months FU	14.6 / 24	2.8 / 60	Unclear / 16	8.8 / 12	7.0 / 12	4.0 / 12	16.9 / 39	4.4 (3mos) / 10	Unclear / 3	10.4 / 20	16.8 / 60	Unclear / 12
Violation of ITT?	Unclear	No	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Yes	No
Jadad score	2	4	1	3	5	5	5	3	1	4	5	2

* = Included mesh, not patients (including bilateral); BMI = Body Mass Index; FU = follow-up; NR = not reported; VAS = Visual Analogue Scale; PP = polypropylene; N/A = not applicable; macroporous = >1mm pore size; ITT = intention to treat.

The risk of any pain showed no significant difference when using a LWM (123/1,362 patients) compared to a HWM (127/1,277 patients) (RR 0.79, 95% CI: 0.52 - 1.20) (Figure 2). There was substantial heterogeneity (chi-square = 24.16, *df* = 9, P = 0.004, I^2 = 63%) among the RCTs. Also, the risk of severe pain was not statistically significant (LWM 3/1,226 and HWM 9/1,079 patients, RR 0.38, 95% CI: 0.11 – 1.35) (see forest plot severe pain, Supplemental Digital Content 4). There was low statistical heterogeneity among the RCTs (chi-square = 2.24, *df* = 3, P = 0.52, I^2 = 0%). TSA indicated shortage of evidence for any pain and severe pain, since the trial sequential monitoring boundaries (TSMB) were not surpassed and the required information size was not reached (Table 2). Sensitivity analyses revealed no significant changes for any pain or severe pain (Table 2). Because the study by Kalra et al. (2017) had outlying results (probably because follow-up was only 3 months), a high risk of bias and carried 27.6% of the meta-analysis, an additional analyses was performed excluding this study which did not change the outcome (RR 0.68, 95% CI: 0.36 – 1.28). Further analyses were performed to correct for the influence of the recurrences in a trial on the outcome chronic pain. No RCTs reported if patients with recurrences were in pain. The study by Roos et al. (2018) weighs highly in the analysis and reports many recurrences for the LWM group compared to the HWM group. Therefore, their database was re-assessed, resulting in 8 LWM patients and 1 HWM patient with a recurrence that were in pain. The TULP-trial found recurrences to be a significant factor for pain at 1 year in a multivariate analysis. Eliminating these patients for the any pain analysis did not change the outcome (RR 0.73, 95% CI: 0.45 – 1.21). Moreover, using their database the influence of changing the definition of severe pain from VAS >7 to >5 was examined, since most studies used this cut-off point. Re-assessment showed 4 patients in the LWM group with VAS >5, instead of 0 with VAS >7, no patients in the HWM group had a VAS >5, thus resulting in a less-outlying RR of 0.70, 95% CI: 0.16 – 3.02.

Recurrence

Eleven RCTs reported on the outcome recurrence (Figure 3).[24-33, 35] The pooled analysis showed that the risk of a recurrence was statistically significantly increased by a factor of 2.21 when a LWM was used compared to a HWM (LWM 32/1,571 and HWM 13/1,508 patients, RR 2.21, 95% CI: 1.14 - 4.31). The NNH was 85 (95% CI: 48 – 305). There was low statistical heterogeneity among the RCTs (chi-square = 6.75, *df* = 8, P = 0.56, I^2 = 0%). Also, TSA indicated firm evidence for an increased risk of recurrences when using LWM, since the Z-score surpassed the TSMB of the low-bias trials, however in the sensitivity analysis with a D^2 of 25% the significance faded (Table 2). The *a priori* 20% intervention effect was not reached (Table 2). The outcome was only changed by excluding studies with repairs performed for recurrences and, further sensitivity analyses did not reveal any changes in significance (Table 2).

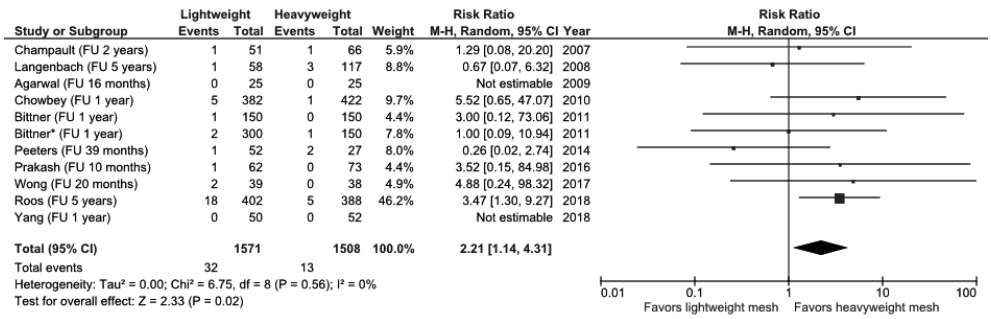

Figure 3 Pooled data from 11 RCTs regarding recurrences after the use of lightweight mesh versus heavyweight mesh in laparo-endoscopic inguinal hernia repair. Prakash et al. (2016) represents unpublished data.

Influence of direct or indirect inguinal hernia repair on recurrences

Seven studies initially reported their recurrence outcome with additional information, making them suitable for meta-analysis.[25, 27-32] Out of the remaining studies that reported recurrence outcomes, Chowbey et al. (2010), Prakash et al. (2016) and Wong et al. (2017), responded with the required additional data upon request.[26, 33, 35]

The risk of a recurrence after direct inguinal hernia repair showed no significant difference when a LWM (19/500 patients) was used compared to a HWM (6/511 patients) (RR 2.31, 95% CI: 0.83 - 6.43) (Figure 4). Heterogeneity was low among the RCTs (chi-square = 6.57, *df* = 6, P = 0.36, I^2 = 9%). The risk of recurrence after an indirect hernia repair was not influenced when a LWM (12/866 patients) was used compared to a HWM (6/842 patients) (RR 1.66, 95% CI: 0.66 - 4.18) (see forest plot recurrences after indirect repairs, Supplemental Digital Content 5). There was low statistical heterogeneity among the RCTs (chi-square = 1.55, *df* = 4, P = 0.82, I^2 = 0%). TSA indicated lack of evidence and sensitivity analyses revealed no change in significance for either direct or indirect repairs (Table 2).

Table 2 Sensitivity analyses and trial sequential analyses

Sensitivity analyses	Any pain	Severe pain	Recurrences	Recurrences after direct repair	Recurrences after indirect repair	Recurrences after direct repair with non-fixated mesh	Foreign body sensation
Longest FU and no studies excluded	0.79 (0.52-1.20)	0.38 (0.11-1.35)	**2.21 (1.14-4.31)**	2.31 (0.83-6.43)	1.66 (0.66-4.18)	**7.27 (1.33-39.73)**	0.94 (0.73-1.20)
Exclusion of high risk of bias studies	0.85 (0.46-1.57)	0.71 (0.04-12.01)	**2.29 (1.15-4.54)**	2.31 (0.83-6.43)	1.66 (0.66-4.18)	**7.27 (1.33-39.73)**	1.01 (0.75-1.36)
Only studies with ≤6 months FU	0.81 (0.44-1.48)	0.36 (0.09-1.43)	N/A	N/A	N/A	N/A	0.93 (0.67-1.29)
Only studies with ≥24 months FU	0.64 (0.19-2.13)	0.43 (0.05-4.03)	N/A	N/A	N/A	N/A	1.08 (0.77-1.52)#
Exclusion of studies with recurrence repairs	0.98 (0.63-1.52)	0.20 (0.02-1.61)#	2.21 (0.90-5.43)*	2.31 (0.58-9.21)	1.66 (0.66-4.18)	**7.27 (1.33-39.73)**	0.91 (0.67-1.24)
Only studies with macroporous LWM	0.96 (0.71-1.30)	0.37 (0.07-1.91)	**2.29 (1.15-4.54)**	2.31 (0.83-6.43)	1.66 (0.66-4.18)	**7.27 (1.33-39.73)**	0.94 (0.73-1.20)
Only studies with only TAPP repairs	0.80 (0.22-2.94)	0.37 (0.07-1.91)	1.06 (0.25-4.56)	1.37 (0.33-5.67)	Not estimable	Not estimable	0.78 (0.50-1.22)
Only studies with only TEP repairs	0.56 (0.21-1.52)	0.43 (0.05-4.03)	2.40 (0.92-6.28)	3.25 (0.64-16.55)	1.60 (0.61-4.20)	**7.27 (1.33-39.73)**	1.10 (0.78-1.55)
Trial sequential analysis (TSA)							
D^2 / sensitivity analysis with D^2=25 (%)	80	0 / 25	0 / 25	10 / 25	0 / 25	0 / 25	0 / 25
DARIS-LBT / for D^2=25%	58,847	38,425 / 51,233	**3,555** / 4,740	2,824 / 3,393	13,304 / 17,738	557 / 742	1,871,353 / 2,495,137
DARIS-AP20% / for D^2=25%	31,736	80,331 / 107,108	83,540 / 111,386	68,756 / 82,604	101,860 / 135,813	112,784 / 150,378	5,616 / 7,488

Outcomes sensitivity analyses expressed as RR (95 % CI); in bold = statistically significant; FU = follow-up; N/A = not applicable; * = change in significance; # only 1 study remains; D^2 = diversity; DARIS = diversity adjusted required information size; LBT = low-bias trial based relative risk reduction; AP20% = based on *a priori* 20% relative risk reduction.

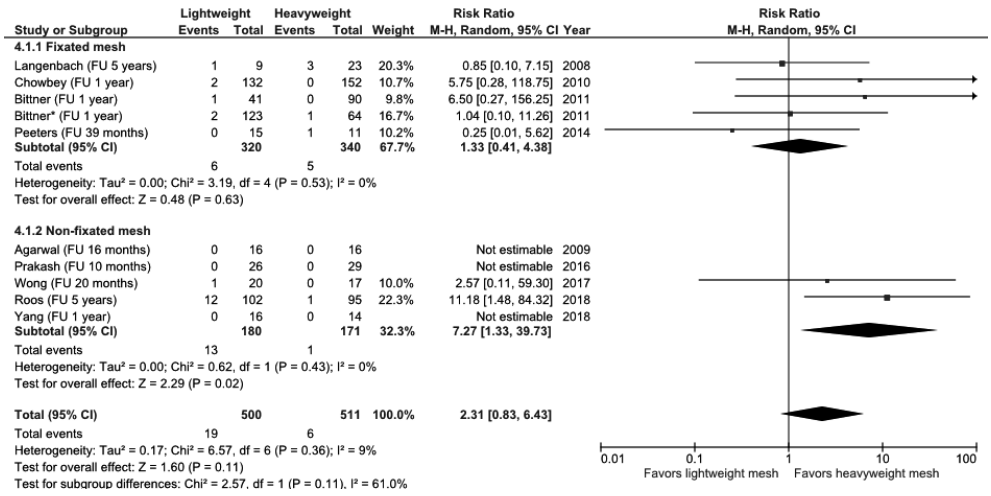

Figure 4 Pooled data from 10 RCTs regarding recurrences after direct repairs comparing the use of lightweight mesh versus heavyweight mesh in laparo-endoscopic inguinal hernia repair. Subgroups of fixated and non-fixated mesh are shown. Chowbey et al. (2010), Prakash et al. (2016) and Wong et al. (2017) represent unpublished data.

Influence of mesh fixation on recurrences

Mesh fixation techniques were performed in 5 of the 11 RCTs that reported on recurrences and in 6 RCTs no mesh fixation was performed (Table 1b). If studies that only performed mesh fixation were included, the significance of an increased risk for recurrences when using LWM disappeared (LWM 10/942 and HWM 7/866 patients, RR 1.20, 95% CI: 0.40-3.61). Heterogeneity was low (chi-square = 4.22, *df* = 4, P = 0.38, I^2 = 5%). Also, no significant difference was seen for recurrences after direct hernia repair with fixated mesh (LWM 6/320 and HWM 5/340 patients, RR 1.33, 95% CI: 0.41-4.38, low heterogeneity (chi-square = 3.19, *df* = 4, P = 0.53, I^2 = 0%)) (Figure 4), and after indirect hernia repairs with fixated mesh (LWM 4/472 and HWM 2/452 patients, RR 1.39, 95% CI: 0.22-8.83, low heterogeneity (chi-square = 1.13, *df* = 1, P = 0.29, I^2 = 12%)). TSA indicated insufficient data for the analyses of fixated mesh (Supplemental Digital Content 3).

If only studies that did not perform mesh fixation were included, the increased risk of developing a recurrence when using a LWM increased and remained of significance (LWM 22/629 and HWM 6/642 patients, RR 3.25, 95% CI: 1.39-7.61). The NNH was 39 (95% CI: 23 - 104), and there was low heterogeneity (chi-square = 0.52, *df* = 3, P = 0.91, I^2 = 0%). Interestingly, using LWM compared to HWM in direct repairs with a non-fixated mesh significantly increased the RR by a factor of 7.27 (LWM 13/180 and HWM 1/171 patients, RR 7.27, 95% CI: 1.33-39.73) (Figure 4). The NNH was 15 (95% CI: 9 - 37), there was low heterogeneity (chi-square = 0.62, *df* = 1, P = 0.43, I^2 = 0%). Recurrences after non-fixated mesh indirect repairs showed no significant difference (LWM 8/394 and HWM 4/390 patients, RR 1.77, 95% CI: 0.59-5.27, low heterogeneity (chi-square = 0.38, *df* = 2, P = 0.83,

I^2 = 0%)). TSA indicated insufficient data for the analyses of non-fixated mesh (Table 2, Supplemental Digital Content 3).

Influence of the primary hernia defect size on recurrence

This outcome was ill-reported as none of the data required for meta-analysis was available from the publications. However, the available data favors using HWM in large defect sizes. Chowbey et al. (2010) found all 5 recurrences in the LWM group to be after the repair of large hernia defects (3 indirect, 2 direct).[26] Prakash et al. (2016) showed 1 recurrence that occurred in the LWM-group after a large primary indirect inguinal hernia.[33] During re-assessment of the database (not published) of Roos et al. (2018), it was found that all of the recurrences after reported primary hernia defect sizes of >3 cm appeared in the LWM group. Out of 23 recurrences, defect sizes were only reported in 8 cases, 6 of which were >3 cm. Peeters et al. (2014) found no difference in recurrence rates between groups attributable to the hernia defect size.[29] Bittner et al. (2011)* excluded hernia defects >3cm.[27] Other RCTs that published recurrence outcomes did not report on primary hernia defect sizes or found no recurrences.

Foreign Body Sensation

Six RCTs initially reported on the outcome foreign body sensation (Figure 5).[27, 30, 31, 33-35] Bittner et al. (2011)* responded with the required data.[28] The risk of foreign body sensation showed no difference when using LWM (100/1,074 patients) compared to HWM (103/913 patients) (RR 0.94, 95% CI: 0.73 – 1.20). There was low heterogeneity among the RCTs (chi-square = 4.69, *df* = 6, P = 0.58, I^2 = 0%). TSA indicated lack of evidence and sensitivity analyses revealed no significant changes (Table 2).

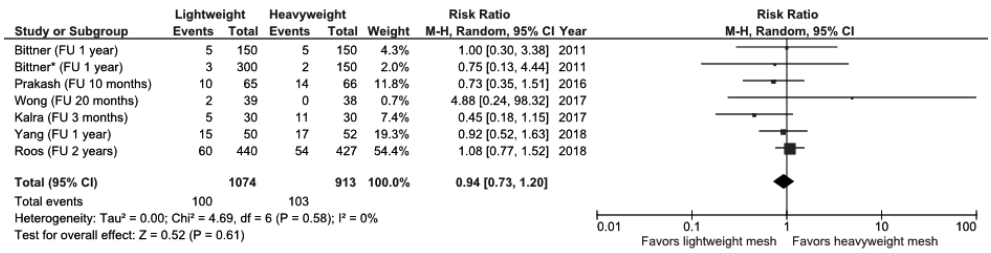

Figure 5 Pooled data from 7 RCTs regarding foreign body sensation after the use of lightweight mesh versus heavyweight mesh in laparo-endoscopic inguinal hernia repair. Bittner et al. (2011)* represents unpublished data.

Rating the quality of the evidence using GRADE[16]

The evidence originated from RCTs, therefore the quality level started at 'High'. We did not downgrade the outcomes for limitations in the methodological quality of the included RCTs (risk of bias), since removing the studies with a high risk of bias from the meta-analysis

did not affect the outcomes and a sufficient number of studies remained. However, the quality of the evidence regarding any pain, severe pain, recurrences in non-fixated mesh repairs, and foreign body sensation was downgraded with one level to 'moderate GRADE' due to imprecision. It was decided to downgrade the following outcomes by 2 levels to 'low GRADE' due to imprecision: recurrences after direct, indirect and fixated mesh. The outcome any pain was further downgraded to 'low GRADE', due to inconsistency of results. Severe pain and the outcomes regarding recurrences with or without mesh fixation were further downgraded to 'low GRADE', due to indirectness of evidence. The quality of the evidence regarding recurrences was not downgraded, since there was no publication bias, no inconsistency of results, no indirectness of evidence, or imprecision.

Discussion

This systematic review and meta-analysis demonstrated that HWM are preferable in laparo-endoscopic repairs of direct or large inguinal hernias. LWM provide no difference in indirect hernias. Using LWM instead of HWM, significantly increased and more than doubled the risk of recurrences, and significantly increased the risk of recurrences in non-fixated mesh repairs of direct inguinal hernia more than sevenfold. As the mesh type does not seem to influence chronic pain or foreign body sensation, there are no benefits of using LWM over HWM in laparo-endoscopic inguinal hernia repair.

Ever since LWM were introduced, and appeared to cause a decrease in chronic pain after open inguinal hernia repair, it has not been resolved what type of mesh to use in laparo-endoscopic inguinal hernia repair. Even with 11 RCTs reporting on chronic pain, LWM showed no statistically significant difference. Nevertheless, due to substantial heterogeneity TSA still detected a shortage of evidence to establish firm conclusions. For recurrences, especially in direct repairs that were not fixated or in large hernia defects, the evidence explicitly favors the use of HWM in laparo-endoscopic inguinal hernia repair. Whether looking at the overall analysis or after only direct or only indirect repair, with fixation of the mesh or not, the RR of a recurrence is always higher when LWM are used compared to HWM. Moreover, the executed TSA of recurrences overall based on the low-bias trials detected firm evidence. Also, the level of evidence regarding recurrences was 'high GRADE'. This means that we are confident that the true effect lies close to that of the estimate of the effect. Moreover, a recent cost-utility analysis comparing HWM and LWM in laparoscopic surgery from a National Health Service perspective found no support for the adoption of LWM as the standard treatment due to higher costs.[36]

Concerning recurrences, it is of importance to distinguish between those after direct and those after indirect hernia repairs in the included studies. In direct inguinal hernia repairs a

tendency towards significance for recurrences is seen when LWM are used, which is mainly driven by the effect of studies that did not perform mesh fixation. Interestingly, if only those studies that performed mesh fixation were included, the significance of the outcome recurrences faded. Potentially, although only small numbers were presented, Peeters et al. (2014) performed the most efficient fixation by using tackers to fixate both the mesh and the fascia transversalis on Cooper's ligament in large direct hernias.[29] On the contrary, only including studies without any mesh fixation led to the observation that recurrences after a direct hernia repair occurred significantly less often when a HWM was used, with a RR of 7.27 and a NNH of 15. There was no influence of these analyses on recurrences after indirect repairs. Although no significant increase in recurrences was determined after direct repairs, using a LWM and fixing the mesh with tackers or sutures to attain a decrease in recurrences, which is already achieved by using HWM, serves no purpose. In fact, this approach has downsides when taking into account the higher price, the inconvenient handling and the non-significant effect on chronic pain of LWM use. Moreover, the sutures or tackers can cause pain due to entrapment neuralgia.[37] Therefore, the use of a HWM is a superior and cost-effective method in laparoscopic hernia repair. Considering these analyses, and all the performed sensitivity analyses that did not show different outcomes, it seems that the evidence for using a HWM in direct hernia repair is strong. Furthermore, although ill-reported, recurrences seem more likely to develop after large hernia defects when a LWM is used. Thus, as far as reported, there is a general tendency for recurrences to develop when using a LWM after direct inguinal hernias and after large hernia defects. There does not seem to be any advantage of LWM use for indirect repairs or repairs of smaller hernias. This finding is in line with results from a recent, high-volume prospective Swedish hernia database study by Melkemichel et al. (2018).[13] They found LWM to be associated with an increased risk of reoperation for recurrences when compared to HWM, and concluded that direct hernias and larger hernia defects may benefit from HWM.

The latest systematic review with the same research question was performed by Sajid et al. (2013), which included 11 RCTs published up to June 2011.[7, 24-28, 32, 38-42] They concluded that the use of LWM during laparo-endoscopic inguinal hernia repair reduced the incidence of chronic groin pain and did not affect the risk of hernia recurrences. For the outcomes of this review 2 studies included in their review were irrelevant.[40, 41] Moreover, data extraction inaccuracies and incorrectly included studies in the systematic review by Sajid et al. (2013) were corrected for in this review. Sajid et al. (2013) stated that a high quality trial with a longer follow-up duration was required, which was provided with the publication of the results from the TULP-trial by Roos et al. (2018).[18, 30] The only downside of this study was the lack of mesh fixation, which led to the demonstrated association between direct hernias and an increased recurrence rate when using LWM. This study is the biggest contributor in the field and has the largest sample size, the longest follow-up duration, a high weight in all meta-analyses outcome fields, and was of an unlikely risk of bias. On the contrary, we are

aware of the influence of this study on the meta-analyses. For example, the many patients of the TULP-trial with LWM recurrences that were in pain, or the different pain definition used for severe pain, could influence the chronic pain outcomes. However, multiple re-assessments of the TULP-database, and therefrom corrections in multiple outcome fields did not change the significance of the outcomes. The long-term outcomes of Peeters et al. (2014) and 4 new trials by Prakash et al. (2016), Kalra et al. (2017), Wong et al. (2017) and Yang et al. (2018) further strengthened the evidence.[29, 31, 33-35] Interestingly, in a comparable systematic review and meta-analysis by Currie et al. (2012), published just a year before Sajid et al. (2013), different conclusions were drawn from the same studies.[12] In this systematic review, however, 2 RCTs were missed, that were correctly included by Sajid et al. (2013).[24, 27] Currie et al. (2012) concluded that the use of LWM in laparoscopic inguinal hernia repair did not offer a reduced risk of chronic pain or any change in the recurrence risk when compared to HWM.

The strength of this systematic review and meta-analysis is that new, valuable information for laparo-endoscopic inguinal hernia repair can be reported regarding crucial outcome measures for decision making in mesh choice. In particular the supplemental analyses to our primary outcomes into the influence of direct and indirect repairs, of fixation of the mesh and of the primary hernia defect size have never been performed. Outcomes that are subjective or easily interpreted differently by outcome assessors and care providers (infection or seroma/hematoma formation) or less important outcomes for decision-making (perioperative complications, operation time, early postoperative pain) were deliberately not assessed. Moreover, corrections were made for imprecisions detected in previously performed systematic reviews and meta-analyses with comparable research questions. We are confident that our search query was well-built, in part because no additional publications that met the inclusion criteria were found in the reference lists of the included RCTs. Also, unpublished data from the authors was extensively received and implemented in the meta-analyses.

Nevertheless, there were limitations to this systematic review. At a review level, publication bias was unlikely. For the outcome 'any pain' statistical heterogeneity was encountered. At a study level, the lack of baseline data and/or differences in in- and exclusion criteria (for example, age, sex, surgical expertise, hernia sizes, and recurrent or bilateral/unilateral inguinal hernias) between studies made clinical heterogeneity plausible. Moreover, studies were encountered with small sample sizes without the performance of a power analysis. Thus, these studies were probably unable to recognize small variances between groups. At the outcome level, the outcomes of interest could have been influenced by the fixation methods that were used and the follow-up duration. Moreover, these factors might have contributed to the encountered heterogeneity, particularly for the chronic pain outcomes. The shorter follow-up periods may have led to a long-term recurrence risk underestimation.

Fixation methods can influence the outcome chronic pain due to possible entrapment neuralgia, although this is similar within the trials.[37] Performing meta-analyses with TSA and sensitivity analyses in this systematic review compensated for these limitations to some extent. Lastly, there was no uniformity regarding the measurement scales or definitions that were used in different studies for chronic pain (e.g. any pain, severe or clinically relevant) and foreign body sensation. The inguinal pain questionnaire (IPQ) can facilitate future RCTs with a uniform assessment for postherniorrhaphy pain.[43, 44]

Randomized comparisons of good quality with an overall impressive sample size were abundantly published. Since the latest meta-analysis twice as many RCTs were performed that amplify our knowledge and provide stronger conclusions. Moreover, unpublished data was received from the authors of the RCTs and published first in this systematic review. Also, sensitivity analyses were performed that provided new insights and addressed possible reasons for doubt of the surgical community. TSA of recurrences overall based on the intervention effect of the low-bias trials indicated firm evidence, however the encountered event size remains relatively small. For chronic pain TSA indicated shortage of evidence due to substantial heterogeneity, however the estimated information size based on current available evidence seems beyond reach. To reach even firmer conclusions more data is required, however future research can gain most from focusing on the benefits that different fixation techniques may provide for recurrence outcomes in direct and large hernia repairs. Maintaining prospective hernia registration databases is advised.

In conclusion, in the current systematic review and meta-analysis an update was provided with RCTs of significance for the conclusions to be drawn. The use of HWM for laparo-endoscopic inguinal hernia repair significantly decreases the risk of recurrences, especially in non-fixated direct or large inguinal hernia repairs. Although proper fixation of LWM in direct or large hernia repairs can resemble the recurrence rates of HWM, it is not in any way superior and at best more expensive. The risk of chronic pain or foreign body sensation was not significantly influenced by the use of LWM. All things considered, the use of HWM in direct and large inguinal hernia repairs is recommended. There are no advantages of using LWM in indirect inguinal hernias.

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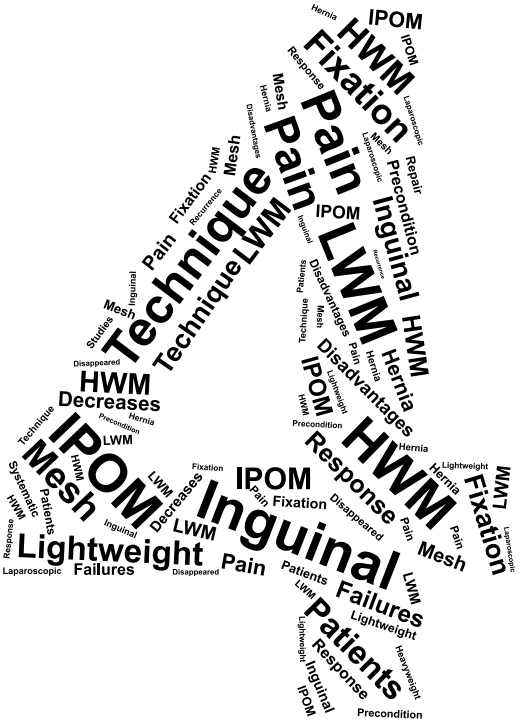
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Response to Comment on
"Heavyweight mesh is superior to lightweight mesh in laparo-endoscopic inguinal hernia repair: a meta-analysis and trial sequential analysis of randomized controlled trials."

Comment
J Li

Reply
WJ Bakker
JPJ Burgmans

Annals of Surgery (2020) [Epub ahead of print]

Comment

Laparo-endoscopic inguinal hernia repair have the advantage of faster recovery times, lower chronic pain.[1] There is an ongoing debate about the mesh type best suited for laparoscopic inguinal hernia repair.[2,3] The recent study by Bakker et al[4] concluded that heavyweight mesh (HWM) should be used in laparo-endoscopic repairs of direct or large inguinal hernias to reduce recurrence rates, and that lightweight mesh (LWM) provides no benefit in indirect hernias. Furthermore, the authors also made valuable subgroup analysis, and showed that the increased recurrence with LWM disappeared when mesh fixation used.

We agree with the author's nice interpretation on mesh choice for laparo-endoscopic inguinal hernia repair based on RCTs studies, however, we want to look into the underlying mechanism of the author's present findings, and furthermore, we aim to provide the possible and definite resolution to this problem, therefore, several comments on this topic were addressed.

First, about the recurrence mechanism. Unlike the recurrence after incisional hernias, which may be associated with the enlargement of defect, the mesh-fascia disruption, or multiple defects, the mechanism of inguinal hernia recurrence after laparo-endoscopic repair with LWM is largely due to mesh dislocation or mesh protrusion,[2,5] as it is more likely that a less strong lightweight mesh will protrude if the primary direct or indirect defect is large, which may occur in the early postoperative period, before the fibrotic response and subsequent fixation of mesh just stared, or occur gradually several months later. Consequently, the recurrent inguinal hernia was usually present with the same size as non-operated, which indicates a technique failure.

Second, about the mesh fixation. The authors reported that the increased recurrence using LWM disappeared when mesh fixation used. However, the efficacy and necessary of mesh fixation in laparo-endoscopic inguinal hernia repair are still debatable. Theoretically, the purpose of mesh fixation in laparo-endoscopic inguinal hernia repair is different from that of laparoscopic ventral/incisional hernia repair. In case of laparoscopic intraoperitoneal onlay mesh repair (IPOM), fixation is mandatory to hold the mesh in place, while, the purpose of fixation in laparo-endoscopic inguinal hernia repair is rather to position the mesh in the proper place, to prevent mesh curling, than to permanently fix the mesh from dislocation. According to the guideline, mesh fixation is not mandatory in the majority of laparo-endoscopic inguinal hernia repair.[1] Furthermore, there are studies with large volume (11228 male patients) clearly showing that mesh fixation did not reduce the recurrence rate.[6,7]

Third, narrowing the defect prior to mesh placement. Since the increase recurrence was attributed to the mesh dislocation or protrusion into the defect cavity,[2,5] which is prone

to occur in either direct hernia or large indirect hernia. Although LWM is more prone to migrate, the HWM can also protrude or slide into the large defect cavity as well, and result in hernia recurrence. Therefore, we routinely close the large direct hernia defect by suture the transversalis fascia with barbed suture instead of fixation the mesh,[8] in not only LWM, but also in the use of HWM. In case of large and scrotal indirect hernia with a wide defect orifice, we proposed dividing the distal hernia sac, and close or the distal sac,[9] or simply narrowing the defect by suture the lower edge of the divided distal sac to the anterior abdominal wall.[10] By doing these, the large hernia defects were closed or narrowed, the possibility of mesh dislocation was minimized, and the hernia recurrence due to mesh dislocation was prevented. In addition, another advantage of the present methods is to decrease the seroma formation after laparo-endoscopic direct or scrotal hernia repair.[8,10] During laparo-endoscopic inguinal hernia repair, if these modifications were addressed prior to mesh placement, the recurrence rate would be decreased for both LWM and HWM. Although we felt the need to discuss these few points, we congratulate Bakker et al. for their nice analysis, and hope and the present discussion and their contribution will be useful for hernia surgeons dealing with direct and large indirect hernia repair.

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Response

We would like to thank Dr. Li for the congratulations on our study and the effort to write a commentary on our publication.[1]

Dr. Li comments with several valuable points that elaborate on the underlying mechanism of the development of recurrences. The author also introduces a technique to further improve outcomes after laparo-endoscopic inguinal hernia repair for direct and large inguinal hernias.

The first comment of Dr. Li addresses the mechanism of the development of a recurrence in direct repairs when using a lightweight mesh. We agree with the author that early recurrences are often due to technical failures which are most likely to occur when using lightweight mesh, as likewise stated by Dr. Li. In theory, using heavyweight mesh decreases early recurrences due to easier mesh handling and less mesh dislocation or protrusion. However, at 3 months follow-up in a randomized controlled trial (RCT) that compared lightweight and heavyweight mesh (TULP-trial) for both arms only 2 recurrences were detected, while 19 recurrences occurred after 3 months follow-up.[2] Therefore, technical failures also seem to be experience-related.

The second issue the author addresses concerns the fixation of the mesh. The author explains that according to the current guidelines mesh fixation for laparo-endoscopic inguinal hernia repair is not mandatory in the majority of patients and recites multiple high-volume studies that show similar recurrence rates for fixated and non-fixated mesh.[3, 4] We agree with Dr. Li that the majority of patients undergoing totally extraperitoneal (TEP) inguinal hernia repair do not need mesh fixation. We feel the need to emphasize an explanatory paragraph in the Discussion section of the systematic review and meta-analysis in which we elaborate on the downsides of fixating a lightweight mesh compared to using a non-fixated heavyweight mesh. Nevertheless, the results of our study clearly show the increased risk of developing a recurrence with direct or large inguinal hernia repairs.[1] Interestingly, both of the recited high-volume studies, in agreement with multiple systematic reviews and meta-analyses on the subject, show a significantly increased risk of developing a recurrence for direct inguinal hernias.[3-5] Moreover, in contrast to the statement by Dr. Li, the study by Mayer et al. with the largest sample size of 11 228 patients found a significant reduction of recurrences in direct inguinal hernia repairs with fixated mesh compared to non-fixated mesh, although on average also significantly larger mesh were used in fixated repairs.[4] This is in agreement with the most recent inguinal hernia guidelines that recommend non-fixation of mesh in nearly all hernia types, however, based on the expert opinion and consensus within the HerniaSurge Group, the guidelines explicitly mention that mesh fixation is recommended for large direct defects (M3 EHS classification).[5] In addition, an adequately sized and overlapping mesh for large direct inguinal hernias is mentioned as a crucial precondition.[5]

Thirdly, Dr. Li proposes their routine technique of closing the direct hernia defect before mesh placement by suturing the transversalis fascia with barbed suture instead of fixating the mesh. This technique is stated to prevent the mesh from migrating, sliding or protruding into the large defect cavity of direct inguinal hernias, and thus prevent recurrences. Although lightweight mesh are most prone to migrate, Dr. Li proposes the technique for heavyweight mesh too. This technique is very interesting and could indeed by advantageous. In literature, mostly the reduction of seroma formation is reported.[6, 7] The technique has not yet proven superior for the prevention of recurrences, and it is plausible that possible advantages would only apply to lightweight mesh. In our opinion, conducting further research on this technique should be encouraged. However, fixation of heavyweight mesh for large direct defects is relatively simple, probably results in comparably low recurrence rates, and could be accompanied by fewer perioperative risks as nerve entrapment, used materials, and costs. Hence, the technique by Dr. Li warrants comparison to simple mesh fixation of heavyweight mesh. Currently, the proposed technique by the author does not have the substantiation to introduce the method as standard practice. Moreover, it remains questionable if the increased steps during an inguinal hernia repair are necessary adjustments. Even without performing mesh fixation recurrences are at an all-time low, with 1.1% at 5-year follow-up.[2] Prospective trials will need to be powered at an excessive number of patients to detect significant differences between techniques in recurrence rates. We would suggest investigating the technique through a prospective registration database.

In conclusion, we strongly agree with the author that no mesh fixation is needed in the majority of patients, however, the verdict should not arise that no patients need mesh fixation. Patient-tailored surgery with properly sized mesh and the consideration of a fixated heavyweight mesh in very large and direct laparo-endoscopic inguinal hernia repairs remains of importance. Hence, we stand by our suggestion for future research to focus on the benefits that different fixation techniques may provide for recurrence outcomes in direct and very large hernia repairs. The proposed technique by the author is interesting and promising. Future research will have to determine the benefits compared to heavyweight mesh fixation for recurrences and show there are no disadvantages of the adjusted laparo-endoscopic technique.

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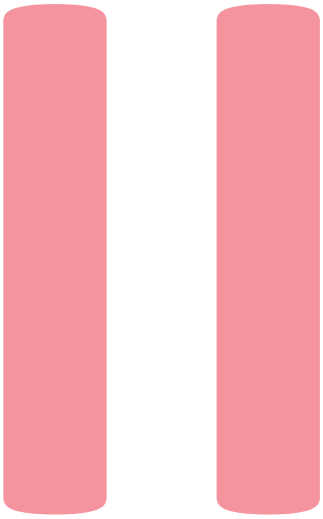
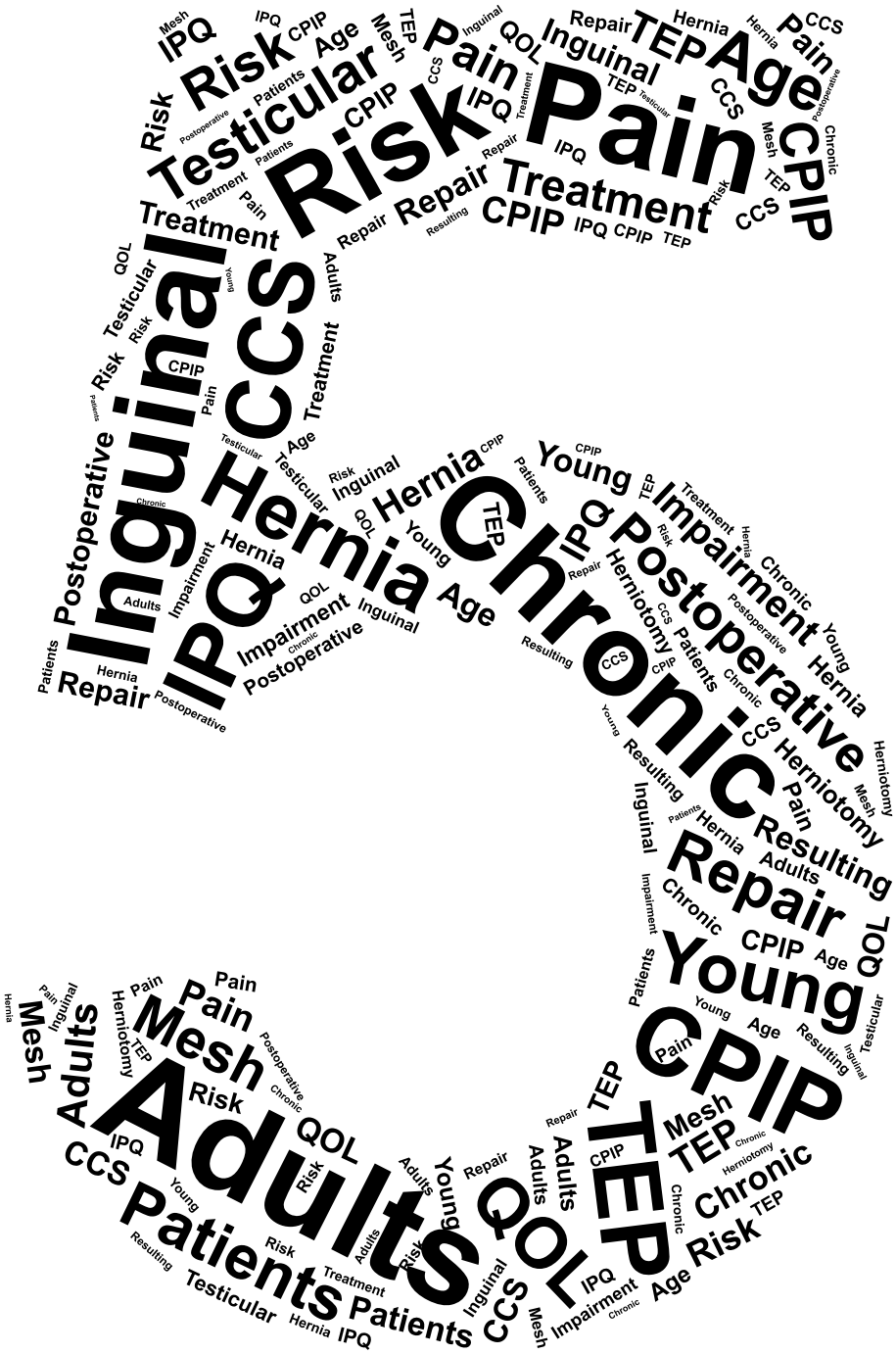
PART II



Part II

Optimizing TEP repair for specific patient populations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Is young age a risk factor for chronic postoperative inguinal pain after endoscopic totally extraperitoneal (TEP) repair?

WJ Bakker
CV van Hessen
EJMM Verleisdonk
GJ Clevers
PHP Davids
N Schouten
JPJ Burgmans

Hernia (2019) 23:1053-1059

Abstract

Purpose

A generally known risk factor for developing chronic postoperative inguinal pain after inguinal hernia repair is young age. However, studies discussing young age as a risk factor are mainly based on open repairs. The aim of this study was to determine if young adults (age 18-30) are also more prone to experience chronic postoperative inguinal pain after totally extraperitoneal (TEP) inguinal hernia repair, compared to older adults (age ≥31).

Methods

A prospective study was conducted in a high-volume TEP hernia clinic in 919 patients. Patients were assessed using the Numeric (Pain) Rating Scale (NRS), Inguinal Pain Questionnaire and Carolina Comfort Scale preoperatively, at 3 months, 1 year and 2 years after TEP mesh repair. The primary outcome was clinically relevant pain (NRS 3-10) in young adults compared to older adults at 3 months follow-up. Secondary outcomes were pain 1 and 2 years postoperatively, the impact of pain on daily living, foreign body feeling and testicular pain. Furthermore, age-categories were analyzed to determine potential age dependent risk factors.

Results

Follow-up was completed in 867 patients. No significant difference was found between young adults and older adults for clinically relevant pain at 3 months follow-up (p=0.723). At all follow-up time points no significant differences were found for clinically relevant pain, any pain (NRS 1-10), mean pain scores, the Inguinal Pain Questionnaire (IPQ) and the Carolina Comfort Scale (CCS). The subgroup analyses showed no age dependent risk factor for chronic postoperative inguinal pain development.

Conclusions

Young age is not associated with a higher risk of chronic postoperative inguinal pain after endoscopic TEP hernia repair.

Introduction

Since the introduction of inguinal hernia repair with placement of a mesh, recurrences have decreased impressively.[1, 2] Ever since, chronic postoperative inguinal pain (CPIP) has become the most common disabling complication of inguinal hernia repair.[3] CPIP is defined as inguinal pain lasting more than 3 months after surgery.[4, 5] Various studies report a wide spread of CPIP incidence after inguinal hernia repair ranging from 0.7–75%.[5] The reported incidence of CPIP in patients after endoscopic totally extraperitoneal (TEP) repair is 12.4%.[6] Daily activities of patients with CPIP are affected in 2–20% of patients.[7] As summarized in the international guidelines, known risk factors for CPIP are young age, female gender, high preoperative pain level, early high postoperative pain, recurrent hernia and open repair.[5] However, there is no consensus with regard to a definition of 'young age'. Most studies discussing young age as a risk factor for CPIP are based on open repair and relevant studies for endoscopic repair are barely available.[7-13] Since endoscopic TEP hernia repair by experienced surgeons results in a significantly lower incidence of CPIP compared to open repair, it remains unclear if young age is a risk factor for CPIP after endoscopic TEP repair.[5]

The aim of this study was to determine if young adults (18-30 years) are more prone to experience CPIP after TEP repair compared to adults of ≥31 years of age.

Methods

Study design

This prospective study was carried out in a high-volume hospital with extensive experience in the endoscopic TEP hernia repair technique (Hernia Clinic Diakonessenhuis Utrecht/Zeist). Hernia repairs were analyzed from the database of a double-blind randomized controlled trial (TULP-trial) comparing a lightweight and heavyweight mesh in patients that underwent TEP inguinal hernia repair. Detailed methodology has been published previously.[14-17] Pre- and postoperative data regarding the presence of chronic pain up to 2 years after TEP repair at 4 time points were prospectively registered. For current analyses the patients in whom 3 months follow-up (minimum for CPIP) was completed were selected. The patients were included between March 2010 and October 2012. Informed consent was obtained in all patients. The study was approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, the Netherlands) and the local ethics board of the hospital.

Patients

Patients deemed eligible for inclusion were male, over 18 years of age, with a primary, reducible, unilateral inguinal hernia and no contraindications for endoscopic TEP repair. Exclusion criteria were patients with collagen or connective tissue disorders and patients

who were unlikely to complete the follow-up regimen since their understanding of the language was insufficient or they had no fixed address.

Intervention

All patients underwent endoscopic TEP repair with tension-free placement of either a lightweight mesh (Ultrapro®, Ethicon, Johnson & Johnson company, Amersfoort, The Netherlands) or a heavyweight mesh (Prolene®, Ethicon, Johnson & Johnson Company, Amersfoort, The Netherlands) (for specifications meshes, see: TULP-trial).[14-17] Fixation of the mesh was not performed. All procedures were performed under general anesthesia. All patients were operated by 4 surgeons with extensive experience (>500 procedures/ surgeon) in performing the TEP inguinal hernia repair.

Postoperative management, outcomes and follow-up

Patients were routinely discharged on the day of surgery, unless complications prohibited early discharge. Patients were advised to take analgesics when in pain, and strenuous physical activity was discouraged during the first week postoperatively. No restrictions were given for activities of daily living.

The primary outcome of this study was clinically relevant pain (NRS 3-10) during rest in 18-30 year old patients compared to patients ≥31 years old at 3 months after endoscopic TEP hernia repair. Secondary outcomes were CPIP (clinically relevant and any pain) during rest 1 and 2 years after TEP, the impact of pain on daily living, foreign body feeling and testicular pain in young adults compared to older adults. Furthermore, a subgroup analysis of age categories (mostly 10 years per category) was performed to determine a potential age dependent risk factor for the development of CPIP.

Patients visited the outpatient clinic at 3 months and 1 year for physical examination by a specialized hernia surgeon. Patients were approached by telephone if pain, discomfort or a bulge in the groin was reported in the 2 year questionnaires and offered a clinical appointment if required. Information regarding the, at the time, current presence of pain and the impact on daily living was obtained through questionnaires preoperatively and at 3 months, 1 and 2 years after TEP repair. Pain was measured using the Numeric (Pain) Rating Scale (NRS, a scale of 0 = no pain, 10 = worst imaginable pain, Dutch). NRS scores were reported during rest. Based on a recent systematic review pain intensity was categorized as mild (NRS 1-2), moderate (NRS 3-6) or severe (NRS 7-10).[18] Moderate and severe pain (NRS 3-10) were considered clinically relevant. The Dutch versions of the Carolina Comfort Scale (CCS) and Inguinal Pain Questionnaire (IPQ) were used to assess the impact of pain on daily life activities.[19, 20] These are both recommended hernia-specific measurement tools incorporating assessments of both pain intensity and quality of life (QOL).[18] The CCS is a validated hernia-specific QOL questionnaire with 23 five-point scale questions of 0 being

'no pain, foreign body feeling or mechanical impairment' and 5 being 'terrible pain, foreign body feeling or mechanical impairment' (maximum total of points = 115).[19, 21] The IPQ uses a 7 step fixed-point rating scale to assess the impact of pain. The questionnaire uses separate questions to report the current inguinal pain, the worst pain experienced during the preceding week and the interference of pain with daily activities. Since the IPQ and the CCS overlap on certain subjects and for the reason of the unpractical extent of the IPQ questionnaire, the questions regarding a description of the worst pain in the past week, the experience of foreign body feeling (mesh) and pain in the testicle on the operated site were considered most relevant for this study. For the description of the worst pain in the past week, step 4-7, in which pain cannot be ignored and interferes with daily activities or worse, were considered clinically relevant.[20]

Statistical analysis

A sample size calculation and power analysis was performed using R, version 3.5.1 (The R Foundation for Statistical Computing, Vienna, Austria). The hypothesis was that the incidence of clinically relevant chronic pain (proportional outcome) is higher in young adults (18-30 years) than in older adults (>30 years), as for open repairs and as described in the international guidelines. The analysis was based on the study by Langeveld et al. (2015), which is the only other study that analyzes the prognostic value of age for CPIP in TEP (and Lichtenstein) repair patients, and uses a proportional outcome.[22] From the proportions encountered in their study (43.3% in the 18-40 group *versus* 23.9% in the >40 group), with a two-sided alpha of 0.05 and a power of 0.80, a total of 92 patients were to be included in each allocation group. However, regarding the study design of a secondary analysis of a previous conducted trial, the number of patients analyzed is fixed to 64 patients in the smallest group (age 18-30) and 855 patients in the other group (age >30). From the study of Langeveld et al. (2015) a power of 0.65 was determined for a group n=64.

Outcome analyses were performed using SPSS statistical software, version 24 (IBM Corp, Armonk, NY). Descriptive statistics were used for baseline data. The incidence of clinically relevant pain and any pain at the 5 different time points were compared by means of chi-square analyses or a Fisher exact test. A univariate analysis was performed for possible confounders (mesh type, BMI, severe preoperative pain, hernia type and operation time). Variables with a *p*-value of <0.25 in any of the relevant follow-up time points were subsequently entered in a multivariable analysis by means of a binary logistic regression in addition to age of 18-30 years to correct for confounding factors for the association between age of 18-30 years and CPIP-experience. The effects of the subgroups of age on clinically relevant pain were described using the relative risk (RR) ratio with the 95% confidence interval (CI). For other endpoints, the Student *t* test (normally distributed continuous), Mann-Whitney U analysis (not normally distributed continuous) or chi-square analysis (categorical variables) was used. A *p*-value of <0.05 (two-sided) was considered significant.

Results

Three month follow-up in the TULP-trial was completed in 919 patients, with a median age of 55 (IQR 44-64) (Table 1). Follow-up information at 1 and 2 years after TEP repair was available in 894 and 867 patients respectively (Figure 1). Significantly more indirect inguinal hernias were seen in young adults compared to older adults (p=0.008). There was no significant difference in mesh distribution (Ultrapro® *versus* Prolene®) for all age categories.

Table 1. Patient characteristics

	All patients *(n = 919)*	Age 18-30 *(n = 64)*	Age ≥31 *(n = 855)*	*p*-value
Age, years, median (IQR)	55 (44-64)	25 (23-28)	57 (46-64)	
BMI, kg/m², mean (SD)	24.9 (2.6)	22.9 (2.3)	25.0 (2.6)	0.000*
Side, n (%)				0.683
Left	394 (42.9)	29 (45.3)	365 (42.7)	
Right	525 (57.1)	35 (54.7)	490 (57.3)	
Hernia type, n (%)				0.008*
Medial	234 (25.5)	6 (9.5)	228 (26.7)	
Lateral	678 (73.9)	57 (90.5)	621 (72.7)	
Femoral	5 (0.5)	0 (0)	5 (0.6)	
Mesh, n (%)				0.734
Ultrapro®	464 (50.5)	31 (48.4)	433 (50.6)	
Prolene®	455 (49.5)	33 (51.6)	422 (49.4)	
Operation time, minutes, median (IQR)	19 (15-23)	20 (17-23)	19 (15-23)	0.496

IQR, Inter Quartile Range; BMI, Body Mass Index; SD, Standard Deviation; * $p < 0.05$

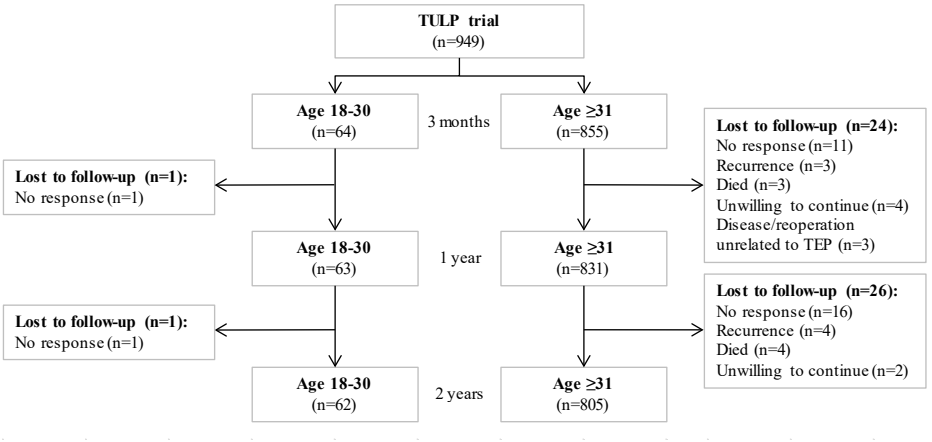

Figure 1 Flowchart

Clinically relevant pain (NRS 3-10) was present preoperatively and at 3 months, 1 and 2 years in, respectively, 345, 33, 24 and 31 patients. Preoperatively, clinically relevant pain was present in 43.8% of young adults *versus* 37.1% of patients ≥31 years of age. Three months postoperatively, 1.6% of patients 18-30 years of age complained of clinically relevant pain compared to 3.7% of patients ≥ 31 years s (p=0.723). For the preoperative data and all follow-up time points no significant difference was found for our secondary outcomes; clinically relevant pain at 1 and 2 years of follow-up, any pain (NRS 1-10), mean pain scores and the CCS. (Table 2) Correcting for confounding factors did not change this finding for both clinically relevant pain and any pain at any of the 3 follow-up time points (Table 3). A higher BMI, severe preoperative pain and the use of an Ultrapro® lightweight mesh remained as independent predictors for clinically relevant pain at 3 months.

Table 2. Pain results

NRS, mean (SD)	Age	18-30	≥31	*p*-value
Pre-operative		2.53 (2.3)	2.34 (2.4)	0.408
3 months		0.17 (0.5)	0.37 (1.0)	0.145
1 year		0.19 (0.6)	0.24 (0.9)	0.963
2 years		0.21 (0.7)	0.25 (0.8)	0.695
Clinically relevant pain (NRS 3-10), n (%)				
Pre-operative		28 (43.8)	317 (37.1)	0.288
3 months		1 (1.6)	32 (3.7)	0.723
1 year		1 (1.6)	23 (2.8)	1.000
2 years		2 (3.2)	29 (3.6)	1.000
Any pain (NRS 1-10), n (%)				
Pre-operative		49 (76.6)	604 (70.6)	0.314
3 months		8 (12.5)	168 (19.6)	0.161
1 year		7 (11.1)	93 (11.2)	0.982
2 years		7 (11.3)	105 (13.0)	0.692
Carolina Comfort Scale*, mean points (SD)				
Pre-operative		15.5 (14.5)	14.4 (14.9)	0.396
3 months		4.1 (12.0)	3.0 (8.0)	0.761
1 year		0.9 (3.7)	1.8 (6.1)	0.094
2 years		2.0 (7.1)	1.7 (5.6)	0.652

NRS, Numeric Rating Scale; SD, Standard Deviation

* Pre-operative maximum 75 points, other time points maximum 115 points.

Concerning the IPQ question of describing the worst pain in the past week no significant differences were detected between young and older adults for clinically relevant pain (step 4-7) both preoperatively and at any time point postoperatively. Neither were significant differences detected for hindrance of foreign body feeling (mesh) or the experience of pain in the testicle on the operated site.

Analysis of the 7 subgroups of age showed that patients 41-51 years old had a significantly higher relative risk (RR) of more clinically relevant pain preoperatively and at 3 months

postoperatively compared to the rest of the sample size. One year after TEP repair, this applied to patients 31-40 years of age. (Table 4)

Table 3. Multivariable analysis

	3 months			1 year			2 years		
Any pain	OR	CI (95%)	*p*-value	OR	CI (95%)	*p*-value	OR	CI (95%)	*p*-value
Age 18 - 30	0.66	0.30 - 1.43	0.293	1.29	0.56 - 2.99	0.554	0.94	0.41 - 2.17	0.890
Ultrapro mesh®	0.97	0.70 - 1.35	0.847	1.05	0.69 - 1.59	0.835	1.38	0.92 - 2.07	0.116
BMI	1.06	0.99 - 1.13	0.085	1.12	1.03 - 1.21	0.007*	1.04	0.97 - 1.13	0.286
Severe pre-operative pain	1.80	0.81 - 4.03	0.150	2.54	1.05 - 6.16	0.038*	1.42	0.53 - 3.82	0.491
Operation time	0.99	0.97 - 1.02	0.591	1.01	0.98 - 1.04	0.703	1.01	0.98 - 1.04	0.689
Clinically relevant pain									
Age 18 - 30	0.66	0.09 - 5.03	0.685	0.99	0.12 - 7.88	0.992	1.24	0.27 - 5.62	0.782
Ultrapro mesh®	1.28	0.63 - 2.60	0.501	2.98	1.16 - 7.65	0.023*	1.97	0.91 - 4.27	0.087
BMI	1.21	1.07 - 1.36	0.003*	1.23	1.06 - 1.42	0.007*	1.09	0.95 - 1.25	0.227
Severe pre-operative pain	2.77	0.78 - 9.88	0.116	4.12	1.11 - 15.23	0.034*	6.45	2.23 - 18.62	0.001*
Operation time	1.00	0.95 - 1.06	0.990	0.99	0.92 - 1.05	0.686	1.03	0.99 - 1.08	0.158

All factors were simultaneously entered into the analysis. BMI, Body Mass Index; * $p < 0.05$

Table 4. Relative risk ratio for experience of clinically relevant pain (NRS 3-10) for different age-categories

		Pre-operative	3 months	1 year	2 years
Age-category		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
18-30	(n=64)	1.18 (0.88 - 1.58)	0.42 (0.06 - 3.01)	0.57 (0.08 - 4.17)	0.90 (0.22 - 3.67)
31-40	(n=112)	0.97 (0.75 - 1.26)	1.94 (0.86 - 4.36)	2.53 (1.03 - 6.23)*	1.53 (0.60 - 3.88)
41-50	(n=185)	1.24 (1.03 - 1.49)*	2.27 (1.14 - 4.52)*	1.63 (0.69 - 3.87)	1.62 (0.76 - 3.45)
51-60	(n=229)	0.84 (0.68 - 1.03)	0.67 (0.28 - 1.60)	0.60 (0.21 - 1.74)	0.58 (0.23 - 1.49)
61-70	(n=241)	0.95 (0.78 - 1.15)	0.50 (0.20 - 1.29)	0.92 (0.37 - 2.30)	0.94 (0.43 - 2.07)
71-80	(n=78)	0.92 (0.67 - 1.26)	0.70 (0.17 - 2.85)	N / A	0.74 (0.18 - 3.04)
≥81	(n=10)	1.34 (0.72 - 2.50)	N / A	N / A	N / A

* Confidence interval does not include 1.00

Discussion

This prospective study with 2 years of follow-up demonstrates that in a center of expertise, young adults (18-30 years) do not experience more CPIP after TEP hernia repair compared to older adults (≥31 years). Moreover, no age dependent risk factor for the development of CPIP could be identified in our subgroup analysis.

Several studies have shared their findings on the influence of age on CPIP. Nevertheless, up to our knowledge this is the first study focusing on young age as a risk factor for CPIP after endoscopic inguinal hernia surgery. Our findings of CPIP (NRS 1-10) in 12.5% at 3 months after surgery decreasing to 11.3% over time for age 18-30, and 19.6% decreasing to 13.0%

over time for age ≥31, is conform with the reported 12.4% of TEP patients with CPIP of a recent systematic review and meta-analysis.[6]

One other study by Langeveld et al. (2015) had a comparable study design to ours, although patients underwent TEP and Lichtenstein, the sample size was smaller and pain was only assessed as a dichotomous value (yes/no).[22] They concluded that younger patients (18-40 years) presented more often with CPIP than middle-aged or elderly patients and TEP did not reduce the pain incidence. They however neglected to correct for confounders, since in their study younger patients also had more frequent preoperative pain and the intensity of pain was higher during the first 3 postoperative days, which are known risk factors for the development of CPIP.

The guidelines defined their statement of young age being a risk factor for CPIP mainly based on studies of patients after open repair.[7, 11, 12] Only 2 studies investigated pain exclusively after endoscopic repair.[9, 10] Dickinson et al. (2008) described a significant correlation of young age and CPIP after TEP, however young age was defined as <50 years.[9] Lau et al. (2004) did not address chronic pain, but found more acute pain after TEP repair in patients <65 years of age in the first days after surgery.[10] Liem et al. (2003) described a randomized comparison of laparoscopic and open inguinal hernia repairs with 5 years of follow-up.[8] Comparable to our study, age was not identified as a significant influence on the development of CPIP. Only preoperative pain, open repair and an intraoperative lesion of the ilioinguinal nerve were identified as predictors for CPIP.

The subgroup analyses of the current study identified a significantly higher RR for CPIP for the age category 41-50 years, preoperatively and at 3 months. This is most likely due to the before mentioned risk factor preoperative pain and not the age category, especially since significance fades at 1 and 2 years of follow-up. We have difficulty explaining the significantly higher RR seen in patients in age category 31-40 years 1 year after TEP repair, although probably the group sample size and multiple outliers resulted in the outcome.

This study did not show more CPIP, foreign body feeling or worse scores concerning QOL in young adults compared to older adults after TEP mesh repair. However, if mesh placement should always be advised in young patients remains questionable. Mesh placement reduces recurrences by reinforcement of the weak inguinal floor. However, in young adults a different etiology of a patent processus vaginalis might be causative for an indirect inguinal hernia without a weakened posterior wall or large defect.[23, 24] The more frequent appearance is confirmed by both the database of Langeveld et al. (2015) and our database that show significantly more indirect inguinal hernias in young adults.[22]

In children (<18 years), with a patent processus vaginalis as the primary cause of an indirect inguinal hernia, an open herniotomy is the procedure of choice. In patients >30 years of age with an inguinal hernia sufficient evidence has been provided that an open herniotomy is accompanied by high recurrence rates which necessitates the use of a mesh.[5] For patients of 18-30 years the available evidence is weak.[5] A recent retrospective study by van Kerckhoven et al. (2016) found recurrence rates after open herniotomy of 0% in patients aged 18-25, 2.7% in patients aged 18-30 years and 4.7% in patients aged 18-40 years, and suggested open herniotomy as a possible treatment of choice in young adults.[25] Osifo and Irowa (2008) found 1 recurrence (0.3%) after open herniotomy in patients with indirect inguinal hernias (mean age 25 ± 5.3 years, range 12-45) with 1-5 years of follow-up.[26] Well-designed prospective trials with adequate follow-up duration for the detection of recurrences are lacking and especially in direct inguinal hernias (current study 9.5% of patients) higher recurrence rates are to be expected. In our sample of patients no recurrences were detected in young adults (age 18-30) after TEP mesh repair with 5 years of follow-up.[16]

Therefore, we recommend performing TEP inguinal hernia repair with placement of a mesh in patients of 18-30 years of age. Nevertheless, open herniotomy could be an alternative in young adults who are unwilling to undergo mesh repair. However, higher recurrence rates after open herniotomy are seen and to be expected compared to TEP mesh repair and hence patients should be informed. Randomized controlled trials to detect recurrence differences between TEP and open herniotomy require lengthy follow-up and inordinate sample sizes. Detecting differences in pain might be virtually impossible. Therefore, we see no necessity for randomizing open herniotomy versus endoscopic mesh repair in young adults.

A strength of this study is the long-term follow-up with the use of recommended and validated questionnaires aimed at analyzing (chronic) pain and interference with daily activities.[18] Moreover, the current study provided a fairly pure analysis of the risk factor age. The study design filtered out other risk factors for CPIP development as female gender, recurrences and open repair, and correction for the remaining confounders through a multivariable analysis was performed. Furthermore, the study was conducted in a single, highly experienced TEP center. Comparable to TEP repair, outcomes of chronic pain in young adults after transabdominal preperitoneal (TAPP) repair are underreported. From multiple high-volume comparisons, the recently published international guidelines concluded that TAPP and TEP show similar complication rates for, amongst other outcomes, inguinal nerve lesions, chronic pain and recurrences.[5] Presuming there is no age-related influence on the comparability of TEP and TAPP, extending the current outcomes to laparo-endoscopic inguinal hernia repairs seems justified.
A limitation to this study is that it was not primarily aimed at distinguishing between age categories. The original TULP-trial was randomized between lightweight and heavyweight mesh and powered for the detection of pain differences, however not for age categories

resulting in different sample sizes. The sample size of 64 in the age-category 18-30 resulted in a power of 0.65, which is below the optimal standard. In a high-volume TEP center 2.5 years of including yielded 64 patients in this age-category. Therefore, achieving a power of >0.80 will be challenging. Presumably due to the difficulty of establishing sample sizes for optimal power in this age-category, this is the first study to analyze patients in the age-category 18-30 years after TEP repair. Maintaining prospective inguinal hernia registration databases is advised and might provide adequate sample sizes for analyses of higher power in time. Moreover, since it was not our primary outcome our subgroup analysis of age-categories was not corrected for confounders, including the type of mesh used. Yet, the mesh distribution showed no significant difference for each of the 7 subgroups separately in comparison with the rest of the sample population.

In conclusion, age did not prove to be a risk factor for the development of CPIP after TEP mesh repair, which justifies this technique in patients 18-30 years of age.

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Chronic
Groin
Hernia
Inguinal
Symptoms
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Pain
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TEP
Repair
Surgery
Results
Physiotherapy
Laparoscopic
Examination
Sports
Mesh
Implantation
KNVB
HAGOS
Polypropylene

Athletes with inguinal disruption benefit from endoscopic totally extraperitoneal (TEP) repair

MM Roos
WJ Bakker
EA Goedhart
EJMM Verleisdonk
GJ Clevers
CEH Voorbrood
FBM Sanders
DB Naafs
JPJ Burgmans

Hernia (2018) 22:517-524

Abstract

Background

Inguinal disruption, a common condition in athletes, is a diagnostic and therapeutic challenge. The aim of this study was to evaluate the effect of endoscopic totally extraperitoneal (TEP) repair in athletes with inguinal disruption, selected through a multidisciplinary, systematic work-up.

Methods

An observational, prospective cohort study was conducted in 32 athletes with inguinal disruption. Athletes were assessed by a sports medicine physician, radiologist and hernia surgeon and underwent subsequent endoscopic TEP repair with placement of polypropylene mesh. The primary outcome was pain reduction during exercise (NRS) 3 months postoperatively. Secondary outcomes were sports resumption, physical functioning and long-term pain intensity. Patients were assessed preoperatively, 3 months postoperatively and after a median follow-up of 19 months.

Results

Follow-up was completed in 30 patients (94%). The median pain score decreased from 8 (interquartile range (IQR) 7-8) preoperatively to 2 (IQR 0-5) 3 months postoperatively ($p<0.001$). At long-term follow-up the median pain score was 0 (IQR 0-3) ($p<0.001$). At 3 months 60% of patients were able to complete a full training and match. The median intensity of sport was 50% (IQR 20-70) preoperatively, 95% (IQR 70-100) 3 months postoperatively ($p<0.001$), and 100% (IQR 90-100) at long-term follow-up ($p<0.001$). The median frequency of sport was 4 (IQR 3-5) times per week before development of symptoms and 3 (IQR 3-4) times per week 3 months postoperatively ($p=0.025$). Three months postoperatively improvement was shown on all physical functioning subscales.

Conclusion

Athletes with inguinal disruption, selected through a multidisciplinary, systematic work-up, benefit from TEP repair.

Introduction

Chronic groin pain can derive from a wide variety of structures and is often multifactorial.[1-3] Many athletes, professional and amateur, suffer from chronic groin pain and in numerous cases no clear pathology exists.[4,5] In these cases inguinal disruption might be present. Inguinal disruption is defined as pain, predominantly in the groin area, either of insidious or acute onset, when no other obvious pathology explains the symptoms.[6] Athletes of sports involving rapid directional changes are most likely to be affected by this condition, with an incidence of 0.5-6.2%.[6-8] Fast resumption of sport activities is important to athletes. Treatment of inguinal disruption should start with conservative options, such as refraining from sports, analgesia, rehabilitation programs and physiotherapy.[5,6,9,10] However, this approach often proves unsuccessful, therefore athletes return for more lasting solutions and surgical intervention may be needed.[5,9,10] There is still considerable controversy surrounding the best surgical technique for the management of inguinal disruption. Depending on the suspected nature of injury, various surgical procedures have been described for groin pain in athletes. These include open repairs, mini-open repairs and endoscopic repairs, with or without a mesh reinforcement or tenotomy. Performing a totally extraperitoneal (TEP) repair in athletes with inguinal disruption is based on reinforcing the weakened posterior wall that might lead to pain relief.[3,11,12] Even though previous studies that investigated laparoscopic repair in athletes show good results in both early and long term follow-up, recent literature reviews stated a paucity of studies regarding TEP repair still exists.[11,13] The aim of this prospective study is to evaluate the effect of TEP repair in athletes with inguinal disruption, selected through a multidisciplinary, systematic work-up.

Methods

Patients

This observational, prospective cohort study was carried out in a high-volume hospital with extensive experience in the endoscopic TEP hernia repair technique (Hernia Clinic Diakonessenhuis Utrecht/Zeist) in collaboration with the Royal Netherlands Football Association (Koninklijke Nederlandse Voetbalbond (KNVB)). From September 2014 to December 2016, 32 professional and amateur athletes were included in our study. Patients deemed eligible for inclusion were selected and referred to our hospital by an experienced sports medicine physician at the sports medical outpatient clinic of the KNVB. The sports medicine physician performed anamnesis, physical examination, functional testing and supplemental examination to investigate possible causes of inguinal pain. The working method and definitions as set by the Manchester Consensus Conference on inguinal disruption were followed.[6] When inguinal disruption was suspected patients were referred to the department of surgery where physical examination by an experienced hernia

surgeon and additional imaging were performed (ultrasound, X-pelvis/hip, and MRI). Two experienced radiologists assessed all examinations independently. A MR imaging protocol for assessing possible sources of referred groin pain was used, including both small field-of-view high resolution studies detailing the pubic symphysis and large field-of-view pelvic surveys.[14] Patients eligible for inclusion were either male or female (>18 years old) who had experienced inguinal pain for at least 3 months (during or after sports activity) and did not receive benefit from conservative treatment (at least 6 weeks refraining from sports and 12 physiotherapy treatments). Exclusion criteria were a history of previous surgery in the groin area or other causes for chronic groin pain on physical examination or imaging (evident inguinal hernia, isolated adductor muscle/tendon pain, (stress)fracture, referred spinal pain, inguinal nerve entrapment, hip joint pathology, urological, gynaecological or bowel related causes, space-occupying lesion). The study protocol was approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, the Netherlands) and the local Ethics Board of the Diakonessenhuis Utrecht/Zeist. Informed consent was obtained from all individual participants included in the study. Preoperative data were obtained through measurements and a questionnaire.

Surgical procedure

All patients underwent endoscopic TEP repair with implantation of a polypropylene mesh. The surgical technique and perioperative care were standardized for all patients.[15] Operations were performed under general anaesthesia. A polypropylene monofilament mesh (Prolene®, 10x15cm, Ethicon, Johnson & Johnson company, Amersfoort, the Netherlands) was placed in a tension-free manner without fixation behind the pubic bone and/or posterior wall of the inguinal canal in all patients. All operations were executed by 3 surgeons with extensive experience (>1000 procedures) in endoscopic hernia surgery. No balloon dilatation or urinary catheterization was applied. Presence of a true inguinal hernia or lipoma and peri- and postoperative complications were registered in the Electronic Patient Chart (Dutch: EPD).

Postoperative management and follow-up

Patients underwent routine postoperative monitoring, were advised to take analgesics when in pain (paracetamol and if required diclofenac) and were discharged on the day of surgery, unless complications prohibited early discharge. Concerning activities of daily living (ADL) no restrictions were given. Strenuous physical activity was discouraged during the first week postoperatively. Return to sports starting from 1 week postoperatively was encouraged. A 6 week rehabilitation schedule was advised by the sports medicine physician and depending on the patient executed by differing physiotherapists. Six weeks postoperatively the athletes were consulted telephonically by their surgeon to monitor possible complications. Three months postoperatively all patients were seen by the sports medicine physician at the outpatient clinic of the KNVB where the 3 months follow-up data were collected.

Additionally, long-term results were registered with a telephone questionnaire in June 2017, with a median follow-up of 19 months varying between 5 months and 31 months. Using this questionnaire we assessed pain intensity and resumption of sport. Missing 3 months data were addressed as loss to follow-up.

Outcomes

The primary outcome of this study is pain reduction 3 months postoperatively. Secondary outcomes are the resumption of sports, physical functioning and long-term pain intensity.

Pain

Pain during exercise was assessed by means of the Numeric (Pain) Rating Scale (NRS) preoperatively and at 3 months postoperatively by means of a written questionnaire. After a median follow-up of 19 months (IQR 14-24 months), long-term NRS scores were assessed telephonically.

Resumption of sports

Resumption of sports was assessed by means of a self-designed written questionnaire in Dutch. Patients were asked to state their maximum intensity of sports activity in percentages preoperatively, at 3 months postoperatively, and after a median follow-up of 19 months (IQR 14-24 months). Also, the weekly sports frequency before the athletes experienced symptoms and the weekly sports frequency after 3 months were registered.

Physical functioning

Physical functioning was assessed by means of the Copenhagen Hip and Groin Outcome Score (HAGOS) preoperatively and at 3 months postoperatively.[16] In this patient-reported written questionnaire, outcomes are presented in 6 individual scales (pain, symptoms, ADL, sport and recreation, participation, quality of life (QOL)) in which the worst possible score reflects 0 and the best possible score reflects 100.

Statistical analysis

All statistical analyses were performed using SPSS statistical software, version 23 (IBM Corp., Armonk, NY, USA). For baseline data descriptive statistics were applied. Differences between pre- and postoperative parameters were analyzed by means of the paired sample t-test for parametric data and the Wilcoxon signed-ranked test for non-parametric data. A p-value of ≤0.05 (two-sided) was considered significant.

Results

Thirty-two male athletes (median age 22 years) were included in our study *(figure 1, table 1)*. The majority of participants (68%) were soccer players *(figure 2)*. At physical examination, tenderness by palpation at the inguinal canal region was found in 97% of patients, and 46.7% of these patients experienced coexisting tenderness by palpation of other structures. One or both radiologists observed abnormalities in 19 patients (59%) on MRI *(table 2)*.

Table 1 Patient characteristics (n=32)

Age (years)	22.0 (19.3-30.8)
BMI (kg/m²)	23.5 (21.8-24.3)
Right leg dominant, n (%)	29 (91)
Duration of symptoms (months)	12 (5.3-23.5)
Frequency of sports before symptoms (weekly)	4.0 (3.0-5.0)
Hours of sports before symptoms (weekly)	6.5 (5.0-8.5)
Presence of symptoms, n (%)	
Pain during exercise	16 (50)
Pain at rest and during exercise	16 (50)
Side of groin pain, n (%)	
Left	14 (44)
Right	16 (50)
Bilateral	2 (6)
Groin pain on dominant side, n (%)	17 (53)
Pain score during exercise (NRS)	8.0 (7.0-8.0)
Tenderness at palpation of inguinal canal, n (%)	30 (97) ǂ
Intensity of sports (%)	40.0 (20.0-65.0)

Continuous data are presented as median (IQR). BMI, Body Mass Index; NRS, Numeric Rating Scale. ǂ n=31

Table 2 MRI findings (n=32)

	n (%)
No abnormalities	13 (41)
Oedema of the pubic bone	14 (44)
Musculotendinous	
Enthesopathy adductor muscles	5 (16)
Enthesopathy rectus abdominis	2 (6)
Microrupture obturator externus	2 (6)
Tendinosis calcarea rectus femoris	1 (3)

The number of patients exceeds the sample size, since multiple patients had oedema of the pubic bone and musculotendinous findings.

In 24 cases (75% of study population) we were able to assess whether a true inguinal hernia was found. A true inguinal hernia was found in 2 athletes (6.3%). In 6 (18.8%) cases a lateral lipoma in the superficial inguinal ring was found. No conversions were needed during TEP repair. One of the 32 patients had a complication of bladder retention for which a catheter

was inserted. He stayed one night for observation and could be discharged the following day without further complications.

Thirty participants completed the 3 months and long-term follow up. Two patients remained unresponsive despite attempts for re-engagement in the study by means of telephone and e-mail.

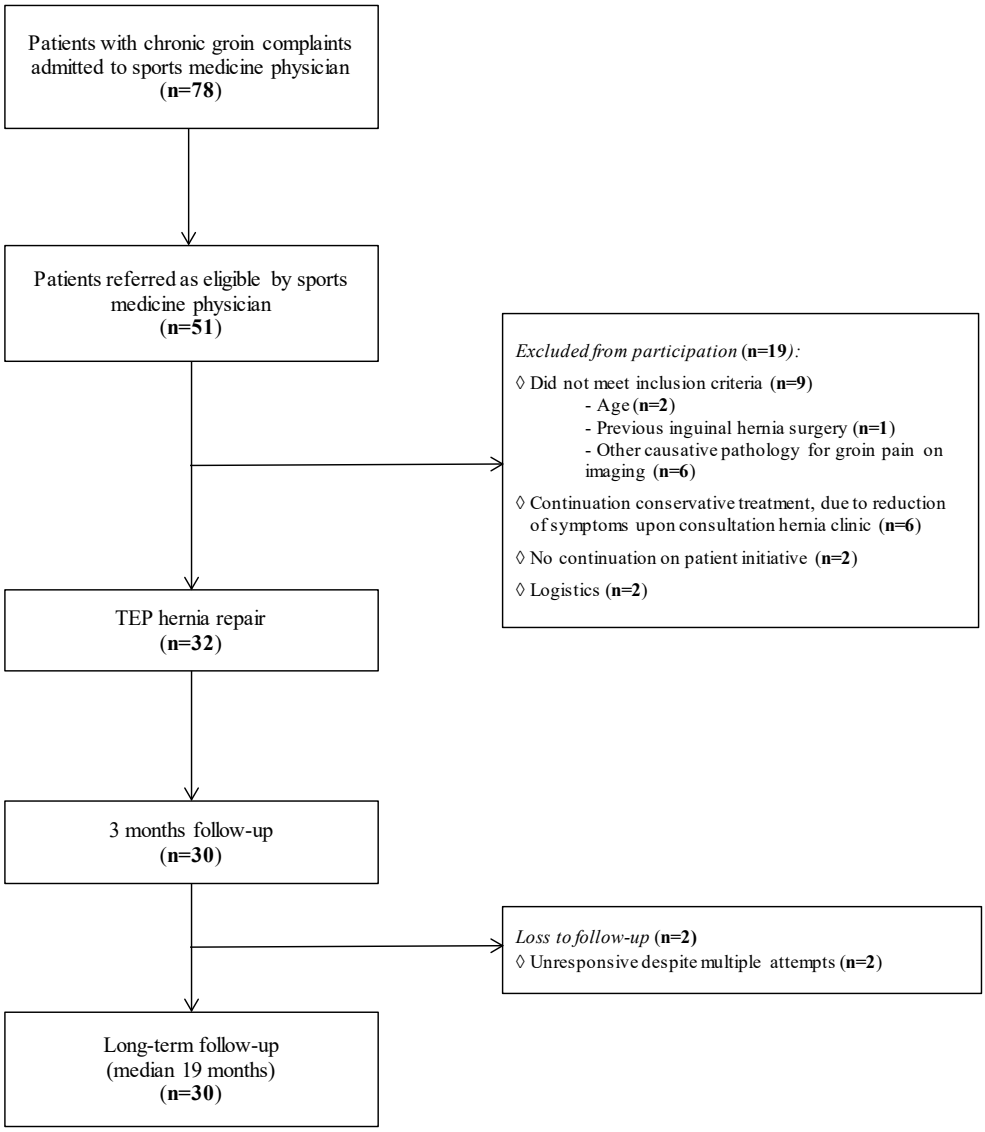


Figure 1 Flowchart patient inclusion and follow-up

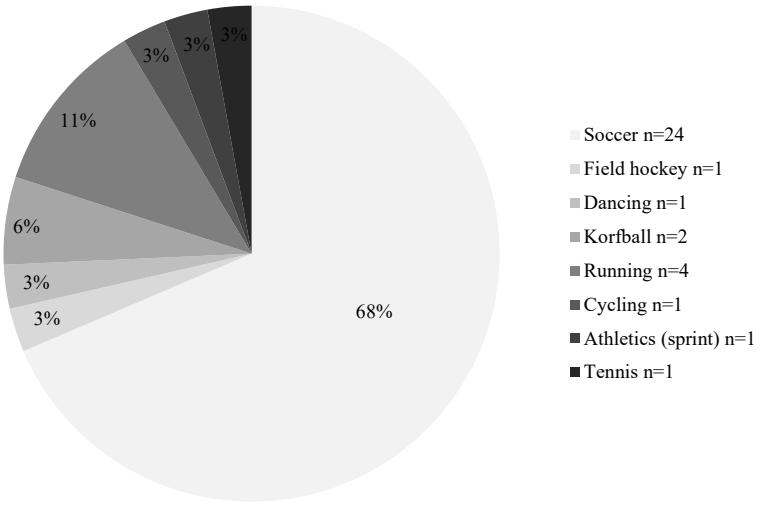


Figure 2 Distribution of sports type

Pain

The median pain score during exercise preoperatively was 8 (interquartile range (IQR) 7-8) and decreased to 2 (IQR 0-5) 3 months postoperatively (p<0.001) *(figure 3)*. In all patients, except for 3 soccer players, the pain decreased 3 months after surgery. In two patients the pain remained constant (NRS 5 and 7) and in the third patient the pain increased from NRS 9 to 10. In the latter patient the pre-existing experienced pain of the inguinal canal no longer existed, but his coexisting pain of hip-related groin pain became worse. At long-term follow-up, with a median of 19 (IQR 14-25) months, the median pain score was 0 (IQR 0-3) (p<0.001) and 62% of patients were totally pain free (p<0.001). One patient who initially responded well was re-operated for femoroacetabular impingement 14 months after TEP repair.

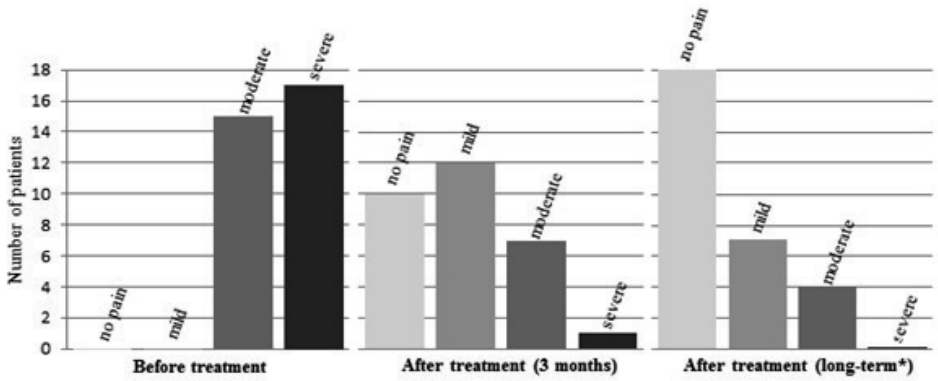


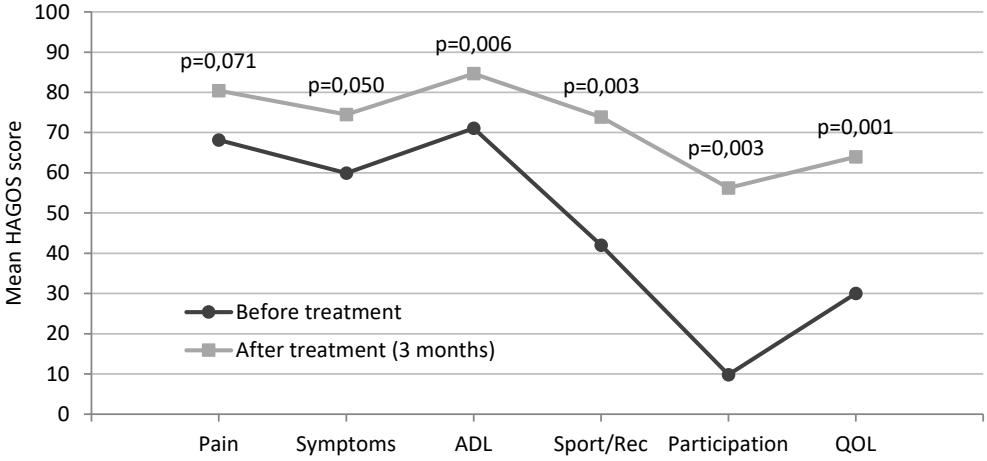
Figure 3 Reduction in pain intensity. In this figure, pain intensity was divided into three categories. No pain: Numeric Rating Scale (NRS) 0, mild: NRS 1-3, moderate: NRS 4-7, severe: NRS 8-10.* median long-term follow-up of 19 months

Resumption of sports

At 3 months postoperatively 60% of patients were able to complete a full training and match. The median maximum intensity of sport increased significantly from 40% (IQR 20-65) preoperatively to 95% (IQR 70-100) 3 months postoperatively (p<0.001). At long term follow-up (median 19 months, IQR 14-25 months) the median maximum intensity of sport was 100% (IQR 90-100) (p<0.001) and 72% of patients were able to exercise with 100% intensity. The median frequency of sport was 4 (IQR 3-5) times per week before patients developed symptoms and 3 (IQR 3-4) times per week 3 months postoperatively (p=0.025).

Physical functioning

The HAGOS showed high scores on physical functioning and improvement on all subscales after 3 months of follow-up (*figure 4)*. Three months after TEP repair our study population scored highest on ADL with a score of 85 and worst on participation with a score of 56. The biggest improvement was detected in participation, with a mean increase of 47.



ADL: activities of daily living, Rec: recreation, QOL: quality of life

Figure 4 Physical functioning

Discussion

This prospective cohort study demonstrates that TEP repair for athletes with inguinal disruption offers pain relief and fast return to full sports activity in the great majority of patients. Also, athletes show high and increased scores on all subscales of physical functioning 3 months after treatment.

Based on these results we believe that athletes with inguinal disruption, selected through a systematic work-up, executed by a multidisciplinary team of a sports medicine physician, radiologist and hernia surgeon benefit from reinforcing the posterior wall by TEP repair. This approach lends itself well for treating athletes in whom inguinal disruption is suspected and no response to conservative treatment is observed.

The pathogenesis of chronic groin pain in athletes has been an ongoing literature debate for decades. Although there is consensus that inguinal disruption results from injury to muscles and/or fascia, the exact anatomical structures involved are constantly disputed. In addition, pathology often coexists, aggravating the confusion. [3,6,12,17] The weakened posterior wall and disruption of the adductor and/or rectus abdominis tendon attachment to the pubis seems to be the most widely accepted pathogenesis theory, with 80 to 85% of athletes with chronic groin pain showing a perioperative deficiency of the posterior inguinal wall.[13,18-22] Both Susmallian et al. and van Veen et al. express their conviction that TEP repair has good results because a deficiency of the posterior inguinal wall is the most common operative finding.[18,23] A literature review suggests that athletes with chronic groin pain undergoing TEP repair do well because strengthening the posterior wall relieves symptoms, even when a macroscopic abnormality is not detected.[11] The tearing of the fascia transversalis and/or overlying fascia or musculature seems to be possible because of the disproportion of the relatively weaker lower abdominal muscles that have to handle forces across the pubic symphysis of the strong pull of the adductors against a fixed lower extremity. These opposing forces, which are especially great in athletes participating in sports with rapid directional changes, could be the mechanism for the origin of inguinal disruption. [12,22,24]

The use of imaging modalities (ultrasound, X-pelvis/hip, MRI) helped us exclude patients not eligible for this study. Our MRI findings are compliant with recognizable patterns of pathology described in athletes with inguinal disruption.[25]

Adding up the peroperative findings of true inguinal hernias and lipomas in the superficial inguinal ring, in a total of 8 athletes with chronic groin pain selected through a multidisciplinary approach (33% of athletes in whom the laparoscopic view of the posterior wall was well documented) abnormalities of the posterior wall were described. This findings are consistent with the peroperative findings reported by Santilli et al, a large series that executed laparoscopic TAPP surgery in athletes with chronic groin pain referred through a center specialized in sports medicine.[26] Defects of the posterior wall were found in 573 out of 1450 athletes with chronic groin pain (40%), of which 498 coincided with the areas affected by pain (34%).

Few studies with sufficient sample size have described treatment results of the TEP technique for inguinal disruption.[11,13] Regarding our primary outcome of pain reduction

we found a median pain score during exercise of 8 (IQR 7-8) preoperatively, 2 (IQR 0-5) 3 months postoperatively and 0 (IQR 0-3) at long-term follow-up. At long-term follow up 61% of patients were totally pain free. Only Paajanen et al. and a small study (n=7) of Kluin et al. reported results 3 months after TEP repair, with 90% and 86% of patients being totally pain free, respectively.[5, 27] Van Veen et al. showed 88% of athletes were without groin pain at exercise after TEP repair within 6-8 weeks.[23] Paajanen et al. reported a long-term outcome of 95% of athletes being painless after TEP repair with a mean follow-up op 51 months.[8] However, not all these studies did accurately describe how postoperative pain reduction was assessed and if a (validated) pain scale was used in all cases.

Concerning sports resumption we found a median maximum intensity of sport of 40% (IQR 20-65) preoperatively and 95% (IQR 70-100) 3 months postoperatively. At 3 months post-operatively 60% of patients were able to return to full sports activity. At long term follow-up the median maximum intensity of sport was 100% (IQR 90-100) and 72 % of patients were able to exercise with 100% intensity. Van Veen et al. reported a 91% resumption of sports at 3 months postoperatively after TEP repair.[23] Paajanen et al. achieved full return to sports activity 1 month after TEP repair in 93% of participants, and Paajanen et al. after 1 and 3 months in 67% and 90% of participants, respectively.[5,28] Susmallian et al. stated 97% was able to resume normal activities after TEP repair, but did not specify the moment of return (6-26 months) or the kind of activities.[18]

A strength of our study is that all patients were selected and referred by the same experienced sports medicine physician of the KNVB as part of the multidisciplinary work-up. Also, a standardized inguinal disruption imaging protocol was followed where the imaging modalities (ultrasound, X-pelvis/hip, and MRI) were conducted in all patients instead of in few selected patients.[14] Furthermore, to our knowledge we performed the only study that assessed physical functioning in athletes with inguinal disruption by means of the HAGOS, a validated questionnaire recommended for assessment of groin pain in athletes.[16] At the start of this study it was decided to use the term inguinal disruption following the leading consensus based on the Sheen et al. Manchester Consensus Conference.[6] Shortly after the study started the Weir et al. Doha agreement meeting on terminology and definitions was held and published.[29] It remains important to specifically categorize chronic groin pain in athletes and to use clear terminology following the definition set by Sheen et al. for inguinal disruption and to use the classification system of Weir et al. for the entire groin area.[6, 29]

A limitation of our study is the absence of a control group with only conservative treatment, a sham operation or an operation with another technique. Initiation of a study design with a control group with another technique will be difficult, since only specialized centers with their own expertise and results perform these techniques. Only 1 study compared TEP repair in athletes to a control group, although not comparing different surgical techniques.[5]

Paajanen et al. showed in a randomized controlled trial that the non-operative group (intensive physiotherapy training program) had worse results than the group that received operative treatment (TEP repair). After 1 and 3 months of intensive physiotherapy training, respectively, 0% and 7% had complete relief of pain and 20% and 27% achieved full return to sports activity. At 12 months of follow up 66% of patients still had disabling symptoms or even stopped participation in their sport.

Another limitation is that in this study a fully standardized postoperative physical rehabilitation regimen was lacking. Daily practice is reflected by having differing physiotherapists provide rehabilitation schedules, but a strict regimen may accelerate recovery.

In conclusion, we have demonstrated pain reduction, fast return to full sports activity and improvement on physical functioning in athletes with inguinal disruption at both 3 months and long-term follow-up after TEP repair. Therefore we would recommend the TEP repair technique with placement of a mesh for athletes with inguinal disruption, selected through a multidisciplinary work-up, who did not benefit from conservative treatment. High-quality randomized controlled trials comparing different surgical treatment techniques are needed.

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Inguinal
Mesh
Prostatectomies
PLND
Repair
Hernia
Patients
Pain
Chronic
CT
Therapy
Risk
Cancer
Prostate
Intervention
Outcomes
Radiotherapy
Cryotherapy
Preoperative
Respondents
Recommendations
Experienced
MRI

Influence of previous laparo-endoscopic inguinal hernia repair on performing radical prostatectomy:
a nationwide survey among urological surgeons

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JPJ Burgmans

Surgical Endoscopy (2020) [Epub ahead of print]

Abstract

Background

There is considerable demographic overlap of inguinal hernia patients and prostate cancer patients. Previous laparo-endoscopic inguinal hernia mesh repairs can complicate subsequent radical prostatectomies due to adhesions and distortion of anatomic planes. This study aims to assess the experience of urological surgeons on the safety and feasibility of performing radical prostatectomies after laparo-endoscopic inguinal hernia mesh repair.

Methods

For this cross-sectional study an online 24 question survey was developed regarding the experience in performing a radical prostatectomy and pelvic lymph node dissection (PLND) with a prior preperitoneal inguinal hernia mesh repair. Between June 2016 and December 2017, the questionnaire was sent to all 68 urological surgeons performing radical prostatectomy in the Netherlands.

Results

The response rate of urological surgeons was 69% (n=47). The majority (77%) of urological surgeons perform robot-assisted laparoscopic prostatectomies. A previous preperitoneal inguinal hernia repair was reported by 40% of urological surgeons in 10-30% of patients undergoing radical prostatectomy. Radical prostatectomy with prior preperitoneal inguinal hernia mesh repair is considered more difficult by 49%, predominantly because of (occasionally to always) experienced longer operating times (88.4%), increased blood loss (46.5%), difficult dissection of Retzius space (88.4%), nerve-sparing difficulties (32.6%), less adequate PLND (69.8%) and bladder- (16.3%) or peritoneal perforations (27.9%). Additionally, 11.6% had performed mesh explantation, 16.3% had aborted radical prostatectomies, and 35.7% experienced increased inguinal hernia recurrences after radical prostatectomies with prior preperitoneal inguinal hernia mesh repair. More experienced urological surgeons reported an increased difficulty for all outcomes.

Conclusions

Laparo-endoscopic inguinal hernia mesh repair has a significant impact on performing a radical prostatectomy and PLND. Surgeons should postpone the inguinal hernia repair of patients in the work-up for a radical prostatectomy, with the preferable option of performing the radical prostatectomy and inguinal hernia repair in the same procedure. Alternatively, a Lichtenstein repair can be performed.

Introduction

Inguinal hernia repair is the most commonly performed elective surgical intervention with over 20 million procedures annually worldwide.[1] Tension-free mesh repair of an inguinal hernia has become standard practice since the introduction of this technique reduced recurrence rates significantly.[2] Laparo-endoscopic repairs resulted in faster postoperative recovery and less chronic pain, and have become increasingly popular in the last decade.[3]

Prostate cancer is the second most common cancer in men worldwide, and currently the most prevalent cancer among older males in Western, industrialized countries.[4] Radical prostatectomy is the standard surgical therapy that is intended to provide a definitive treatment for clinically localized prostate cancer. The technique is performed using an open- or a minimally invasive (laparoscopic or robot-assisted) approach and should be combined with pelvic lymph node dissection (PLND) in case of a significant risk of lymph node involvement.[5]

There is demographic overlap of inguinal hernia patients and prostate cancer patients considering the lifetime occurrence in men of groin hernias is 27-43%, and prostate cancer is 7-18%, both increasingly diagnosed in the aging male.[1, 6, 7] Therefore, a considerable number of patients who undergo inguinal hernia repair will be scheduled for radical prostatectomy later. Previous laparo-endoscopic inguinal hernia mesh repair might complicate a subsequent radical prostatectomy due to adhesions and distortion of anatomic planes, complicating surgical dissection of Retzius space. Performing an adequate PLND can be technically difficult due to adhesions and the mesh that usually covers the obturator fossa. However, previous reports on the impact of endoscopic inguinal hernia repair on radical prostatectomy afterwards, range widely in their findings and recommendations.[8] Outcomes vary from no adverse effects to termination of the prostatectomy procedure.

In the end, the responsibility for the safety of the patient, hence the chosen treatment approach for prostate cancer lies with the urological surgeon performing surgery. Among urological surgeons the adverse effects of previous inguinal hernia mesh repair are well known, hence to date, all performed studies are from a urological perspective. Possibly surgeons should adjust their surgical approach when patients are in the work-up for a prostatectomy. The purpose of this study was to assess the experience of urological surgeons on the safety, feasibility, and outcomes of performing a radical prostatectomy after endoscopic inguinal hernia mesh repair.

Materials and Methods

This cross-sectional study involved the development and distribution of an online questionnaire regarding the performance of radical prostatectomy and PLND after previous laparo-endoscopic inguinal hernia repair. The questionnaire has been developed in collaboration with an experienced urological surgeon. Between June 2016 and December 2017, the questionnaire was sent to all 68 urological surgeons performing radical prostatectomy in the Netherlands. The survey was created using the software developed by SurveyMethods (Methods Group LLC, http://www.surveymethods.com), and was distributed electronically through the Dutch Urological Association (Dutch: Nederlandse Vereniging voor Urologie (NVU)).

The questionnaire consisted of 24 multiple choice items based on subjects and questions raised in a systematic review.[8] Participants were instructed to make estimations in case they did not know the exact numbers. The first part of the questionnaire consisted of characteristics of the respondents involving their experience, used surgical approaches, and the volume of procedures in their center (Figure 1). The second part involved questions regarding the preoperative work-up, peroperative findings and/or obstacles, and postoperative complications in case of endoscopic inguinal hernia repair prior to radical prostatectomy.

All statistical analyses were performed using SPSS statistical software, version 23 (IBM Corp., Armonk, NY, USA). For all outcomes descriptive statistics were applied. Categorical variables were compared using chi-square analyses or a Fisher exact test. A p-value of <0.05 (two-sided) was considered to be significant.

1. How many radical prostatectomies are being performed in your center annually?
   A: <20 B: 20-50 C: 51-100 D: >100
2. How many radical prostatectomies do you perform annually?
   A: <10 B: 10-20 C: >20
3. How many radical prostatectomies have you performed in total?
   A: <50 B: 51-100 C: 101-150 D: >150
4. How many years of experience do you have in performing radical prostatectomy?
   A: <5 B: 6-10 C: 11-20 D: 21-30 E: >30
5. What radical prostatectomy approach do you use or is used in your center? (check all answers that apply)
   A: Open retropubic radical prostatectomy (RRP) B: Radical perineal prostatectomy (RPP)
   C: Laparoscopic radical prostatectomy (LRP) D: Robot-assisted laparoscopic prostatectomy (RALP)
6. How many pelvic lymph node dissections (PLND) are performed in your center annually?
   A: <20 B: 20-50 C: 51-100 D: >100
7. How many PLND do you perform annually?
   A: <10 B: 10-20 C: >20
8. How many years of experience do you have in performing PLND?
   A: <5 B: 6-10 C: 11-20 D: 21-30 E: >30
9. What PLND approach do you use or is used in your center? (check all that apply)
   A: Open PLND B: Laparoscopic PLND C: Robot-assisted PLND
10. How many patients undergoing radical prostatectomy in your center had previous inguinal hernia repair?
    A: <10% B: 10-30% C: >30%
11. Do you perform additional pelvic imaging before radical prostatectomy because of the inguinal hernia repair?
    A: Never B: Occasionally C: Routinely
12. If you answered B or C to question 11: What type of additional pelvic imaging do you perform?
    A: CT B: MRI C: If other, please specify: *free text*
13. How often do you perform different approaches or therapies due to the prior inguinal hernia repair (e.g. perineal prostatectomy, radiotherapy, cryotherapy) instead of radical prostatectomy?
    A: Never B: Occasionally C: Routinely
14. In general, would you consider the radical prostatectomy procedure more difficult with prior inguinal hernia repair?
    A: Yes B: No
15. In case of prior inguinal hernia repair, do you (A: always B: usually C: occasionally D: never) experience:
    - Longer operating time?
    - Higher amounts of blood loss?
    - Difficult dissection of Retzius space?
    - Trouble in nerve sparing?
    - Less adequate PLND?
16. In case of prior inguinal hernia repair, do you experience:
    - More frequent bladder perforation? A: Yes B: No
    - More frequent bowel perforation? A: Yes B: No
    - More frequent peritoneal perforation? A: Yes B: No
    - More frequent pelvic vascular injury? A: Yes B: No
    - Higher conversion rate? A: Yes B: No
17. Did you ever abort radical prostatectomy due to previous inguinal hernia repair?
    A: Yes B: No
18. Did you ever perform mesh explantation?
    A: Yes B: No
19. Do you experience a higher rate of positive surgical margins with prior inguinal hernia repair?
    A: Yes B: No
20. Do you experience prolonged urinary catheterization with prior inguinal hernia repair?
    A: Always B: Usually C: Occasionally D: Never
21. Do you experience longer hospital stay with prior inguinal hernia repair?
    A: Always B: Usually C: Occasionally D: Never
22. In case of prior inguinal hernia repair, do you experience:
    - More frequent urethral stricture? A: Yes B: No
    - More frequent anastomotic leakage? A: Yes B: No
    - More frequent urinary incontinence? A: Yes B: No
    - More frequent erectile dysfunction? A: Yes B: No
23. Did you ever observe an inguinal hernia recurrence after radical prostatectomy?
    A: Yes B: No
24. Did you ever observe mesh infection after radical prostatectomy?
    A: Yes B: No

Figure 1 Questionnaire amongst urological surgeons

Results

Respondent characteristics

The overall response rate to the questionnaire was 69% (47 out of 68 respondents), and by 41 respondents the questionnaire was fully answered (87%). The majority of urological surgeons (75%) work in a center where over 50 radical prostatectomies are performed annually, 77% of respondents perform over 20 radical prostatectomies annually, 76% previously performed over 150 radical prostatectomies, and 53% have over 10 years of experience (Table 1). Seventy-two percent of respondents perform over 20 PLND annually, and 59% have over 10 years of PLND experience. For both radical prostatectomy and PLND the majority of urological surgeons (77%) perform a robot-assisted laparoscopic approach (RALP), although 16% of the centers perform multiple techniques for radical prostatectomy and 36% of the centers for PLND. Only 14% of respondents routinely perform different approaches or therapies instead of radical prostatectomy due to the inguinal hernia repair, e.g. perineal prostatectomy, radiotherapy, or cryotherapy, the majority of respondents (62%) never perform different approaches or therapies.

Table 1 Characteristics of urological surgeons and centers

	n					
Annually performed procedures of the center		<20	20-50	51-100	>100	
Radical prostatectomy	47	5 (10.6)	7 (14.9)	13 (27.7)	22 (46.8)	
PLND	46	7 (15.2)	14 (30.4)	14 (30.4)	11 (23.9)	
Annually performed procedures by respondent		<10	10-20	>20		
Radical prostatectomy	44	8 (18.2)	2 (4.5)	34 (77.3)		
PLND	46	7 (15.2)	6 (13.0)	33 (71.7)		
		<50	51-100	101-150	>150	
Performed radical prostatectomies in total	45	7 (15.6)	4 (8.9)	0 (0.0)	34 (75.6)	
Years of experience performing		<5	5-10	11-20	21-30	>30
Radical prostatectomy	47	12 (25.5)	10 (21.3)	17 (36.2)	7 (14.9)	1 (2.1)
PLND	46	8 (17.4)	11 (23.9)	19 (41.3)	7 (15.2)	1 (2.2)
Used prostatectomy approaches of the center (all that apply)	44	Open RRP 7 (15.9)	RPP 0 (0.0)	LRP 10 (22.7)	RALP 34 (77.3)	
Used PLND approaches of the center (all that apply)	44	Open 12 (27.3)	Laparoscopic 18 (40.9)	Robot-assisted 34 (77.3)		
Different therapies* used instead of radical prostatectomy	42	Never 26 (61.9)	Occasionally 10 (23.8)	Routinely 6 (14.3)		

All outcomes are expressed as: *n (%).* RRP = retropubic radical prostatectomy; RPP = radical perineal prostatectomy; LRP = laparoscopic radical prostatectomy; RALP = robot-assisted laparoscopic prostatectomy; PLND = pelvic lymph node dissection; * = e.g. perineal prostatectomy, radiotherapy or cryotherapy

Preoperative work-up

Forty percent of urological surgeons report that 10-30% of patients undergoing prostatectomy have had a previous inguinal hernia repair, 60% report a history of inguinal hernia repair of fewer than 10% (Table 2). Additional pelvic imaging is never performed by 79% of the urological surgeons with a prior inguinal hernia repair, however, if ordered 78% perform Magnetic Resonance Imaging (MRI) and 22% Computed Tomography (CT).

Table 2 Perioperative radical prostatectomy findings with a prior laparo-endoscopic inguinal hernia mesh repair

	n				
		<10%	10-30%	>30%	
Patients with a prior inguinal hernia repair	45	27 (60.0)	18 (40.0)	0 (0.0)	
		Never	Occasionally	Routinely	
Performed additional pelvic imaging	43	34 (79.1)	4 (9.3)	5 (11.6)	
		Yes	No		
The procedure is considered more difficult	43	21 (48.8)	22 (51.2)		
		Yes	No		
Aborted radical prostatectomy	43	7 (16.3)	36 (83.7)		
Performed mesh explantation	43	5 (11.6)	38 (88.4)		
Observed mesh infection	42	0 (0.0)	42 (100.0)		
Observed hernia recurrence after prostatectomy	42	15 (35.7)	27 (64.3)		
		Always	Usually	Occasionally	Never
Longer operating times	43	2 (4.7)	8 (18.6)	28 (65.1)	5 (11.6)
Higher amounts of blood loss	43	1 (2.3)	1 (2.3)	18 (41.9)	23 (53.5)
Difficult dissection of Retzius space	43	3 (7.0)	16 (37.2)	19 (44.2)	5 (11.6)
Trouble in nerve sparing	43	0 (0.0)	4 (9.3)	10 (23.3)	29 (67.4)
Less adequate PLND	43	1 (2.3)	7 (16.3)	22 (51.2)	13 (30.2)
Prolonged urinary catheterization	42	0 (0.0)	0 (0.0)	9 (21.4)	33 (78.6)
Longer hospital stay	42	0 (0.0)	0 (0.0)	15 (35.7)	27 (64.3)
More frequent		Yes	No		
Bladder perforations	43	7 (16.3)	36 (83.7)		
Bowel perforations	42	0 (0.0)	42 (100.0)		
Peritoneal perforations	43	12 (27.9)	31 (72.1)		
Pelvic vascular injury	42	2 (4.8)	40 (95.2)		
Conversions	43	3 (7.0)	40 (93.0)		
Positive surgical margins	41	0 (0.0)	41 (100.0)		
Urethral strictures	41	0 (0.0)	41 (100.0)		
Anastomotic leakage	40	1 (2.5)	39 (97.5)		
Urinary incontinence	41	0 (0.0)	41 (100.0)		
Erectile dysfunction	41	2 (4.9)	39 (95.1)		

All outcomes are expressed as: *n (%)*

Peroperative findings

With a history of inguinal hernia repair prior to radical prostatectomy, 49% of the respondents consider the procedure more difficult. Sixteen percent ever aborted a radical prostatectomy due to a previous inguinal hernia repair. When performing a radical prostatectomy in case of prior inguinal hernia repair, the majority of respondents (4 options for each question) occasionally experience longer operating times (65%), never experience higher amounts of blood loss (53%), occasionally experience a difficult dissection of Retzius space (44%), never experience trouble in nerve-sparing (67%), and occasionally experience less adequate PLND (51%). The majority (2 options for each question) does not experience more frequent bladder perforations (84%), bowel perforations (100%), peritoneal perforations (72%), pelvic vascular injury (95%), and conversions (93%). Twelve percent of urological surgeons ever performed mesh explantation during radical prostatectomy.

Postoperative findings

When performing a radical prostatectomy in case of prior inguinal hernia repair, the majority of respondents (4 options for each question) never experience prolonged urinary catheterization (79%), and never experience longer hospital stay (64%). The majority (2 options for each question) do not experience a higher rate of positive surgical margins (100%), urethral strictures (100%), anastomotic leakage (98%), urinary incontinence (100%), and erectile dysfunction (95%). An inguinal hernia recurrence after radical prostatectomy has been observed by 36% of respondents. Not one respondent ever observed a mesh infection.

As a sensitivity analysis only the urological surgeons were selected that previously performed over 150 radical prostatectomies (76%). All outcomes were comparable to the outcomes of the full group size, with a range of 0% to 5% difference. Interestingly, the selection of more experienced urological surgeons reported an increased difficulty for all outcomes compared to the less experienced urological surgeons, among other outcomes with prior inguinal hernia mesh repair relatively more urological surgeons considered the procedure more difficult (54% versus 33%, p=0.410), experienced less adequate PLND (71% versus 67%, p=1.000), aborted radical prostatectomy (20% versus 0%, p=0.567), performed mesh explantation (14% versus 0%, p=1.000), and experienced postoperative inguinal hernia recurrences (40% versus 20%, p=0.633).

Additionally, the urological surgeons that considered the procedure more difficult (49%) were compared to the urological surgeons that did not consider the procedure more difficult (51%). Regarding the characteristics of the urological surgeons and their centers no significant or striking differences were encountered for radical prostatectomy and PLND concerning the annually performed procedures, performed radical prostatectomies in total, years of experience, and used approaches. However, significantly more urological surgeons

that considered the procedure more difficult (62% versus 24%, p=0.013) reported a higher incidence of patients with a previous inguinal hernia repair (10%-30% instead of 0%-10%), again suggesting the more experienced urological surgeons report an increased difficulty compared to the less experienced urological surgeons. Urological surgeons that consider the procedure more difficult significantly more often describe the experience of (occasionally to always) longer operation times (100% versus 73%, p=0.021), (occasionally to always) difficult dissection of Retzius space (100% versus 73%, p=0.021), bladder perforations (33% versus 0%, p=0.004), peritoneal perforations (48% versus 9%, p=0.005), aborted prostatectomies (33% versus 0%, p=0.004), and extended hospital stay (52% versus 19%, p=0.024). Other outcomes were not significantly different between groups.

Discussion

This nationwide cross-sectional study among urological surgeons gave a clear insight into the encountered obstacles of performing a radical prostatectomy after a previous laparo-endoscopic inguinal hernia repair. An inguinal hernia repair prior to radical prostatectomy is a situation of frequent occurrence reported in 10-30% of patients by 40% of the urological surgeons. Especially peroperative difficulties are frequently encountered. Half of the urological surgeons consider the procedure more difficult with the occasional abortion of the procedure, mesh explantation, and bladder- or peritoneal perforations. Frequently longer operating times, higher amounts of blood loss, trouble in nerve-sparing, difficult resection of Retzius space, and a less adequate pelvic lymph node dissection (PLND) were reported. Postoperatively, prolonged urinary catheterization, longer hospital stay, and inguinal hernia recurrences are seen. The more experienced urological surgeons reported an increased difficulty for all outcomes compared to the less experienced urological surgeons, suggesting awareness of the risks increases with experience.

These results need to be taken under consideration in the work-up of both inguinal hernia patients and prostate cancer patients, considering their demographic overlap. Patients scheduled for a radical prostatectomy should be made aware of the increased urological risks and possibly additional procedures. Currently the adverse effects of a previous laparo-endoscopic inguinal hernia repair on performing a radical prostatectomy are not sufficiently recognized or acted upon by surgeons.

This is the first study that assesses the experience of urological surgeons, however, multiple prior studies have gathered patient data for the same research question, including 2 systematic reviews by Haifler et al. (2012) and Picozzi et al. (2015).[8, 9] Unfortunately the available data of patients with a prior mesh repair is limited compared to the control group, and only few studies with few patients remain for data-pooling.[8] Data pooling was possible

for 2 studies concerning open retropubic radical prostatectomies, and 2 studies regarding laparoscopic radical prostatectomies. No data were available for data pooling regarding RALP, which is unfortunate since most urological surgeons (77%) in this survey perform RALP. After the systematic reviews, a case-matched study of 64 patients was performed on RALP with and without prior inguinal hernia repair, which concluded that the procedure is feasible and safe after hernia repair, however takes longer with a higher risk for lymphoceles and bladder injuries.[10] In this study no procedures were aborted, no postoperative inguinal hernia recurrences were detected, and no difference in the number of removed lymph nodes was seen. Although overall for most outcomes hard data in systematic reviews is lacking to substantiate conclusions, the current verdict is that a radical prostatectomy is feasible and safe after an inguinal hernia repair, although may be technically demanding. However, the available literature does report multiple important complications that cannot be denied and are now substantiated accordingly by a significant number of urological surgeons, which are hernia recurrences, mesh explantation, possible abortion of the radical prostatectomy, and a less adequate nodal staging.

PLND is of importance in the process of accurate tumor staging in prostate cancer, and hence to decide who qualifies for adjuvant therapy. The estimated risk of lymph node involvement in prostate cancer patients is based on nomograms that incorporate the local tumor extent, Gleason score, and serum prostate-specific antigen (PSA).[11] The calculated risk determines the need for PLND, which is usually performed in intermediate- and high-risk patients and omitted in patients with low-risk disease.[11] To date, PLND is the only accurate technique for the assessment of pelvic lymph node involvement, since other methods as Partin tables or PET-, CT- or MRI-scans are not proven superior.[12-14] As the majority of urological surgeons occasionally or even usually experience a less adequate PLND after inguinal hernia mesh repairs, prostate cancer patients with intermediate- or high risk of lymph node involvement are at risk of under-staging and under-treatment. In the review by Picozzi et al. 42% of PLND were aborted with open radical prostatectomies, and 63% with laparoscopic radical prostatectomies, and on average 3 to 4 lymph nodes were removed in patients with a prior mesh repair, which was significantly lower than the 7 to 8 in the control group.[8] Excision of 4-10 lymph nodes is considered adequate.[15] Apart from the therapeutic consequences of less adequate PLND, the number of positive lymph nodes (1, 2, or >2) is also of predictive value for the (disease-free) survival.[16, 17]

Sixteen percent of the urological surgeons reported having aborted radical prostatectomies due to prior inguinal hernia mesh repair. Although our results would suggest more frequent occurrence, we are aware of only 5 reported cases in the literature.[18-22] In these patients, particularly prior bilateral mesh repairs induced challenges. Additionally, the extent of the mesh, excess fibrosis, anatomic distortion, and the proximity to nerves and vessels were reported as influential factors. In the majority of patients, the dense adhesions are cephalad

to the pubis and anterior to the bladder, and by dissection through superficial adhesions, the plane that allows for the standard procedure can be reached.[8, 9]

Besides the problematic PLND and aborted radical prostatectomies, also more frequent inguinal hernia recurrences after radical prostatectomy and explantation of mesh are encountered. Inguinal hernia recurrences, probably due to the displaced mesh with PLND, and the need for mesh explantation might lead to further surgical interventions with additional risks of per- and postoperative complications. Moreover, further surgery, in addition to the experienced, and in the literature reported, longer operating times, longer hospital stay and aborted radical prostatectomies, increase healthcare costs.

The described encountered difficulties by urological surgeons after a prior laparo-endoscopic inguinal hernia mesh repair are insufficiently known to surgeons. If patients are in the work-up for a prostatectomy, and present with an inguinal hernia, postponing an inguinal hernia repair or performing an anterior inguinal hernia mesh repair (Lichtenstein) is appropriate and should always be considered. Since the incidence and risk of developing a complicated inguinal hernia (strangulated or incarcerated) is low, postponing in case of minor complaints should be possible in most patients. In multiple studies laparo-endoscopic inguinal hernia surgery after a radical prostatectomy showed to be difficult, but nevertheless feasible and safe.[23-29] When postponing the inguinal hernia repair, these approaches can be considered. In case of complaints interfering with daily activities, a Lichtenstein repair can be performed without the associated per- and postoperative obstacles to urological surgeons. Moreover, many studies have shown the safety and feasibility of a concomitant performance of extraperitoneal inguinal hernia mesh repair and radical prostatectomy.[30-39] This option eliminates the risks involved with a second procedure, saves operative time, and allows the surgeon to perform a preperitoneal hernia repair. Moreover, this option is preferable for bilateral inguinal hernias considering a laparo-endoscopic repair is advised compared to an open repair.[40] Theoretical concerns with a concomitant repair of mesh infection in the presence of a vesicourethral anastomosis exist. However, a literature search of the available evidence (10 studies) resulted in not one mesh infection for a total of 820 patients with an inguinal hernia repair simultaneously with the radical prostatectomy.[30-39] Performing a Lichtenstein repair or concomitant inguinal hernia repair and radical prostatectomy is preferable compared to a postponed laparo-endoscopic inguinal hernia repair after a radical prostatectomy.

Many studies have been performed aimed at changing urological operative techniques, decrease complications, or adjust the work-up of prostate cancer patients with a prior inguinal hernia repair. From a urological perspective performing a radical prostatectomy with a prior inguinal hernia mesh repair is for experienced urological surgeons only. However, this is the first study that approaches the problem from a surgical angle and proposes

changes for surgeons in the work-up of these patients, and if needed in their operative approach for an inguinal hernia repair. The use of a survey gave us a clear insight into the experience of the urological surgeons at group level, although evidently this should not be considered hard data. The professional experience of urological surgeons was a necessary addition to the ongoing discussion considering the lack of available patient data, although the current research question would benefit from a urological registry study. A limitation is an impossibility for further clarification of the individual answers. Also, the answers to the dichotomous "yes/no" questions provided us with the insight that events occur, however, refrain us from insights in how often events occur. This cross-sectional study was performed among all Dutch urological surgeons, nevertheless, the given answers to the questionnaire are probably applicable to urological surgeons worldwide.

In conclusion, inguinal hernia and prostate cancer patients have a considerable demographic overlap that results in urological surgeons frequently performing a radical prostatectomy after a previous laparo-endoscopic inguinal hernia repair. In these situations, urological surgeons experience technical surgical difficulties that may lead to aborted radical prostatectomies, additional surgery for inguinal hernia recurrences or mesh explantation, and increased healthcare costs. However, clinically most important, a prior inguinal hernia repair frequently leads to a less adequate PLND, possibly resulting in under-staging and under-treatment of patients with prostate cancer. Surgeons need to be more aware of the impact of a laparo-endoscopic inguinal hernia mesh repair. If patients are in the work-up for an inguinal hernia repair and (impending) radical prostatectomy, surgeons need to postpone the inguinal hernia repair, with the preferable option of performing the radical prostatectomy and inguinal hernia repair in the same procedure. Alternatively, a Lichtenstein repair can be performed without the associated per- and postoperative obstacles to urological surgeons.

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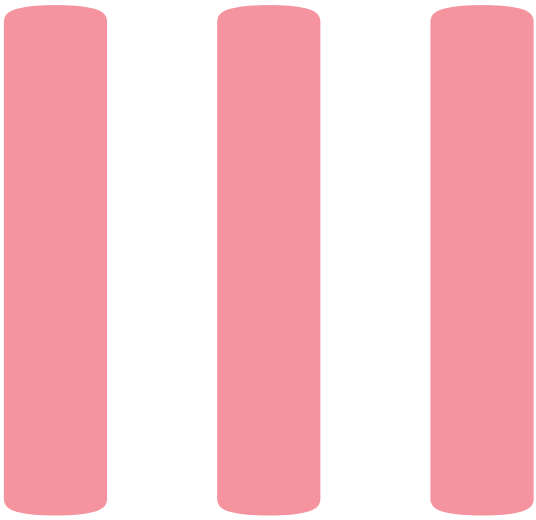
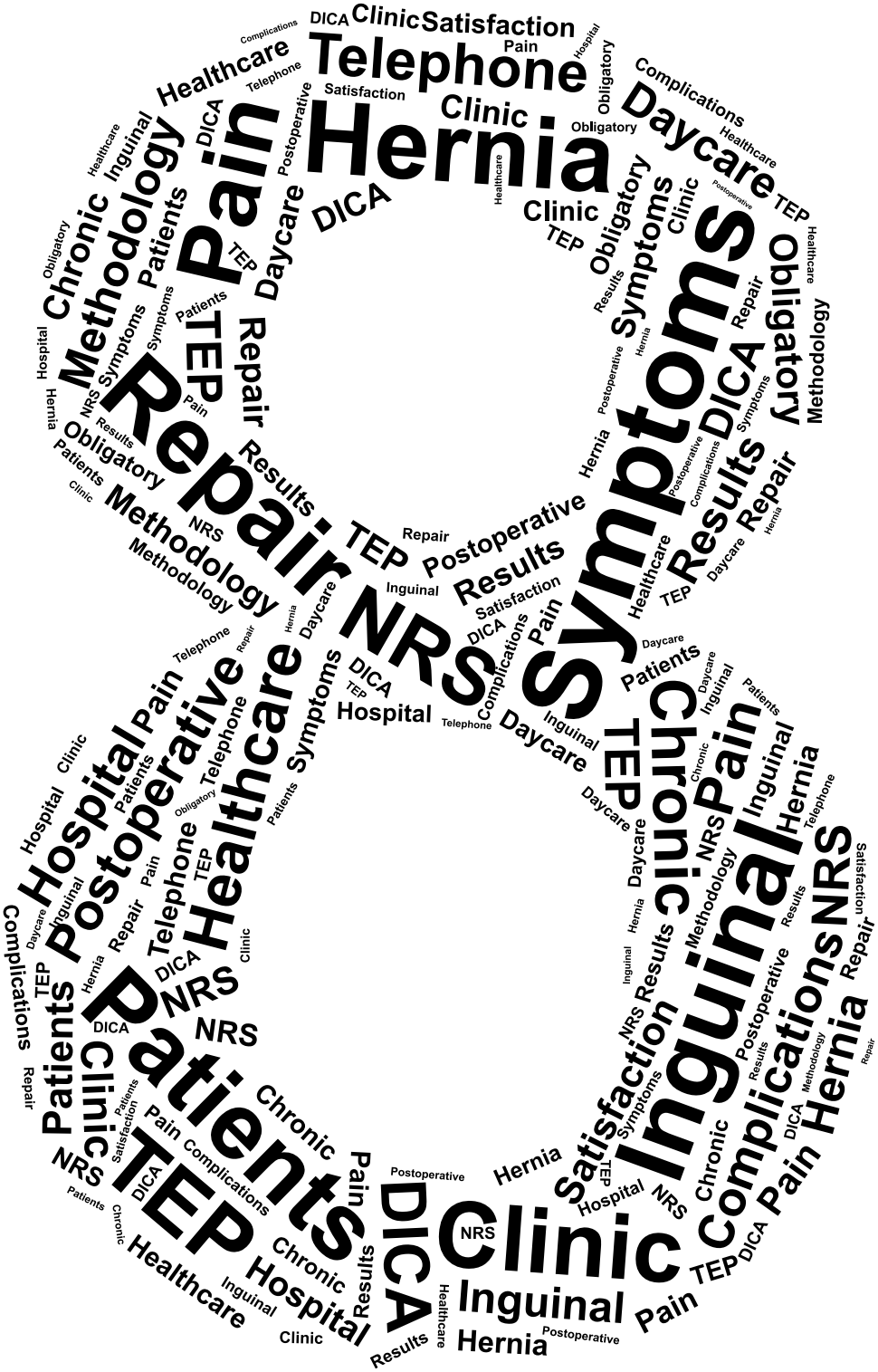
PART III



Part III

Optimizing follow-up


Hernia
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DICA
TEP
NRS

Value and patient appreciation of follow-up after endoscopic totally extraperitoneal (TEP) inguinal hernia repair

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Hernia (2020) 24:1033-1040

Abstract

Purpose

There is some consensus on inguinal hernia surgery follow-up in research settings. However, consensus on regular follow-up is lacking. Therefore, patients and surgeons are unnecessarily burdened and not cost-efficient. Moreover, the purpose of follow-up is barely questioned. This study aims to evaluate follow-up after inguinal hernia repair and determine patient satisfaction.

Methods

This prospective cohort study was executed in a high-volume specialized hernia clinic. All totally extraperitoneal (TEP) repair patients between July and October 2016 were included. Telephone follow-up was performed at 1 day, 6 weeks and 1 year postoperatively. One year postoperatively it was assessed whether patients visited other healthcare organizations, had remaining inguinal complaints, a Post-INguinal-repair-Questionnaire by telephone (PINQ-PHONE) was executed, and appreciation with follow-up was determined.

Results

Respectively, 6 weeks and 1 year postoperatively, 138 (79.3%) and 130 (74.7%) of 174 included patients were reached. One year postoperatively 15 patients (11.5%) had remaining inguinal complaints, of which only 4 patients (3.1%) had not already reported their symptoms. Nineteen patients (14.6%) presented with self-reported complaints between 6 weeks and 1 year, and no patients went to other hospitals. Respectively, 107 (82.3%), 61 (46.9%) and 117 (90.0%) patients considered follow-up useful at 6 weeks, 1 year and in general. One-hundred-nineteen patients (91.5%) preferred telephone follow-up to outpatient clinic appointments.

Conclusions

TEP patients value a telephone follow-up time-point, however, long-term follow-up is not considered useful. Patients report postoperative complaints themselves, therefore performing follow-up serves no clinical purpose. The purpose of follow-up is patient satisfaction and registration for quality objectives.

Introduction

Since the introduction of inguinal hernia repair with placement of a mesh, recurrences have decreased impressively.[1, 2] Ever since, postoperative attention shifted to chronic postoperative inguinal pain, which became the most common disabling complication of inguinal hernia repair.[3]

Many studies focus on the content of follow-up after inguinal hernia repair. Follow-up should assess recurrences, (chronic) pain, quality of life, and resumption of work and sports.[4] Interestingly, the purpose of follow-up after inguinal hernia repair is barely questioned and based on assumptions. Follow-up is performed for various reasons. First, with respect to a patient-related purpose; to assess potential postoperative complaints, and have the possibility to inform patients about complications and 'the normal postoperative course'. Second, with intent to register data to assess quality objectives for internal quality control, and national and international benchmarking. Finally, follow-up is of value in research settings. Extensive research has resulted in some consensus on the methodology of follow-up in research settings, e.g., baseline measurement, follow-up at standardized time-points and the need for at least 1 year of follow-up using standardized validated scales is advocated to assess chronic pain.[5] However, there is no consensus on adequate methodology, content, frequency and timing of follow-up with a clinical purpose and with respect to data registration after inguinal hernia surgery. Therefore, patients are probably unnecessarily burdened and surgeons are not time- and cost-efficient. Moreover, barely anything is known about outcomes that are of importance to patients, and if patients value (long-term) follow-up.[6]

In the Netherlands there is substantial inter-hospital variability concerning the organization of follow-up after inguinal hernia surgery. In our high-volume specialized hernia clinic follow-up is performed by means of telephone consultation at 1 day and 6 weeks after surgery. The aim of this prospective study is to evaluate the efficiency and purpose of our follow-up methodology, the value of additional follow-up at 1 year after surgery and determine patient satisfaction.

Methods

Patients

This prospective cohort study was carried out in a high-volume hernia clinic with extensive experience in the endoscopic totally extraperitoneal (TEP) inguinal hernia repair technique (Hernia Clinic Diakonessenhuis Utrecht/Zeist). All patients that received a TEP inguinal hernia repair in the third quarter of 2016 (July to October) were included in the study. The study protocol was approved by the local Ethics Board of the Diakonessenhuis Utrecht/Zeist.

Informed consent was obtained orally by telephone from all individual participants included in the study.

Postoperative management and follow-up

Patients were routinely discharged on the day of surgery, unless complications prohibited early discharge. Patients were advised to take analgesics when in pain, and strenuous physical activity was discouraged during the first week postoperatively. No restrictions were given for activities of daily living. Patients did not routinely get an outpatient clinic appointment. When discharged, all patients got a 6 weeks follow-up appointment by telephone and were instructed that they could contact the hospital for questions or consultation at all times.

One day postoperatively patients were called by the daycare ward to inquire about the state of patients, provide information and answer remaining questions. The daycare ward was consulted about their experience with the 1-day postoperative telephone consultation. We will present part of the process the daycare ward has gone through from December 2017 till March 2018 to effectuate a reduction in workload and improvement in cost-efficiency regarding the postoperative telephone consultation. The 6 weeks follow-up time-point by telephone consultation, based on the EuraHS-QOL questionnaire, is aimed at the detection of remaining complaints that need further attention, and registration of pain outcomes, postoperative recovery and patient satisfaction.[7] The 6 weeks prospectively registered patient data were extracted from the electronic patient file. In the context of this study, 1 year postoperatively patients were inquired if they had visited other healthcare organizations for inguinal complaints, experienced remaining complaints and/or swelling of the inguinal region, a modified Post-INguinal-repair-Questionnaire by telephone (PINQ-PHONE) was executed, and their appreciation with follow-up was determined (Figure 1).[8] At 1 year follow-up, patients were called by 2 researchers (W.B. and C.H.), if needed in close consultation with a blinded hernia surgeon (J.B.). To reflect daily practice, a maximum of 3 attempts were made to reach a patient 1 year postoperatively. If patients experienced remaining complaints, an outpatient clinic appointment with a hernia surgeon was offered.

Additionally, 10 inguinal hernia repair centers in the Netherlands were contacted. Inquiries were made about the postoperative time-point of follow-up, and whether follow-up was executed by telephone or at the outpatient clinic.

Outcomes

The aim of the current study was to assess the efficiency of our standard follow-up methodology, and the value of additional follow-up 1 year after surgery. The primary outcome was the fraction of patients with new complaints relative to 6 weeks follow-up that patients had not reported themselves. Secondary outcomes were patient appreciation with both follow-up time-points, the fraction of patients that had visited other organizations

(general practitioner, other hospital) with remaining inguinal complaints, the fraction of patients that reported complaints spontaneously between 6 weeks and 1-year follow-up, recurrences, and pain 1 year postoperatively using the Numeric Rating Scale (NRS).[9] Pain was considered to be clinically relevant with NRS>3 and severe with NRS>6.[5]

Have you visited your general practitioner or another hospital for complaints of your operated groin since your 6 weeks follow-up appointment?

If *'Yes'*: What were the complaints? Did you visit your general practitioner or another hospital? Was something diagnosed? Have you received treatment? Has a re-operation been performed?

The following questions regard your previous week:

- Do you have any symptoms or have you noticed any swelling at your operated groin?
  If *'Yes'*: Numeric Rating Scale (NRS) in rest and with sports?
- Have you noticed something at the operated groin when coughing, sneezing or squeezing?
- Could you stand up and put your other hand flat in your operated groin. Now put the phone down and put this hand to your mouth and blow. Do you feel something in your operated groin?

Regarding patient appreciation:

- Were you called 1 day after surgery?
- Do you think the 6 weeks after surgery follow-up time-point is useful?
- Do you think this follow-up time-point at 1 year after surgery is useful?
- Do you think a follow-up moment after surgery in general is useful?
- What has your preference: follow-up by means of a telephone consultation or an outpatient clinic appointment?
- Was it clear to you that you could at all times contact the hospital for questions or consultation?

Figure 1 Telephone questionnaire at 1 year postoperatively

In the Netherlands, having healthcare insurance is obliged, which comes with an obligatory deductible excess. However, if the healthcare costs exceed the deductible excess further healthcare accompanies no additional personal expenses for patients. Patients undergoing inguinal hernia surgery will have exceeded their deductible excess. Therefore, 1, or 2 or more follow-up appointments, whether by phone or at the outpatient clinic, will not come along with additional expense for patients. The appointment costs will not have influenced their response to the questionnaire.

Statistical analysis

All statistical analyses were performed using SPSS statistical software, version 23 (IBM Corp., Armonk, NY, USA). Descriptive statistics were applied for baseline data. Categorical variables were compared using chi-square analyses or a Fisher exact test. A *p*-value of <0.05 (two-sided) was considered to be significant.

Results

In the selected period 174 patients received a TEP repair with a mean age of 56.5 years (standard deviation (SD) 14.2) (Table 1). Primary repairs were performed in 155 patients (89.1%) (Table 2). Complications occurred in 5 patients (3.8%). At 6 weeks follow-up we were able to reach 138 patients (79.3%), with an average time to follow-up of 6.3 weeks (SD 1.2). We reached 130 patients at 1-year follow-up (74.7%), with an average time to follow-up of 12.8 months (SD 1.4) (Figure 2). In 15 patients (8.6%) both follow-up time-points at 6 weeks and 1 year were not assessed. Seventeen patients (13.1%) were scheduled at the outpatient clinic in the first year after surgery.

Table 1 Patient characteristics (n=174)

Age, years, mean (SD)	56.5 (14.2)
Male, n (%)	163 (93.7)
BMI, kg/m², mean (SD)	24.7 (2.8)
Smoking, n (%)	
Yes	27 (15.5)
No	127 (73.0)
Quit	20 (11.5)
Prescribed anticoagulants, n (%)	21 (12.1)
ASA, n (%)	
1	82 (47.1)
2	79 (45.4)
3	13 (7.5)

SD, Standard Deviation; BMI, Body Mass Index; ASA, American Society of Anesthesiologists Physical Status

Follow-up 1 day postoperatively

In this study of TEP repairs performed in 2016, 91 patients (70.0%) were reached the first day after surgery by the daycare ward, 16 patients (12.3%) did not remember, and 23 patients (17.7%) were not consulted.

Besides the included cohort of this study, as part of a *productive ward* assignment by the hospital from December 2017 till March 2018, the daycare ward reported a high workload that was in part due to the telephone consultations performed for each inguinal hernia patient the first day postoperatively. With TEP repairs increasing annually the workload increased, resulting in on average 2 hours a day of contacting patients (2 weeks measurement period). Moreover, in the experience of the nurses a telephone consultation the first postoperatively had no additional value, since patients had already received the required postoperative information through information on the website, explanation upon discharge and a patient information letter. In a process improvement attempt, patients were asked upon discharge if they wanted to be contacted the next day. Only 20.0% of patients desired to be contacted, resulting in an 80.0% reduction of telephone consultations. A monthly evaluation produced

that merely 30 minutes a day was spent on contacting patients, resulting in a 1.5-hour reduction of workload.

Table 2 Characteristics TEP repairs (n=174)

Inguinal hernia, n (%)	
Primary	155 (89.1)
Recurrence	13 (7.5)
Primary and recurrence (bilateral)	6 (3.4)
Side, n (%)	
Left	65 (37.4)
Right	75 (43.1)
Bilateral	34 (19.5)
EHS-classification, n (%)	
Unilateral direct	27 (15.5)
Unilateral indirect	100 (57.5)
Unilateral femoral	5 (2.9)
Unilateral mixed	8 (4.6)
Bilateral direct/direct	15 (8.6)
Bilateral indirect/indirect	13 (7.5)
Bilateral indirect/direct	5 (2.9)
Bilateral femoral/direct	1 (0.6)
Lipoma present, n (%)	43 (24.7)
Complications, n (%)	
Conversion	1 (0.6)
Haematoma	2 (1.1)
Wound infection	1 (0.6)
Scrotal neuropathy	1 (0.6)
Recurrence	0 (0.0)
Heavyweight polypropylene mesh, n(%)	174 (100)
Operation time, minutes, median (IQR)	19 (15-22)

IQR, Inter-Quartile Range

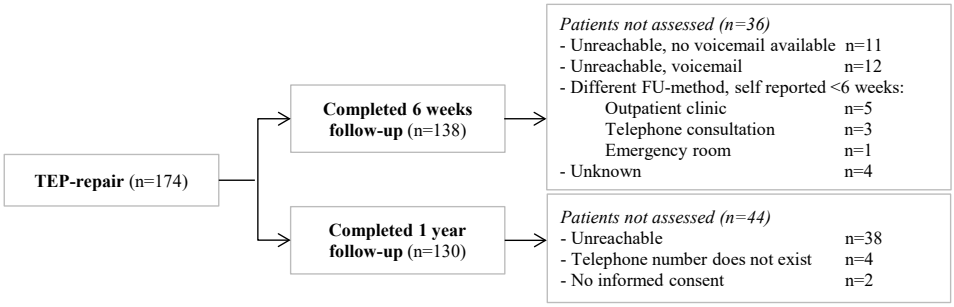

Figure 2 Flowchart. The patients that were not assessed at 6 weeks and 1-year follow-up are not the same individuals.

Self-reported patients from surgery to 1 year follow-up

Nineteen patients (14.6%) had been in contact with our hospital after surgery with self-reported questions or complaints apart from their regular follow-up. Fourteen patients (73.7%) were seen at the outpatient clinic and 5 patients (26.3%) were addressed by telephone. Five of these 19 patients (26.3%) had also visited their general practitioner for their complaints. Three out of 130 patients (2.3%) visited their general practitioner with complaints without consulting our hospital. In no cases treatment or re-operation was indicated. Moreover, no patients went to other hospitals for surgery-related complaints.

Follow up 1 year postoperatively

Four out of 130 patients (3.1%) had either clinically relevant pain or a positive response to the PINQ-PHONE questions and did not report their symptoms between 6 weeks and 1-year follow-up (Figure 3).

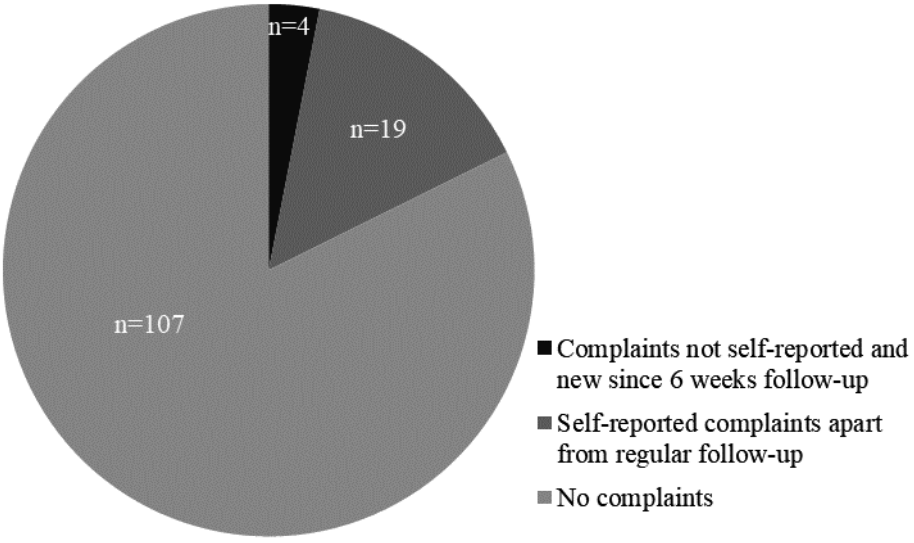

Figure 3 Distribution of the reporting of complaints at 1-year follow-up

At 1 year postoperatively, 15 of the 130 patients (11.5%) had complaints of their operated groin (Table 3). The overall mean NRS was 0.1 (SD 0.6) in rest, and 0.3 (SD 1.0) with sports. The mean pain score of the patients with complaints was NRS 1.1 (SD 1.3) in rest, and 2.2 (SD 2.2) with sports. Three patients experienced complaints related to certain positions only. Three patients had clinically relevant pain, of which 1 patient had severe pain (NRS 1 in rest, NRS 8 with sports) comparable to before surgery. The latter patient was already under treatment and referred to a sports medicine physician with the working diagnosis of a musculotendinous origin of his pain. Therefore, 2 symptomatic patients were newly encountered at 1-year follow-up.

Table 3 Results of the telephone questionnaire at 1 year postoperatively (n=130)

Follow-up 1 year postoperatively	
Complaints not self-reported and new since 6 weeks FU, n (%)	4 (3.1)
Self-reported complaints apart from regular FU, n (%)	19 (14.6)
Complaints of the operated groin at 1 year postoperatively, n (%)	15 (11.5)
NRS in rest, mean (SD)	0.1 (0.6)
NRS with sports, mean (SD)	0.3 (1.0)
Clinically relevant pain, n (%)	3 (2.3)
Positive PINQ-PHONE, n (%)	5 (3.8)
Patient appreciation	
FU time-point considered useful	
In general, n (%)	117 (90.0)
At 6 weeks postoperatively, n (%)	107 (82.3)
At 1 year postoperatively, n (%)	61 (46.9)
Preference of FU by telephone compared to outpatient clinic, n (%)	119 (91.5)
Awareness of possibility to at all times consult the hospital, n (%)	110 (84.6)

FU, follow-up; NRS, numeric rating scale; SD, standard deviation; PINQ-PHONE, Post-INguinal-repair-Questionnaire by telephone

Four patients (3.1%), of which 2 also had clinically relevant pain, noticed something in the operated groin upon moments of coughing, sneezing or squeezing (PINQ-PHONE). Upon self-examination of the do-it-yourself Valsalva maneuver (PINQ-PHONE) in 1 out of 120 patients (0.8%, 10 patients were unwilling or at the time unable to perform the maneuver) something was felt in the operated groin. This patient had been seen at the outpatient clinic 2 months postoperatively, because of extended follow-up due to pain at 6 weeks follow-up, and at the time no recurrence was detected. The complaints of this patient (NRS 2 in rest, related to certain positions only) were insignificant and no further analysis was sought.

Patient appreciation

One hundred seven patients (82.3%) considered the 6 weeks follow-up time-point to be useful, 61 patients (46.9%) considered the 1 year follow-up time-point to be useful, and 117 patients (90.0%) considered a follow-up moment in general to be useful. The vast majority, with 119 patients (91.5%), prefer telephone follow-up compared to an outpatient clinic appointment. Of the 11 patients that preferred follow-up at the outpatient clinic, 2 had visited the outpatient clinic in their postoperative course. One hundred ten patients (84.6%) were aware that they could contact the hospital for questions or consultation at all times.

Additionally, we investigated patient appreciation with follow-up of the 19 patients that presented themselves between surgery and 1 year of follow-up. Respectively 95%, 95%, and 74% of patients consider a follow-up moment in general, at 6 weeks, and 1 year postoperatively to be useful, with correspondingly p=0.691, p=0.193, and p=0.011 in comparison with the population that did not present themselves between 6 weeks and 1 year of follow-up. Follow-up by telephone was preferred compared to an outpatient clinic

visit in 84% of these 19 patients (p=0.203), and 95% of these patients were aware that they could contact the hospital for questions or consultation at all times (p=0.304).

Inter-hospital variability

Ten hospitals were interviewed regarding their organization of follow-up. There was substantial inter-hospital variability. Respectively 2, 2, and 1 hospitals report follow-up by telephone at 2, 4 or 6 weeks postoperatively. Two hospitals report the organization of follow-up differs per surgeon. One hospital reports that most surgeons perform follow-up at 6 weeks by telephone, while some surgeons perform follow-up on indication only. One hospital reports telephone follow-up at 1 week postoperatively and offers additional follow-up at 6 weeks if desired by the patients. One hospital performs follow-up at 2 and 30 days postoperatively by telephone.

Discussion

This prospective cohort study showed that the vast majority of patients report postoperative complaints themselves. Performing telephone follow-up at 1 year postoperatively, in addition to 6 weeks follow-up, is clinically useful in 3% of patients at best. Respectively 90%, 20%, 82%, and 47% of patients, consider a follow-up moment in general, at 1 day, 6 weeks, and 1 year postoperatively to be useful. Ninety-two percent of patients prefer telephone follow-up compared to an outpatient clinic visit.

These results change our view on the purpose of follow-up after inguinal hernia repair. Regular follow-up was always thought to be useful both clinically and with respect to registration purposes. With follow-up at fixed time-points, the majority of patients will currently have to contact the hospital themselves considering that the presentation of symptoms will usually not be in line with the planned follow-up. This study demonstrates that patients report their postoperative complaints themselves, and when treated in a high-volume specialized hernia clinic, no patients visit other hospitals for surgery-related complaints. Therefore, from a clinical point-of-view follow-up at a fixed time-point serves no purpose, as long as patients know they can contact the hospital for questions or consultation at all times. Follow-up does serve another patient-related purpose, which is meeting expectations and striving for patient satisfaction. Ninety percent of patients consider a follow-up moment in general to be useful, however, patients do not necessarily seem to prefer a certain time-point. As described in the Results section, we changed the policy of the 1-day postoperative telephone consultation by the daycare ward, resulting in an 80% reduction of workload. The question remains if follow-up should be performed at all. Thus, similar to follow-up 1 day postoperatively, it would be of interest to question postoperative patients that are informed on an uncomplicated postoperative course and instructed when to consult the hospital if follow-up is desired. A

trend towards performing less follow-up is already ongoing. A recent study by Adamu-Biu et al (2019) found that only 23% of postoperative inguinal hernia patients that did not receive follow-up felt clinical follow-up was necessary.[10] Although hospitals in the Netherlands show substantial inter-hospital variability, all questioned hospitals nowadays carry out follow-up by telephone and do not perform long-term follow-up. Regarding patient satisfaction, more than 90% of patients preferred telephone follow-up compared to an outpatient clinic appointment. This finding is conform satisfaction surveys that found preference with telephone follow-up compared to outpatient clinic appointments in more than 70% and 90% of patients in other medical fields, respectively, in the management of female urology and thyrotoxicosis.[11, 12] Using telephone follow-up 11.5% of patients with remaining complaints were detected 1 year postoperatively. This finding is conform the detected 10.9% of patients with any pain at the outpatient clinic in a previously conducted randomized controlled trial in our center.[13] Therefore, telephone follow-up is the preferred and cost-efficient method of follow-up compared to outpatient clinic appointments after inguinal hernia repair.

However, another important purpose of follow-up is data registration for quality objectives. The registration of data is of importance to hospitals for internal quality control, and national and international benchmarking. Given the circumstance that clinical purpose is lacking and the majority of patients do not consider long-term follow-up after inguinal hernia surgery to be useful, the surgical community should be judiciary to the methodology of the registration of outcomes. Internal quality control is of importance with new or modified treatments, however, once a hospital is aware of their performance not every patient needs to be exhaustively monitored. In this study patients report their complaints themselves and are not lost to other healthcare organizations. Thus, if patient records are examined periodically, the value of additional follow-up time-points is negligible. However, a limitation to this study can be that it was performed in a high-volume specialized center. Patients of non-specialized centers might be more likely to visit other healthcare organizations, in particular with a complicated postoperative course. Hence, additional follow-up time-points can provide more reliable data registration in these organizations. When to perform follow-up is mostly determined by chronic pain, defined as postoperative pain for more than 3 months by the International Association for the Study of Pain (IASP).[14] Based on current outcomes, with regard to cost-efficiency, patient satisfaction and the registration of chronic pain, we advise telephone follow-up once at 3 months postoperatively.

Nevertheless, using this methodology lacks quality control for asymptomatic outcomes, the outcome recurrence, and the loss to follow-up rate is high. Follow-up should be at least 2 years to assess recurrences, and prolonging the follow-up length will strengthen the registration.[13, 15, 16] Studies with large population databases that have the strength of imitating clinical reality and thus provide a high level of external validity are exemplar.[4] Worldwide 7 hernia registries have been established.[17] The most effective examples are the Danish

and Swedish hernia registries.[15, 18] However, these methodologies are not implementable in other healthcare systems, since they use nationwide patient numbers to effectuate that no data is lost when patients visit other hospitals or move to other regions. In the Netherlands, and many other nations with no nationwide electronic patient file, this methodology is not implementable. In the Netherlands an example of a well-organized oncology registration is the Dutch Institute for Clinical Auditing (DICA).[19] The EuraHS was developed to achieve a comparable hernia registry that generates data for quality of life, recurrences and pain with 2 years of follow-up.[20] Although the EuraHS provides extensive data for research, quality control, and benchmarking, the methodology demands manpower, excessive efforts by doctors and has been unsuccessful so far, probably in part because participation is not obligated.

The question remains how follow-up after inguinal hernia surgery should be organized? This study shows that regarding patient satisfaction adequate provision of information, a telephone consultation once, and an "open door" with the possibility of at all times contacting the hospital for questions or consultation is sufficient. However, this methodology is insufficient with respect to data registration for quality objectives aimed at internal quality control, and national and international benchmarking. Ideally, follow-up is simple and performed with adequate information provision, minimal costs, and efficient gathering of the necessary data with minimal burden for patients, surgeons and healthcare organizations.

To overcome current monitoring limitations of inguinal hernia patients we propose a future perspective of follow-up by means of a smartphone and tablet application. A promising innovative application for inguinal hernia repair follow-up was launched in 2019, which has incorporated preferred questionnaires and poses questions of which the timing, content, and frequencies are adapted to the daily life and assumed recovery of each patient.[21] Data registration through a smartphone application possibly provides accurate patient-reported outcomes measures, including asymptomatic outcomes, with a reduction of workload, and probably costs. In the near future a smartphone registration tool has the potential to be nationally or internationally used for large-scale benchmarking and research on inguinal hernia surgery, while at the same time preserve patient satisfaction and lower healthcare costs of inguinal hernia treatment. However, an application will need to be validated with the preferred validated questionnaires, and eventually the feasibility with elderly patients or patients with no smartphone accessibility, and cost-efficiency will need to be determined.

In conclusion, this study provided valuable information regarding the purpose of follow-up and the methodology of regular follow-up after inguinal hernia repair. The vast majority of inguinal hernia patients report postoperative complaints themselves, thus from a clinical point-of-view follow-up serves no purpose. Patients value a follow-up time-point, preferably by telephone, however do not consider long-term follow-up useful. Therefore, the purpose

of follow-up is patient satisfaction and registration for quality objectives, ideally in a national or international database. A smartphone and tablet application can possibly overcome current follow-up limitations.

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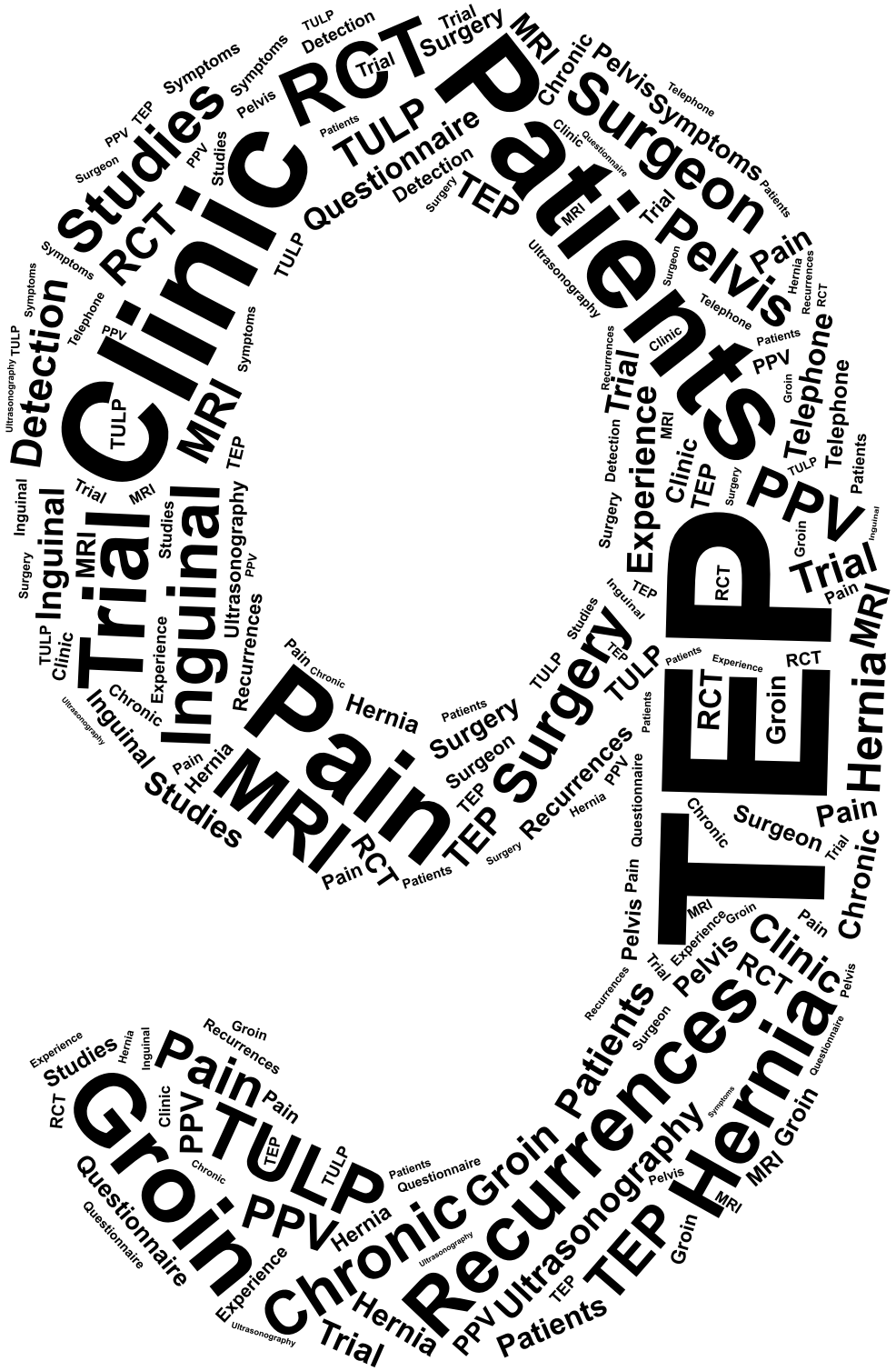
Clinic
Patients
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Detection
Questionnaire
Ultrasonography
MRI
PPV
Telephone
Experience

Experience with the PINQ-PHONE telephone questionnaire for detection of recurrences after endoscopic inguinal hernia repair

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Hernia (2019) 23:685-691

Abstract

Purpose

The PINQ-PHONE is a 4-question telephone questionnaire designed and validated as a recurrence detection method after laparo-endoscopic inguinal hernia repair. The study aim was to evaluate the PINQ-PHONE by describing our experience with the questionnaire in a high-volume randomized controlled trial.

Methods

The PINQ-PHONE was performed five years postoperatively after endoscopic totally extraperitoneal (TEP) repair. Positive PINQ-PHONE responses were compared with clinical assessments for a recurrence. An "experience with the PINQ-PHONE"-survey was conducted among the executing researchers. Furthermore, positive predictive values (PPV) for the separate questions and overall PINQ-PHONE were determined.

Results

Fifty-two of 769 responding patients (6.8%) had positive PINQ-PHONE responses and were invited to visit the outpatient clinic, thus preventing follow-up visits in 93.2% of included patients. Two recurrences were detected (0.3%). The overall PPV of the PINQ-PHONE was low (0.057). The PPV of question 1 (0.040) and 2 (0.100) was lower than that of question 3 (0.222) and 4 (0.286). The PPV of only question 3 and 4 combined was 0.183, and no recurrence would have been missed. The researcher survey unanimously produced that the PINQ-PHONE was user-friendly and executed in <5 minutes, and questions 3 and 4 were considered adequate for recurrence detection. The majority found questions 1 and 2 to be inadequate questions.

Conclusions

The PINQ-PHONE proved to be a valuable tool in TEP repair follow-up for recurrences. Enhancement of the PINQ-PHONE using only question 3 and 4 is recommended, since more patients refrain from outpatient clinic visits and nevertheless recurrences are safely detected.

Introduction

The quality of inguinal hernia surgery is predominantly determined by chronic groin pain, recurrences and patient satisfaction.[1] Investigating recurrence rates is only valuable if follow-up is at least two years after inguinal hernia surgery.[2] Many have stated that for an adequate measurement of recurrence rates all patients need to be routinely examined at the outpatient clinic by a hernia surgeon.[3, 4] This method of follow-up is time-consuming, expensive and patient unfriendly.

In 2014 a telephone questionnaire was designed and validated as a method of follow-up for the detection of recurrences after laparo-endoscopic inguinal hernia repair; the Post-INguinal-repair-Questionnaire by telephone (PINQ-PHONE).[5] In its validation study, the PINQ-PHONE proved to be a reliable, practical and simple method of follow-up.

To our knowledge, the PINQ-PHONE has not been used for any clinical studies after it was validated. Therefore, the aim of this study was to evaluate the PINQ-PHONE by describing our experience with the questionnaire in a high-volume randomized controlled trial (RCT) with 5-year follow-up after endoscopic totally extraperitoneal (TEP) inguinal hernia repair.

Materials and methods

Design

Five-year follow-up by means of the PINQ-PHONE in a double-blind RCT (TULP-trial) comparing lightweight and heavyweight mesh in patients that underwent endoscopic TEP inguinal hernia repair was previously conducted.[2] The study was carried out in a high-volume hospital with extensive experience in the endoscopic TEP hernia repair technique (Hernia Clinic Diakonessenhuis Utrecht/Zeist). Patient enrollment commenced in March 2010 and ended in October 2012. Patient in- and exclusion criteria were published previously.[2, 6, 7] At the start of the trial, 949 patients were included and TEP inguinal hernia repairs were performed by hernia surgeons who completed the learning curve (>500 procedures). The primary outcomes were development of (chronic) pain and recurrences. In this study all patients were assessed in whom a 5-year follow-up for recurrences by means of the PINQ-PHONE was completed. Attempts to reach patients for 5-year follow-up were made by five independent researchers between August 2016 and April 2017. The trial was approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, the Netherlands) and the local ethics board of the Hospital.

PINQ-PHONE

The PINQ-PHONE includes the following four elements: three questions concerning the operated groin of the patient and instructions for a Valsalva maneuver performed by the patient on the operated groin (Figure 1). If all four questions are answered negatively a recurrence can reliably be excluded.[5] If one or more of the four questions is answered positively, the PINQ-PHONE is scored positive and the patient should be invited for clinical assessment of a possible recurrent inguinal hernia.

Q1: Do you have any symptoms at your operated groin?
Q2: Have you noticed anything at your operated groin?
Q3: Have you noticed something at the operated groin when coughing, sneezing or squeezing?
Q4: Could you please stand up and put your other hand flat in your operated groin. Now please put the phone down and put this hand to your mouth and blow. Do you feel something in your operated groin?

Figure 1 PINQ-PHONE questionnaire

Patients with a positive PINQ-PHONE were invited for consultation and examination by an experienced hernia surgeon at the outpatient clinic. The outcomes of the PINQ-PHONE questionnaire were compared with the clinical assessment for a recurrence. A recurrence was defined as a symptomatic or asymptomatic bulge or weakness in the abdominal wall of the operated groin with herniation of abdominal contents exacerbated by the Valsalva maneuver. In case of complaints without clear findings of an inguinal hernia on physical examination, imaging was offered (X-ray of the pelvis and/or ultrasonography and/or magnetic resonance imaging (MRI) of the groin).

A survey in Dutch on the practicality and ease of use of the questionnaire was conducted independent from each other among the five researchers who executed the PINQ-PHONE in the TULP-trial. The survey consisted of questions regarding the average time for execution and the experience of the researcher with the overall questionnaire and the separate questions (Figure 2). Furthermore, the positive predictive value (PPV) for each separate question of the PINQ-PHONE, and subsequently for the overall questionnaire, was determined.

Statistical analysis

Analyses were performed using SPSS statistical software, version 24 (IBM Corp, Armonk, NY). Descriptive statistics were used for baseline data.

Q1: How long on average did it take you to execute the PINQ-PHONE questionnaire?
A: 0-3 minutes B: 3-5 minutes C: 5-7 minutes D: 7-10 minutes

Q2: In general, did you think of the PINQ-PHONE as a user-friendly questionnaire?
A: Yes B: No If 'No', why not? *Free text.*

Q3: With respect to detecting an inguinal hernia recurrence, do you think question 1 of the PINQ-PHONE is an adequate question? A: Yes B: No If 'No', why not? *Free text.*

Q4: With respect to detecting an inguinal hernia recurrence, do you think question 2 of the PINQ-PHONE is an adequate question? A: Yes B: No If 'No', why not? *Free text.*

Q5: With respect to detecting an inguinal hernia recurrence, do you think question 3 of the PINQ-PHONE is an adequate question? A: Yes B: No If 'No', why not? *Free text.*

Q6: With respect to detecting an inguinal hernia recurrence, do you think question 4 of the PINQ-PHONE is an adequate question? A: Yes B: No If 'No', why not? *Free text.*

Figure 2 Survey among researchers regarding ease of use of PINQ-PHONE

Results

At 5-year follow-up, execution of the PINQ-PHONE was attempted in 875 patients and completed in 769 patients (87.9%) (Figure 3). The 5-year study population had a median age of 55 years (IQR 44-64) (Table 1). Fifty-two patients (6.8%) responded positively to one or more of the four questions and were invited to visit the outpatient clinic. Thirty-five of the positive respondents were examined for a clinical recurrent inguinal hernia. Seventeen positive respondents were not scheduled for assessment.

Table 1 Patient characteristics

	All patients *(n=769)*	Patients examined at outpatient clinic *(n=35)*
Age, years, median (IQR)	55 (44-64)	53 (43-63)
BMI, kg/m², mean (SD)	24.8 (2.6)	25.9 (3.3)
Side, n (%)		
Left	336 (43.7)	14 (40.0)
Right	433 (56.3)	21 (60.0)
Hernia type, n (%)		
Medial	186 (24.2)	7 (20.0)
Lateral	578 (75.2)	28 (80.0)
Femoral	4 (0.5)	0 (0.0)
Mesh, n (%)		
Ultrapro	386 (50.2)	21 (60.0)
Prolene	383 (48.8)	14 (40.0)
Operation time, minutes, median (IQR)	19 (15-23)	20 (16-22)

BMI, Body Mass Index; IQR, Inter Quartile Range; SD, Standard Deviation

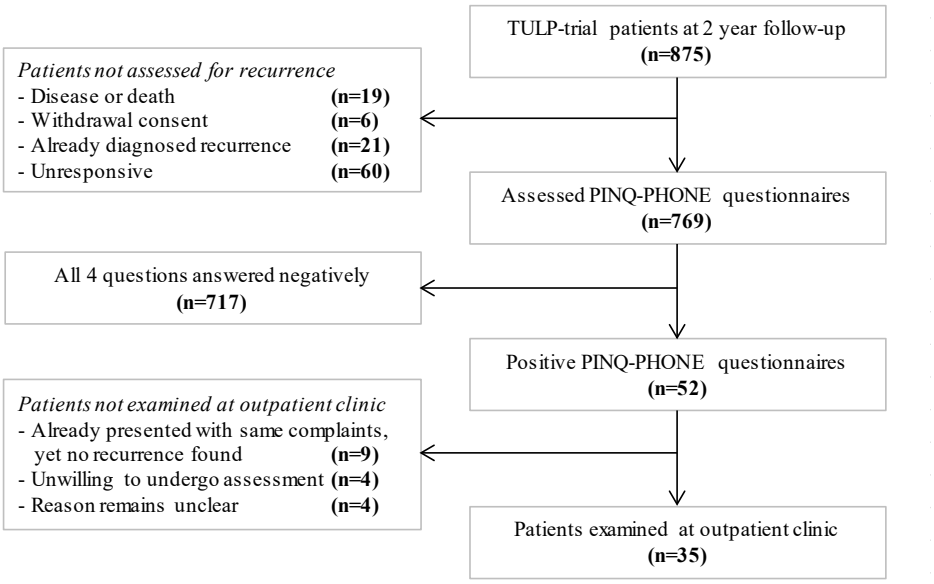

Figure 3 Flowchart

Experience of the researchers with the PINQ-PHONE

All five independent researchers (R1 until R5) completed the survey. Three out of five researchers executed the questionnaire (entire phone call) in 0-3 minutes and two researchers in 3-5 minutes on average. It was unanimously agreed that overall the questionnaire is a user-friendly method of follow-up.

Three researchers did not think of question (Q) 1 as an adequate question for the detection of inguinal hernia recurrences. R1 remarked: "Q1 detects a lot of noise, because of the wide range of irrelevant complaints patients address. Nevertheless, it is a better question than question 2." R4 comparably states: "'Any symptoms' is too widely interpretable, resulting in many unnecessary and irrelevant responses." R5 proclaimed: "The word 'symptoms' is a very broad concept. Moreover, if pain symptoms existed after placement of the mesh the question did not distinguish between a recurrence and chronic pain after surgery."

Four out of 5 researchers did not think of question 2 as an adequate question. R1 commented: "The concept 'noticed anything' is too vague. If the patient means 'symptoms' Q1 addresses this. If the patient means the only other notion of relevance 'inguinal swelling' or 'complaints with increased intra-abdominal pressure' Q3 or Q4 tackles the notion. This broad concept does not enhance the questionnaire." R3 remarked: "Q1 encompasses the objective of Q2, therefore making Q2 irrelevant. 'No symptoms' probably means 'nothing noticed' and if something is noticed patients will address this in Q1. I often received this as a response from

patients as well." R4 stated: "Q2 is too vague and has no added value, since any of the other three questions will always be answered positively if Q2 is answered positively. Moreover, Q2 makes surgeons unnecessarily see many patients at the outpatient clinic with irrelevant complaints." R5 commented: "'Noticed anything' is too vague, furthermore the question to the utmost extent overlaps with Q1. Many typical 'foreign body feeling' patients, but clearly no recurrence, would respond positively to this question. This question can be left out."

All researchers agreed that Q3 and Q4 of the PINQ-PHONE were adequate questions for the detection of inguinal hernia recurrences.

Contribution of separate PINQ-PHONE questions

The first question of the PINQ-PHONE concerning the presence of any symptoms in the operated groin was answered positively in 36 out of 769 patients (4.7%) (Table 2). Of the patients with a positive PINQ-PHONE seen at the outpatient clinic (n=35), 71.4% of patients responded positively to the first question (Figure 4). The second question referring to whether the patient noticed anything in the operated groin was answered positively in 29 patients (3.8%). Of the 35 patients seen at the outpatient clinic 57.1% of patients answered positively to the second question. The third question inquiring whether the patient noticed anything in the operated groin upon moments of sneezing, coughing or squeezing (increased abdominal pressure) was answered positively in nine patients (1.2%). All nine were seen, thus the contribution to patients seen at the outpatient clinic was 25.7%. The fourth question contained instructions for the do-it-yourself Valsalva maneuver. Two patients were unwilling to perform the maneuver. Upon self-examination in seven patients (0.9%) something was felt in the operated groin, therefore accounting for 21.2% of the examined patients.

Table 2 Positive PINQ-PHONE results

	Positive response (%)	Recurrences detected (%)	PPV
Question 1	25/35 (71.4)	1/2 (50.0)	0.040
Question 2	20/35 (57.1)	2/2 (100)	0.100
Question 3	9/35 (25.7)	2/2 (100)	0.222
Question 4	7/33 (21.2)	2/2 (100)	0.286

In two patients (0.3%) an inguinal hernia recurrence was detected on physical examination. In four doubtful cases additional imaging was performed, yet no additional recurrences were detected. Both patients were minimally symptomatic, therefore a watchful waiting approach was decided for and instructions on what to do if symptoms would increase were given. One patient requested surgery three months later and a Lichtenstein repair was performed.

Question 1 of the PINQ-PHONE detected one of two inguinal hernia recurrences. Thus the first question had a PPV of 0.040. Both recurrences were detected in the patients evaluated with a positive second, third and fourth question. The questions therefore had a PPV of 0.100, 0.222 and 0.286, respectively. (Table 2)

The overall PPV of the PINQ-PHONE was 0.057.

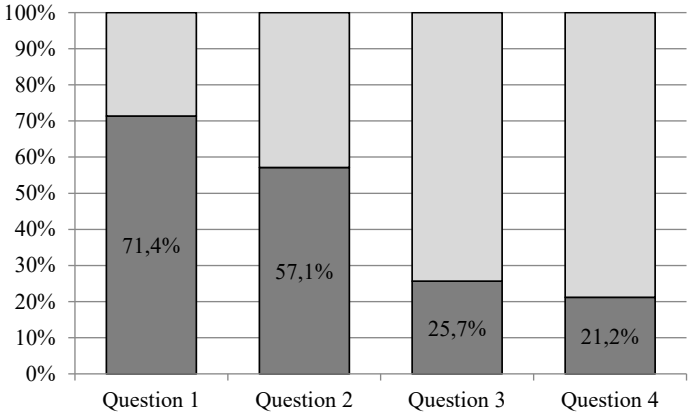

Figure 4 Contribution of separate questions to positive PINQ-PHONEs

Discussion

This study gave a clear insight into the practicality of the PINQ-PHONE by sharing our experience and demonstrating the value of the instrument as a method of follow-up by telephone for inguinal hernia recurrence detection. The PINQ-PHONE proved to be a simple and practical tool in a high-volume RCT with five years of follow-up, that prevented unnecessary and time consuming follow-up visits in 93.2% of included patients.[2] The researcher survey unanimously produced that the PINQ-PHONE was user-friendly and executed in <5 minutes. Questions 3 and 4 were considered adequate for recurrence detection, however the majority of researchers found questions 1 and 2 to be inadequate. Evaluation of the separate PINQ-PHONE questions showed a much lower PPV of question 1 (0.040) and 2 (0.100) compared to the PPV of question 3 (0.222) and 4 (0.286). To our knowledge this is the first study that performed follow-up using the PINQ-PHONE in a clinical trial since the design and validation of the questionnaire.

We applaud the work done by van den Heuvel et al. in designing and validating the PINQ-PHONE, however through our experience in a large sample of patients we see opportunities to enhance the PINQ-PHONE.[5] Pragmatically we would like to suggest to use only questions 3 and 4 of the questionnaire as they were. The PPV of question 3 and 4 combined is 0.183,

and is therefore over three times higher than the PPV of 0.057 of the original PINQ-PHONE. Furthermore, only question 3 and 4 would not have missed an inguinal hernia recurrence. Although we realize in the validation study of the PINQ-PHONE the negative predictive value was a more decisive outcome, the PPV as an objective outcome does substantiate the experience of the researchers and thus our idea for modification. The suggestion for enhancement has a practical nature, since it would allow clinics to schedule fewer outpatient clinic visits; in our sample group this would imply clinically evaluating only 11 out 769 patients (1.4%) instead of 52 patients (6.8%), while still being able to detect all recurrences.

We can only relate our findings to the study of van den Heuvel et al.[5] In their validation study they found an overall PPV of 0.100, which is slightly higher than our PPV of 0.057. Nevertheless, their PPV remains considerably lower than 0.183 of our suggestion for a renewed PINQ-PHONE. Van den Heuvel et al. stated that if a patient responds negatively to all questions of the PINQ-PHONE, from their findings the physician can be 100% sure that the patient has no recurrence. Among the positive respondents they found five recurrences in 300 patients (1.7%) of which one recurrence in their opinion, and to our agreement, should not be taken into account for the reason that progressive dementia made the outcomes unreliable. In their sample of patients all recurrences would have also been detected with only questions 3 and 4, thus the overall sensitivity of the renewed PINQ-PHONE is still 1.00. From these provided results of van den Heuvel et al. the conclusion can be drawn that our suggestion for enhancement is safe. Furthermore, similarly as in our sample of patients, the first question of the PINQ-PHONE is only answered positively in 50.0% of recurrences while at the same time it is evidently the biggest contributor to having to schedule patients at the outpatient clinic due to false positive responses. In the study of van den Heuvel et al. 48 out of 300 patients (16.0%) were invited to the outpatient clinic because of a positive PINQ-PHONE, and 1.7% turned out to have a recurrence. Thirty-nine patients answered question 1 positively, therefore 81.3% of patients is seen at the outpatient clinic due to question 1 even though it misses 50.0% of recurrences. This finding was substantiated by the experience of three of our researchers. The suggestion to leave out the second question is solemnly based on our findings and the experience of four of the researchers. Van den Heuvel et al. found seven out of 300 positive responses (2.3%) to question 2 of the PINQ-PHONE, while in our study the question was a big contributor to having to see patients at the outpatient clinic due to false positive responses. Possibly, this question is therefore ambiguous for both patient and researcher. Unfortunately, from their provided results we were unable to extract whether patients answered positively to only one question or more, thus a negative predictive value could not be calculated.

Two additional asymptomatic recurrences (0.3%) were detected in the TULP-trial. The overall 5-year recurrence rate was 2.4%. The low percentage of additional recurrences compared to literature and few positive PINQ-PHONE responses compared to van den Heuvel et al. can be

explained through the excluded patients with already diagnosed inguinal hernia recurrences (n=21) up until two years in the TULP-trial. Thus, leaving a sample of patients less prone to develop a recurrence. This does not influence the evaluation of effectiveness of the PINQ-PHONE, although as a result the number of patients with a final positive outcome for the questionnaire (recurrence) was smaller. Unfortunately, at the two-year follow-up point the PINQ-PHONE was not yet available. Until 2 years of follow-up all patients that reported pain, discomfort or swelling were scheduled to visit the surgeon for physical examination. Hence, the PINQ-PHONE provided a substantial practical improvement at 5-year follow-up. Usually asymptomatic recurrences require no surgical action, however in a prospective trial with recurrence as an outcome the value of the PINQ-PHONE was proven by detecting symptomatic and asymptomatic recurrences.

Our experience with using the PINQ-PHONE made us supportive of the questionnaire, since it refrains 84.0% of patients in the study of van den Heuvel et al. and 93.2% of our sample of patients from visiting the outpatient clinic for scheduled follow-up. Especially, in a prospective clinical trial with attempted follow-up in every patient it proves to be a valuable method. Nevertheless, having to unnecessarily schedule 14.3% (van den Heuvel et al.) and 6.5% (TULP-trial) of all operated inguinal hernia patients for visits at the outpatient clinic to exclude a recurrence remains time-consuming. From our experience this can relatively easy and safely be improved by eliminating the major sources of false positive responses.

We advise implementing the PINQ-PHONE for detecting inguinal hernia recurrences. Considering the growing awareness of learning from registration databases in addition to clinical trials, the renewed PINQ-PHONE provides questions that should be part of any registration aimed at detecting inguinal hernia recurrences.

A limitation of this study is that the negative PINQ-PHONE responses were not scheduled for a visit to the outpatient clinic. In this experience study logically not all patients were scheduled, since the meaning of the PINQ-PHONE is decreasing the burden at the outpatient clinic for both patients and doctors. From our data (asymptomatic) recurrences (false negatives) might have been missed and it makes us unable to determine a sensitivity or specificity of our suggestion for a renewed PINQ-PHONE with only questions 3 and 4. However, from the original validation data the renewed PINQ-PHONE, in addition to a higher PPV, shows a sensitivity of 1.00, implying that recurrences can be excluded with 100% reliability in patients with a negative response. Furthermore, a specificity of 0.85 was previously presented, which will only improve after elimination of the major source of false positive responses.[5] Therefore, the renewed questionnaire can safely be performed. Nevertheless, ideally a validation study of the renewed PINQ-PHONE would make the questionnaire even more reliable.

The PINQ-PHONE itself also comes with limitations. The PINQ-PHONE is only reliable when patients comprehend the language and do not suffer from cognitive impairment. Moreover, patients are often unresponsive (6.9% in current study), in which case patients should be addressed as loss to follow-up.

The PINQ-PHONE was validated for laparo-endoscopic inguinal hernia repair. Van den Heuvel et al. performed TAPP repair in 92.0% and TEP repair in 8.0% of cases. In our study 100% of cases underwent TEP repair. Future research should validate the PINQ-PHONE in its renewed version after open inguinal hernia repair. In both studies the questionnaire was executed in Dutch and validation of the PINQ-PHONE in other languages needs to be undertaken.

In conclusion, the PINQ-PHONE proved to be a valuable tool in TEP repair follow-up for recurrences and prevents time-consuming outpatient clinic visits for both patients and surgeons. However, enhancement of the PINQ-PHONE using only question 3 and 4 is recommended, since more patients refrain from visits to the outpatient clinic and nevertheless recurrences are safely detected.

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PROMs
Health
Hernia
Protocol
Inguinal
Pain
NRS
Clinic
Patients
Repair
Surgery
Mesh
Study
Data
Reliability
Hospital
Application
Outpatient
Clinicards
TEP
App
Postoperatively

Reliability and Validity of the Inguinal Hernia Smartphone Application for Follow-up after Inguinal Hernia Repair:
protocol of a prospective cohort study

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N Bax
JPJ Burgmans

In progress

Abstract

Background

Limitations of monitoring inguinal hernia patients can be overcome by using a smartphone and tablet application (app). Data registration through an innovative app can provide accurate patient-reported outcomes measures (PROMs) and has the potential to be used for large-scale benchmarking with a probable reduction of healthcare costs and workload. In 2020 a promising app was launched that has incorporated the preferred questionnaires for follow-up after inguinal hernia surgery. The aim of this study is to assess the reliability and validity of the Inguinal Hernia App in patients undergoing endoscopic totally extraperitoneal (TEP) inguinal hernia repair.

Methods

The Inguinal Hernia App was developed using a scalable and modular technology. Inguinal hernia patients over 18 years of age, scheduled for elective TEP repair and with smartphone or tablet access are eligible to participate in this prospective cohort study. Questionnaires of the app will be administered pre-operatively, and at 6 and 6 weeks and 2 days postoperatively, and additionally the NRS and EuraHS-QOL questionnaires will be completed preoperatively and at 6 weeks postoperatively. The primary outcome is the reliability and validity of the Inguinal Hernia App in comparison with previously validated scales and questionnaires by determining the construct validity (internal consistency, convergent and discriminant validity) and the test-retest reliability. Secondary outcomes are patient satisfaction with the app, perioperative complications and postoperative recovery.

Discussion

The Inguinal Hernia App can be an efficient method of follow-up to collect uniform and accurate PROMs after inguinal hernia surgery. If the app proves to be of high reliability and validity, using an app for follow-up after inguinal hernia surgery has the potential to substitute follow-up by telephone or at the outpatient clinic. Hence, reducing the workload and improving cost-efficiency and patient satisfaction.

Introduction

Follow-up after inguinal hernia surgery is performed with a purpose of clinical postoperative assessment, patient satisfaction, research, or data-registration for internal quality control and benchmarking. There is considerable inter-hospital variability regarding the organization of follow-up, however, in general, follow-up is performed at fixed time-points after surgery by telephone or at the outpatient clinic. In a recent study that critically assessed the purpose and methodology of regular follow-up after inguinal hernia repair the conclusion was formulated that from a clinical point-of-view follow-up at fixed time-points serves no purpose.[1] The vast majority of patients report their postoperative symptoms themselves, which is conceivable considering that complaints will usually not present in line with the fixed follow-up time-points.[1] Moreover, uniformity of registered inguinal hernia outcomes after surgery is lacking in research settings and hernia registries.[2-5] Therefore, currently patients are unnecessarily burdened with their regular follow-up, and healthcare professionals are not time- and cost-efficient. Considering the lack of clinical purpose and the organizational inefficiency, especially in the present-day society with restricted healthcare budgets and persistently increasing healthcare costs, the surgical community might need to get rid of certain rigidities and be judiciary to their follow-up methodology.

Current inguinal hernia patient monitoring limitations can be overcome by using a smartphone and tablet application (app). The use of mobile phones to measure inguinal hernia surgery outcomes is appealing since they are portable, easy-accessible, and fast, resulting in high compliance to follow-up. In 2019, 92.2% of the Dutch population older than 12 years had access to internet on a mobile phone.[6] Multiple studies have shown that mobile health (m-Health) apps are effective, efficient and user-friendly.[7-11] Data registration through an innovative app can provide accurate patient-reported outcomes measures (PROMs) and has the potential to be used for large-scale benchmarking with a probable reduction of healthcare costs and workload. In 2020 a promising app was launched that has incorporated the preferred questionnaires for follow-up after inguinal hernia surgery. The aim of this study is to assess the reliability and validity of the Inguinal Hernia App in patients undergoing endoscopic totally extraperitoneal (TEP) inguinal hernia repair by comparing the app with the currently widely used and previously validated scales and questionnaires.

Methods

Study design

This prospective cohort study will be carried out in a high-volume hernia clinic with extensive experience in the endoscopic TEP inguinal hernia repair technique (Hernia Clinic Diakonessenhuis Utrecht/Zeist) in collaboration with the app developer Synappz.

The reliability and validity of the Inguinal Hernia App is investigated in comparison with previously validated questionnaires: the Numeric (Pain) Rating Scale (NRS) and the European Registry for Abdominal Wall Hernias - Quality of Life (EuraHS-QOL) instrument.[12] The study is approved by the regional Medical Ethics Committee (MEC-U, Nieuwegein, the Netherlands) and the local ethics board of the hospital. Informed consent will be obtained in all included patients.

Inguinal Hernia App

The Inguinal Hernia App (in Dutch: Liesbreuk App) is developed by Synappz using their Clinicards platform technology. This technology is scalable and modular, and has been proven patient-friendly and efficient in multiple other medical apps. If required, the app is compatible with electronic patient files and the data is easily extracted and imported in statistical software, such as for example SPSS, for analysis. Received patient data is projected on a digital web-based portal (Clinicards portal). Although patients could be actively monitored in the Clinicards portal, the current app is not meant to be a diagnostic nor treatment modality, and will be used to collect prospective patient data. Therefore, patients will be informed that there will be no anticipation from the treating physician on given answers in the app. All patients will be instructed to contact the treating hospital or physician in case of (urgent) medical complaints or questions regarding their treatment, as they would without using the app. When having downloaded the app, the user is guided through the (Dutch) privacy laws and regulations and provides informed consent that the healthcare provider will not act on the provided data and for using their pseudonymised data for scientific purposes.

Follow-up by means of the app is performed using short questionnaires pre-operatively, and at 6 follow-up moments in the 2 years after surgery (Supplemental Table 1). The questionnaires become less extensive after 3 months postoperatively and take on average 5 minutes to fulfil. Patients are kept engaged and motivated to answer by posing dynamic questions based on previous answers using an adaptive question engine. For example, when the question of resumption of work has been answered positively, this question will no longer be asked. Or when the question of resumption of sports has been answered negatively, the question of pain with sports will not be posed. The app is constructed using the EuraHS-QOL questionnaire and an adjusted question of the Short-Form Inguinal Pain Questionnaire (SF-IPQ) to assess PROMs of pain and limitations, and the questions of the Post-INguinal-repair-Questionnaire by telephone (PINQ-PHONE) to assess possible recurrences.[12-15] Additionally, patient satisfaction, medical consumption, and resumption of daily activities, work, sports and sexual activity will be registered. The NRS is incorporated to quantify the outcomes.

Supplemental Table 1 Inguinal Hernia App (translated from Dutch into English for the purpose of this thesis)

General Pop-up/reminder for questionnaires on the day itself at 8:30 am. If questions are not answered: repeat at 7:30 p.m. and repeat daily until questions are answered.

	PROFILE		
Q	**Question**	**Answers**	**Dynamics**
1	I am a:	Male / Female / Genderfree	
2	Date of birth:	Date	
3	Length (meters with 2 decimal places):	Free text for entering number with 2 decimal places.	
4	Weight (kilogram with 1 decimal place):	Free text for entering number with 1 decimal place.	
5	Do you smoke?	Yes / No / Stopped	
6	Are you using blood thinners?	Yes / No	
7	My inguinal hernia is:	Right sided / left sided / on both sides	
8	Have you had an inguinal hernia operation before?	Yes / No	
9	That inguinal hernia operation was:	In my childhood / Without a mesh / Open surgery with a mesh / Laparo-endoscopic surgery with mesh / I don't know / Otherwise	(if Q8 YES)
10	Which side has had an inguinal hernia operation before?	Left / Right / Both sides	(if Q8 YES)
11	Have you had surgery in the lower abdomen (under the umbilicus) for any other reason than an inguinal hernia?	Yes / No	
12	That was because of:	The prostate / The appendix / A C-section / Gynecological cause / Other	(if Q11 YES)
13	Do you have a paid job?	Yes / No / Retired	
14	What is your profession?	Free text	(if Q13 YES)
15	Do you normally exercise?	Yes / No	
16	Are you sexually active?	Yes / No	
17	Which operation is going to be performed?	Endoscopic surgery (TEP) / Open or classic operation with mesh (Lichtenstein) / Other	
18	When is your operation scheduled?	Date	

	PRE-OPERATIVE		
Q	**Question**	**Answers**	**Dynamics**
1.1	How much pain have you had in the last week?	NRS 0-10, 0=no pain, 10=worst possible pain	
1.2	How much pain do you have in rest (sitting, lying down)?	NRS 0-10, 0=no pain, 10=worst possible pain	
1.3	How much pain do you have during activities (walking, cycling, sports in general)?	NRS 0-10, 0=no pain, 10=worst possible pain	
1.4	How much pain do you have when you have sex?	NRS 0-10, 0=no pain, 10=worst possible pain	(if Q16 YES)
1.5	The pain of the inguinal hernia affects your daily activities:	Always / Often / Sometimes / Never	
1.6	How much does the inguinal hernia limit you during in house activities?	NRS 0-10, 0=no restrictions, 10=completely limited	
1.7	How much does the inguinal hernia limit you during outdoor activities (walking, cycling, driving)?	NRS 0-10, 0=no restrictions, 10=completely limited	
1.8	Do you experience discomfort from your inguinal hernia while working?	Yes / No	(if Q13 YES)
1.9	Did your inguinal hernia stop you from working?	Yes / No	(if Q13 YES)
1.10	How much does the inguinal hernia limit you during hard work?	NRS 0-10, 0=no restrictions, 10=completely limited	(if Q13 YES)
1.11	Have you stopped exercising because of your inguinal hernia?	Yes / No	(if Q15 YES)
1.12	How much does the inguinal hernia limit you during sports?	NRS 0-10, 0=no restrictions, 10=completely limited	(if Q15 YES)

	POSTOPERATIVE at week 2, week 6, week 6 and 2 days, 3 months		
Q	**Question**	**Answers**	**Dynamics**
2.1	How much pain have you had in the last week?	NRS 0-10, 0=no pain, 10=worst possible pain	
2.2	Where is the pain located? (multiple answers possible)	Wound / Operated groin / Scrotum / Other	(if Q2.1 NRS ≥1)
2.3	How much pain do you have in rest (sitting, lying down)?	NRS 0-10, 0=no pain, 10=worst possible pain	
2.4	How much pain do you have during activities (walking, cycling, sports in general)?	NRS 0-10, 0=no pain, 10=worst possible pain	
2.5	The pain after surgery affects your daily activities:	Always / Often / Sometimes / Never	
2.6	How much does the inguinal hernia surgery limit you during in house activities?	NRS 0-10, 0=no restrictions, 10=completely limited	
2.7	How much does the inguinal hernia surgery limit you during outdoor activities (walking, cycling, driving)?	NRS 0-10, 0=no restrictions, 10=completely limited	
2.8	Can you fully carry out your daily activities again?	Yes / No	(Stop asking if previously answered YES)
2.9	How many days after the operation could you fully carry out your daily activities again?	Free text to enter a number.	(if Q2.8 YES; stop if previously answered YES)
2.10	Are you fully working again?	Yes / No	(if Q13 YES; stop if previously answered YES)
2.11	How many days after the operation could you fully work again?	Free text to enter a number.	(if Q2.10 YES; stop if previously answered YES)
2.12	How much does the inguinal hernia surgery limit you during hard work?	NRS 0-10, 0=no restrictions, 10=completely limited	(if Q2.10 YES; stop if previously answered YES)
2.13	Are you exercising fully again?	Yes / No	(if Q15 YES; stop if previously answered YES)
2.14	How many days after the operation could you fully exercise again?	Free text to enter a number.	(if Q2.13 YES; stop if previously answered YES)
2.15	How much does the inguinal hernia surgery limit you during sports?	NRS 0-10, 0=no restrictions, 10=completely limited	(if Q2.13 YES; stop if previously answered YES)
2.16	Are you sexually active again?	Yes / No	(if Q16 YES; stop if previously answered YES)
2.17	How much pain do you have when you have sex?	NRS 0-10, 0=no pain, 10=worst possible pain	(if Q2.16 YES)

	Questionnaire posed once at 3 months and 3 days.		
Q	**Question**	**Answers**	**Dynamics**
3.1	Have you contacted the hospital for questions or complaints after the operation?	Yes / No	
3.2	How many times have you been in touch?	1 / 2 / 3 / more than 3 times	(if Q3.1 YES)
3.3	Have you been to a doctor due to postoperative symptoms?	Yes / No	
3.4	What doctor have you been to? (multiple answers possible)	General practitioner / Surgeon / Otherwise: (free text)	(if Q3.3 YES)
3.5	Why did you see a doctor? (multiple answers possible)	Pain / Bruise / Wound infection / Swelling in the groin / Otherwise: (free text)	(if Q3.3 YES)
3.6	Did you have surgery in the groin again?	Yes / No	
3.7	Why did you have surgery again?	Bleeding / Infection / Pain / Another inguinal hernia on the same side / Otherwise: (free text)	(if Q3.6 YES)
3.8	How satisfied are you with your treatment?	NRS 0-10, 0=very dissatisfied, 10=very satisfied	
3.9	Would you recommend this treatment to family and/or friends?	NRS 0-10, 0=definitely not, 10=definitely	

	POST-OPERATIVE at 6 months, 1 year and 2 years		
Q	**Question**	**Answers**	**Dynamics**
4.1	Have you been to a doctor since completing the last questionnaire due to postoperative complaints?	Yes / No	
4.2	What doctor have you been to? (multiple answers possible)	General practitioner / Surgeon / Otherwise: (free text)	(if Q4.1 YES)
4.3	Why did you see a doctor? (multiple answers possible)	Pain / Bruise / Wound infection / Swelling in the groin / Otherwise: (free text)	(if Q4.1 YES)
4.4	Haveyou had surgery in the groin again since completing the last questionnaire?	Yes / No	
4.5	Why did you have surgery again?	Pain / Another inguinal hernia on the same side / Otherwise: (free text)	(if Q4.4 YES)
4.6	How much pain have you had in the last week?	NRS 0-10, 0=no pain, 10=worst possible pain	
4.7	How much pain do you have in rest (sitting, lying down)?	NRS 0-10, 0=no pain, 10=worst possible pain	
4.8	How much pain do you have during activities (walking, cycling, sports in general)?	NRS 0-10, 0=no pain, 10=worst possible pain	
4.9	The pain after surgery affects your daily activities:	Always / Often / Sometimes / Never	
4.10	How much does the inguinal hernia surgery limit you during in house activities?	NRS 0-10, 0=no restrictions, 10=completely limited	
4.11	How much does the inguinal hernia surgery limit you during outdoor activities (walking, cycling, driving)?	NRS 0-10, 0=no restrictions, 10=completely limited	
4.12	Have you noticed anything at the operated groin when coughing, sneezing or squeezing?	Yes / No	
4.13	Do you feel something with your hand in the operated groin when you blow on the back of your other hand?	Yes / No	

Apart from the collection of data, a chronological time path is presented that allows patients to track their own recovery by re-assessing previously answered questionnaires. Moreover this care path provides patients with credible information related to the recovery phase of each individual. Different care paths exist for varying surgical approaches: the Lichtenstein and the TEP technique. In the care path, preoperative information on the forthcoming inguinal hernia repair is provided and postoperative patients are informed at multiple time points on a 'normal' postoperative course, frequent self-healing complications as seroma, haematoma, or early postoperative pain, and when to contact the hospital. Additionally, the ability to provide practical instructions are a meaningful built-in of the app, e.g., when to remove the adhesive plasters, or resume taking showers, work, sports, or driving a bike or car. The information provision in the care path is often accompanied with informational videos or relevant research articles. This digital care path can be easily edited or further expanded by the healthcare provider, and can be modelled differently for each particular hospital. Using this app, we hope to achieve higher patient satisfaction, better patient understanding of the inguinal hernia intervention and postoperative recovery, and hence, reduce unnecessary postoperative consultations by telephone or at the outpatient clinic.

Patient population

All consecutive patients over 18 years of age with an inguinal hernia that are scheduled for elective endoscopic TEP inguinal hernia repair and with access to a mobile smartphone or tablet with Apple iOS® or Google Android® as operating system are eligible to participate in this study. Patients that do not comply with the inclusion criteria or that are deemed unlikely to complete follow-up due to a language barrier or cognitive impairment, will be excluded. No further exclusion criteria will be applied. All patients are surgically treated under general anaesthesia by hernia surgeons that completed the learning curve (>1500 procedures). A heavyweight polypropylene mesh (Prolene®, Ethicon, Johnson & Johnson Company, Amersfoort, the Netherlands) is placed in all patients. An empirically chosen sample size of 100 patients is considered adequate to investigate our objective of validating the Inguinal Hernia App.

Postoperative management, follow-up and outcomes

Patients are discharged on the day of TEP repair, unless complications prohibited early discharge. No restrictions will be given for activities of daily living (ADL). Strenuous physical activity during the first week postoperatively is discouraged. Patients are advised to use analgesics when in pain.

Patients are expected to fill out the questionnaires of the Inguinal Hernia App pre-operatively, and at 6 and 6 weeks and 2 days postoperatively, and additionally complete the NRS and EuraHS-QOL questionnaire preoperatively and at 6 weeks after TEP repair. The questions will be separately validated. Additionally, the questions of the app that require validation will be allocated in 2 domains: pain and restrictions of activities, and consequently validated in comparison with the corresponding section of the EuraHS-QOL. The NRS (questioned in Dutch) is an 11-point scale ranging from 0 = no pain to 10 = worst imaginable pain. Pain is considered clinically relevant with an NRS >3 and severe with an NRS >6.[5] The EuraHS-QOL instrument is a hernia-specific QOL questionnaire with 9 eleven-point scale questions across 3 domains: pain, esthetical discomfort, and restriction of activities.[12] The esthetical discomfort questions are not considered relevant with the development of the Inguinal Hernia App. Therefore, in the current validation study these questions are also omitted from the EuraHS-QOL questionnaire, resulting in a maximum of 70 points.

The primary outcome is the reliability and validity of the Inguinal Hernia App in comparison with previously validated scales and questionnaires by determining the construct validity (internal consistency, convergent validity and discriminant validity) and the test-retest reliability (at 6 and 6 weeks and 2 days postoperatively).

Secondary outcomes are patient satisfaction with the app, perioperative complications, pain in the last week, in rest, with activities and with sexual activity, resumption of work, sports, ADL, and sexual activity, and limitations with work, sports and ADL.

Statistical analysis

All statistical analyses will be performed using SPSS statistical software, version 23 (IBM Corp., Armonk, NY, USA). Descriptive statistics will be applied for demographic and baseline data. The Fisher exact test or chi-square analysis is executed to evaluate differences in categorical or dichotomous variables between time-points. The Student *t* test (normally distributed continuous) or Mann-Whitney U analysis (not normally distributed continuous) is used for other endpoints. The Cronbach's alpha will be used to assess the internal consistency of the EuraHS-QoL and Inguinal Hernia App. A threshold of 0.80 is considered an indication of good internal consistency and a value >0.90 is considered excellent. Convergent validity will be studied by calculating Spearman correlation coefficients for the agreement of pain subscales of the EuraHS-QoL and Inguinal Hernia App instruments with the NRS pain scale. Test-retest reliability is evaluated by correlating scores obtained at 6 weeks and 6 weeks and 2 days using Spearman correlation coefficients. Systematic differences will be studied by calculating the mean test-retest bias (with 95% confidence interval) and testing its significance according to the Wilcoxon signed rank test.

Discussion

The Inguinal Hernia App has been developed as an efficient method of follow-up to collect uniform and accurate PROMs after inguinal hernia surgery. In the current study protocol we have presented our methodology of determining the reliability and validity of this promising smartphone and tablet app that has incorporated the preferred questionnaires for follow-up after inguinal hernia surgery.

To the best of our knowledge, the Inguinal Hernia App is the first app that collects data by assessing PROMs and that informs patients on a normal postoperative course after inguinal hernia surgery. Many recent studies have shown that m-Health uses can aid, improve or substitute processes in our current healthcare system. Many different innovative m-Health programs provide possibilities of alternatives for collecting PROMs, providing credible health information, enabling patients to actively participate in their own recovery or treatment, and allow for efficient communication between healthcare providers and patients. Correspondingly, in the field of postoperative patient monitoring several studies have effectively investigated different programs in a variety of surgical populations.[9, 10, 16-19] The current evidence reports high satisfaction with the use of mobile apps in both patients and healthcare providers.[10, 11, 20-24] Additionally, substantial time, cost and travel savings for patients were established.[10, 11, 19, 20] Cost savings on the level of healthcare systems are to be suspected, although currently only limited data is available.[19, 20, 25]

This study will be executed in a high-volume hernia clinic in the Netherlands. The app will be validated in patients undergoing TEP inguinal hernia repair, however, if valid and reliable, will in our centre be used for other inguinal hernia repairs as well. In our opinion, the app will need no separate validation for different surgical techniques, since it is the methodology of follow-up that is validated. Moreover, the app is validated in comparison to questionnaires that are used regardless of the performed inguinal hernia repair technique. Currently the app is only available in the Dutch language. However, the app can easily be translated to other languages, as will be important if the app is to have a chance of success for international benchmarking.

Unfortunately at this time we are only able to present the study protocol, since the study has been on hold due to the COVID-19 pandemic. At the time of interruption 145 patients were screened at the outpatient clinic of whom 102 patients (70.3%) were included in the study. Of the excluded patients most were unwilling to participate, however 15 patients (10.3%) were excluded due to the inaccessibility to a smartphone or tablet. Of the included patients only 55 patients (53.9%) completed the pre-operative questionnaire and until now postoperative data is barely available.

With this study, we aim to determine the validity and reliability of the Inguinal Hernia App. If the app proves to be of high reliability and validity, the app can substitute follow-up at the outpatient clinic or by telephone to reduce the workload and improve cost-efficiency and patient satisfaction. The observations and recommendations that come forward from the qualitative research will be used to further improve the app. In time, the widespread use of this app will be encouraged to establish an inguinal hernia registration database that might nationally or internationally be used for large-scale benchmarking and high-volume research.

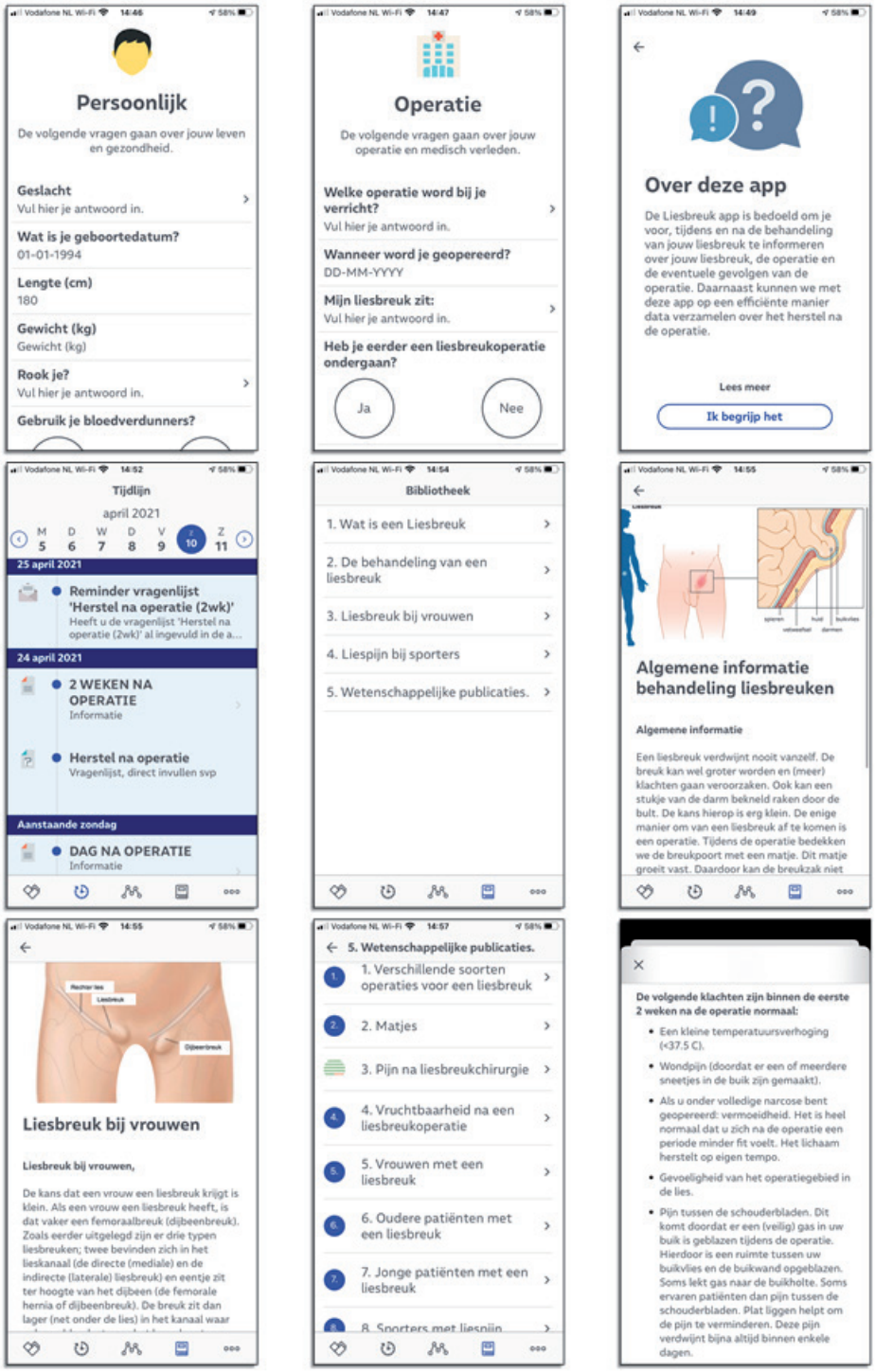

Figure 1 Multiple screenshots of the design of the Inguinal Hernia App (in Dutch)

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PART IV

IV

Part IV

General discussion and summary

Repair
Heavyweight
TEP
Adults
Risk
Asymptomatic
Repair
Research
Chronic
Treatment
Hernia
TEP
Inguinal
Recurrences
Surgery
Heavyweight
Pain
Pain
TEP
Recurrences
Hernia
Mesh
Pain
Repair
Pain
Increased
TSA
Mesh
Chronic
Repair
Hernia
Inguinal
Treatment
Adults
Pelvic
Risk
Risk
Increased
Hernia
Pain
Inguinal
Pain
Patient
Lightweight
GRADE
Hernia
Mesh
Pelvic
Chronic
Chronic
Patient
Research
Chronic
RCT
Risk
GRADE
Pelvic
TSA
Mesh
Recurrences
Repair
Hernia
Asymptomatic
Techniques
Chronic
Hernia
Asymptomatic
TSA
Adults
Lightweight
RCT
RCT
Heavyweight
Increased
Patient
Chronic
Heavyweight
Patient
RCT
Repair
TSA
Treatment
Adults

GRADE
Pain
Pelvic
Increased
Research
Mesh
Mesh
TEP
Inguinal
Research
Techniques
Adults
Inguinal
RCT
Lightweight
TSA
Asymptomatic
Hernia
Recurrences
Adults
Pain
TEP
GRADE
Hernia
Patient
GRADE
Treatment
Pain
Recurrences
Research
Mesh
Surgery
Increased
Lightweight
Adults
Risk
Treatment
TSA
Pain
Pelvic
Repair
Heavyweight
Mesh
Asymptomatic
Lightweight
Techniques
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Chronic
Research
Surgery
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Techniques
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TEP
Pelvic
Adults
TSA
Hernia
RCT
Patient
Inguinal
Chronic
Pain
RCT
Pelvic
TEP
Treatment
Adults
Risk
Techniques
RCT
Risk
GRADE
Surgery
Surgery
Heavyweight
Research
Inguinal
TSA
TSA
Adults
TEP
Techniques
GRADE
Heavyweight
RCT

Summarizing discussion, conclusions and future perspectives

Summarizing discussion

The lifetime occurrence of an inguinal hernia is high, especially in men.[1] A watchful waiting approach can be considered for asymptomatic or minimally symptomatic inguinal hernia patients since their risk of hernia-related emergencies is low.[2] However, most inguinal hernias will be or become symptomatic and should be treated surgically.[3, 4] The performed surgical inguinal hernia repair technique should be tailored to hernia- and patient-related characteristics, available resources, and expertise of the surgeon.[3] Mesh repairs are the gold standard, either by open or laparo-endoscopic technique.[3, 5] Worldwide the Lichtenstein repair technique is most commonly performed. However, provided that expertise and resources are available, laparo-endoscopic repair techniques have considerable advantages over open procedures and have become increasingly popular.[6, 7]

The aim of this thesis has not just been to expose problems, obstacles, or lacking consensus, but to provide pragmatic solutions and recommendations to optimize inguinal hernia surgery. This thesis focusses on three key-aspects of inguinal hernia surgery that remain controversial in the present-day treatment of inguinal hernia patients. What type of mesh should be used for open and laparo-endoscopic inguinal hernia surgery? Do specific patient populations benefit from patient-tailored surgery? And what is the purpose and necessity of follow-up after inguinal hernia surgery, and how should follow-up be organized?

An end to the debate on mesh

From 2004 onwards, the surgical community has had a lively scientific debate concerning the use of lightweight or heavyweight mesh for inguinal hernia repairs. Regardless of previous systematic reviews that analyzed numerous RCTs, the favorable results of lightweight mesh did not lead to a decisive implementation of lightweight mesh for open inguinal hernia surgery. As a result, many more RCTs were executed and published. This resulted in publications of 21 randomized controlled trials (RCT) for open inguinal hernia repair. In **Chapter 2** all data from the RCTs that compare lightweight and heavyweight mesh in open inguinal hernia repairs is summarized in a systematic review and meta-analysis. With the inclusion of over 4.500 inguinal hernia patients, the results and conclusions were convincing and confirmed the outcomes of a previous systematic review. The use of lightweight mesh decreases the risk of developing chronic pain (22% reduction) and foreign body feeling (36% reduction), while no difference in risk of recurrence was established. The outcomes of chronic pain and foreign body feeling were of high GRADE (Grading of Recommendations, Assessment, Development and Evaluation). Moreover, the recurrence rates showed no significant differences when lightweight and heavyweight mesh were compared with respect to the hernia defect size or hernia type (indirect or direct). Therefore, the use of lightweight mesh in open inguinal hernia repairs is recommended. To end the debate on using lightweight- or heavyweight mesh and safeguard research groups from the urge to perform more RCTs, additionally to

Chapter 2 a trial sequential analysis (TSA) was performed. TSA (for in-depth elaboration on TSA, see: Chapter 4 – Statistical analysis) indicated firm evidence for an increased risk of chronic pain and foreign body feeling when using heavyweight mesh. TSA indicated a shortage of evidence for recurrences due to the low event rate, although the required information size is not within a realistic reach. Therefore, there is no need to perform further research that compares lightweight and heavyweight mesh for open inguinal hernia repair, hence the focus of the surgical community should be on implementing the use of lightweight mesh.

For laparo-endoscopic inguinal hernia repairs, it remains questionable if the mesh type is of influence at all, and if so, if the reduction of pain and foreign body feeling when using lightweight mesh is comparable to Lichtenstein repairs. Unlike in open inguinal hernia surgery, not as many RCTs were performed that compared lightweight and heavyweight mesh for laparo-endoscopic inguinal hernia repair. Moreover, a RCT with adequate follow-up length and sample size to provide convincing results was lacking. In the TULP-trial, 950 patients were randomized to TEP inguinal hernia repair with either a lightweight (Ultrapro®) or heavyweight (Prolene®) mesh. A higher incidence of chronic pain, no difference in foreign body feeling, and a significantly increased risk of developing a recurrence when using a lightweight mesh at 3 months, 1 year, and 2 years postoperatively was previously demonstrated.[8-10] In **Chapter 3** the 5-year follow-up results of the TULP-trial with regard to recurrences were presented. To date, the TULP-trial has been the study with the longest follow-up duration and the largest sample size. The risk of developing a recurrence in the lightweight mesh group was significantly higher (lightweight mesh 3.8% versus heavyweight mesh 1.1%). Analysis of the primary hernia types showed a significantly higher recurrence rate for lightweight mesh in direct hernias. Subsequently, on multivariate analysis, lightweight mesh and primary direct inguinal hernias both independently remained significantly associated with the development of a recurrence. Considering the lightweight mesh characteristics compared to heavyweight mesh, the latter can be due to less adequate mesh fixation as a result of less fibrosis formation, intrinsic weakness, or mesh protrusion through the hernia defect, in particular in large direct defects. Based on these outcomes the use of lightweight mesh for laparo-endoscopic inguinal hernia repairs should be discouraged. However, the results were not entirely conform other RCTs that were performed on the subject. Especially for the outcome chronic pain multiple RCTs appeared to show advantages of lightweight mesh, and most RCTs found no significant difference for the outcome recurrences.[11-18] The TULP-trial is the biggest contributor in the field, nevertheless solemnly based on these outcomes a definite recommendation on using lightweight or heavyweight mesh for laparo-endoscopic inguinal hernia repairs could not be provided. In **Chapter 4** all available data of RCTs that compare lightweight and heavyweight mesh for laparo-endoscopic inguinal hernia repairs (TEP or TAPP), including the TULP-trial, was clustered and analyzed in a systematic review with meta-analysis. Based on 12 included RCTs, encompassing over 2.900 inguinal hernia

patients, this meta-analysis demonstrated that a heavyweight mesh should be used in laparo-endoscopic inguinal hernia repairs of direct or large inguinal hernias. For indirect inguinal hernias, no difference was detected. Using lightweight mesh significantly increased, and more than doubled, the risk of developing a recurrence, especially in non-fixated lightweight mesh. This outcome was of high GRADE. The influence of the hernia defect size on the development of recurrences was ill-reported, although the available data clearly favors using heavyweight mesh for a large defect. The recurrence rate of heavyweight mesh can be resembled by proper fixation of lightweight mesh in large or direct hernia repairs. However, this methodology is more expensive, not in any way superior, and tackers or sutures can cause pain through entrapment neuralgia.[19] Chronic pain and foreign body feeling were not influenced by using a lightweight or heavyweight mesh. The performed TSA indicated firm evidence for recurrences, although substantial heterogeneity resulted in a shortage of evidence for chronic pain. The estimated information size is, however, beyond an attainable reach, therefore the focus should be on the implementation of these outcomes.

This thesis has provided an end to the debate on the type of mesh, which has been ongoing for almost 2 decades. Open (Lichtenstein) inguinal hernia repairs can be optimized using a lightweight mesh. Laparo-endoscopic inguinal hernia repairs can be optimized using a heavyweight mesh. The physiology of these different recommendations is conceivable. A mesh induces an inflammatory reaction with subsequent fibrosis that is essential for fixation and incorporation in the abdominal wall of the mesh.[20] However, exaggerated fibrosis in close proximity to the inguinal nerves can contribute to chronic pain and instigate foreign body feeling.[21, 22] This applies especially to Lichtenstein repairs, considering an intermuscular mesh is placed adjacent to the three inguinal nerves (see: Chapter 1 – Figure 2, 3a). In laparo-endoscopic inguinal hernia repair techniques the mesh is placed in the preperitoneal anatomic plane avoiding direct contact with the inguinal nerves (see: Chapter 1 – Figure 3b). Hence, in general, laparo-endoscopic repairs are associated with less early postoperative and chronic pain compared to open repairs.[23, 24] Likewise, using a lightweight mesh does not provide the same advantages on chronic pain and foreign body feeling as for open repairs.

Going forward, implementation of these outcomes is essential. Especially for open inguinal hernia surgery the previously published systematic reviews that showed favorable results for lightweight mesh did not lead to a decisive implementation. As for inguinal hernia surgery, Oberkofler et al. showed that the adoption of recommendations following the outcomes of RCTs is problematic in many other surgical domains too, mainly due to expressed doubts regarding the validity of the used methodology in the RCTs.[25] Implementation is traditionally accomplished by updating national and international guidelines, and by distributing the results through conferences and publications in scientific journals. However, our present-day society provides modern pathways as social media and online platforms that allow for the dissemination of results to a broader audience. The penetrance and adoption of

recommendations into surgical practice can be increased by using these pathways to their full-potential, for example through online interactive seminars, shared video presentations, shared articles, or relatively easily organized international consensus meetings.

Optimizing TEP repair for specific populations of patients

In this thesis the treatment strategy was optimized for three specific patient populations with inguinal complaints: young patients with an inguinal hernia, athletes that suffer from inguinal disruption, and inguinal hernia patients in the work-up for a radical prostatectomy.

Chronic postoperative inguinal pain (CPIP) remains the most common disabling complication of an inguinal hernia repair.[26] Systematic reviews, and guidelines, have found similar predictors for the development of CPIP: young age, high preoperative pain level, female gender, early high postoperative pain intensity, open repair, and recurrent hernia.[3, 27-29] As a result, the current guidelines propose to investigate non-mesh repairs in young adults.[3] However, most studies that discuss young age as a risk factor are outdated and based on open repairs.[27, 30-35] Relevant studies for endoscopic repair were barely available until in **Chapter 5** it was demonstrated that young adults (18-30 years) compared to older adults (≥31 years) do not experience more CPIP after TEP hernia repair in a high-volume hernia clinic. Moreover, a subgroup analysis of 10-year age categories could not identify an age-dependent risk factor for the development of CPIP. Furthermore, Bisgaard et al. concluded that the risk of developing a recurrence with non-mesh repairs compared to mesh repairs in young adults significantly increases.[36] Therefore, considering the latter and the absence of increased pain, TEP mesh repair is the appropriate treatment strategy in young adults with an inguinal hernia.

Another patient population in which the treatment work-up remains a challenge is athletes with chronic groin pain. Inguinal disruption might be present in patients with unclear pathology, which is diagnosed by exclusion and defined as groin pain when no other obvious pathology explains the symptoms.[37-40] TEP repair might be indicated when conservative treatment by refraining from sports, analgesia and physiotherapy fails to improve the symptoms and athletes return for more lasting solutions.[39, 41, 42] However, literature reviews concluded studies regarding TEP repair were lacking to confirm this hypothesis.[43, 44] In **Chapter 6** we demonstrated that athletes with inguinal disruption, selected through a multidisciplinary work-up, benefit from TEP repair. The athletes showed reduction of pain, improvement in physical functioning, and fast return to full sports activity after TEP repair. At 3 months the median pain score significantly decreased from NRS 8 to NRS 4, and the maximum intensity of sports significantly increased from 40% to 95%. At long-term follow-up (median 19 months) 72% of patients were able to exercise with the maximum intensity and 62% of patients were pain-free. The emphasis of the favorable results of this study is on the optimization of the work-up by implementing a multidisciplinary team of a sports

medicine physician, a radiologist, and hernia surgeon to carefully select patients who are most likely to benefit from reinforcement of the posterior wall by performing a TEP repair. This approach is applicable to other centers. In organizing the work-up probably most can be gained from educating the sports medicine physicians regarding the careful selection of inguinal disruption patients. Upon patient presentation, groin pain is frequently adductor-related or has another musculotendinous origin that can be treated conservatively. Nevertheless, the underlying pathology often remains unclear and not one solution offers a reduction of symptoms in all patients. If the underlying pathology remains unclear the symptoms can be classified as inguinal disruption. Thus, the sports medicine physician, in close cooperation with the radiologist, has a key role in diagnosing pathology that can be treated conservatively. Patients should only be referred to a surgeon if no other obvious pathology exists that explains the symptoms, conservative treatment fails, and palpation of the inguinal canal is painful. The exact anatomical structures that are involved with inguinal disruption are constantly disputed, and pathology often seems to coexist, aggravating the confusion.[39, 45-47] Nevertheless, the most widely accepted theory is (a combination of) a weakened posterior wall and disruption of the adductor or rectus abdominis tendon at their attachment to the pubis.[43, 48-51] The disproportionate forces across the pubic symphysis of the strong adductor muscles in fixed lower extremities against the relatively weaker lower abdominal muscles could cause the fascia transversalis or overlying musculature or fascia to weaken.[47, 52, 53] These opposing forces are seen especially in athletes of sports with rapid directional changes. Considering the suspected deficiency of the posterior inguinal wall, strengthening the posterior wall by performing a TEP mesh repair provides a solution in the majority of inguinal disruption patients, even when macroscopically an abnormality is not detected.[44]

Furthermore, optimization is needed in the work-up and treatment of another specific patient population that suffers from an inguinal hernia and prostate cancer simultaneously. A previous laparo-endoscopic inguinal hernia mesh repair can complicate the radical prostatectomy and pelvic lymph node dissection thereafter through adhesions, the position of the mesh, and the distortion of anatomic planes. The available studies on the safety and feasibility of performing a radical prostatectomy with a prior inguinal hernia repair are of poor quality, lack hard data to substantiate conclusions, range widely in their recommendations and findings, and are all from a urological perspective.[54, 55] Therefore, the professional opinion and experience of urological surgeons was a necessary addition to the ongoing discussion. In **Chapter 7** urological surgeons describe their experience with performing a radical prostatectomy after a previous laparo-endoscopic inguinal hernia mesh repair. Urological surgeons report technical surgical difficulties that can lead to aborted radical prostatectomies, additional interventions for mesh explantation or inguinal hernia recurrences, and increased healthcare costs. Based on scarcely available patient data, in literature, a radical prostatectomy with a prior inguinal hernia mesh repair is considered

feasible and safe. However, multiple important complications are exposed that are now substantiated accordingly by the experience of urological surgeons: hernia recurrences, possible abortion of the radical prostatectomy, mesh explantation, and a less adequate nodal staging. In particular, a less adequate pelvic lymph node dissection is undisputed and considered clinically most important since it can result in under-staging and under-treatment of prostate cancer patients. These outcomes deserve adjustments in the work-up of patients with an inguinal hernia that have a scheduled or impending radical prostatectomy. Surgeons will need to be more aware of the impact of a previous laparo-endoscopic mesh repair and will have to be more prominent in preventing that urological surgeons end up performing complicated radical prostatectomies. An inguinal hernia repair should be postponed under the circumstance of an impending radical prostatectomy, with the preferable option of a concomitant performance of the radical prostatectomy and inguinal hernia repair. Alternatively, a Lichtenstein repair can be performed without the associated obstacles to urological surgeons.

Follow-up after inguinal hernia surgery

Performing follow-up after interventions or monitoring treatment therapies has long been incorporated into the organization of healthcare. To optimize healthcare patterns casting a critical eye 'from the outside in' once in a while is a necessity. To that effect, healthcare organizations must get rid of certain rigidities that stifle the development of a dynamic organization and an entrepreneurial mentality. In our present-day society, with persistently increasing health care costs and restricted health care budgets, cost-efficiency is high on the agenda, and optimization of inguinal hernia surgery should no longer only focus on clinical outcomes.

Follow-up after inguinal hernia surgery is performed with a patient-related purpose, in research settings, and to register data for internal quality control and national or international benchmarking. Many studies have focused on the outcomes that should be addressed with follow-up after inguinal hernia surgery, such as recurrences, chronic pain, foreign body feeling, resumption of work and sports, and quality of life.[3] In particular, the methodology of performing follow-up in research settings has been extensively lectured. Interestingly, the purpose and necessity of inguinal hernia surgery follow-up was barely questioned and revolved around assumptions. Evidently, regular follow-up after inguinal hernia surgery should be organized differently than in research settings, however, no clear advice is available. In **Chapter 8** the efficiency and purpose of regular follow-up after TEP inguinal hernia repair was evaluated, and patient appreciation with follow-up was determined. From a patient-related perspective, the vast majority of patients reported postoperative complaints or complications themselves. Follow-up at 1 year after surgery, in addition to 6 weeks follow-up (standard in our hospital), proved only clinically useful in 3% of patients at best. With the currently (multiple) fixed time-points of follow-up, the majority of patients

present themselves to the hospital considering that complaints will usually not arise in line with the planned follow-up. Therefore, follow-up after inguinal hernia surgery does not serve a purpose from a clinical point-of-view. Patients did value a follow-up moment in general, although long-term follow-up was not considered useful. Follow-up was preferably performed by telephone instead of at the outpatient clinic in 92% of patients. Regular follow-up can thus be optimized by performed follow-up once by telephone with the purpose of patient satisfaction and data registration. Considering that chronic pain is the most important outcome to register for internal quality control and national- and international benchmarking we advise performing follow-up by telephone at 3 months postoperatively.[56]

Nevertheless, using this follow-up method lacks quality control for the outcome recurrences after inguinal hernia surgery. It has been widely advertised that patients need to be routinely examined by hernia surgeons at the outpatient clinic to adequately assess recurrence rates.[57, 58] Moreover, to veraciously investigate recurrence rates follow-up should be performed at least 2 years postoperatively.[32, 59-61] This follow-up methodology, purely with the aim of data registration, is patient unfriendly, time-consuming for patients and surgeons, expensive, and comes with high loss to follow-up rates. In 2014, the Post-INguinal-repair-Questionnaire by telephone (PINQ-PHONE) was developed and validated as a method of follow-up to detect recurrences. However, the questionnaire lacked implementation with the consequence that the PINQ-PHONE had not been used in any clinical trials. In **Chapter 9** we shared our experience with the PINQ-PHONE in a high-volume randomized controlled trial. The study demonstrated the value of the PINQ-PHONE questionnaire as a follow-up method to assess inguinal hernia recurrences by telephone. The tool proved to be simple, practical, user-friendly, and prevented follow-up visits at the outpatient clinic in 93% of patients. The questionnaire was further optimized based on the data and the experience of the executing researchers to have more patients refrain from visiting the outpatient clinic and still safely detect all recurrences. It is recommended to use only question 3 and 4 of the original PINQ-PHONE, in which the patients are asked if they notice something at the operated groin when coughing, sneezing or squeezing, and if they feel something in the operated groin when instructed to perform a do-it-yourself Valsalva maneuver on the operated groin.[62] Especially in a prospective clinical study with mandatory follow-up in all patients the PINQ-PHONE proves to be valuable. Moreover, considering the increasing awareness of the importance of registration databases instead of research through clinical trials, the enhanced PINQ-PHONE should be implemented in any registration aimed at assessing inguinal hernia surgery outcomes.

Current inguinal hernia patient monitoring limitations can be overcome by using a smartphone and tablet application. Data registration through an innovative application can provide accurate patient-reported outcomes measures (PROMs) and, in time, has the potential to be used for large-scale benchmarking with a probable reduction of healthcare costs and

workload. In **Chapter 10** we introduced a promising application that has incorporated the preferred questionnaires for follow-up after inguinal hernia surgery. The study is designed with the aim of assessing the reliability and validity of the Inguinal Hernia Application in patients undergoing endoscopic totally extraperitoneal (TEP) inguinal hernia repair with the potential to substitute follow-up by telephone or at the outpatient clinic. Unfortunately this study has been on hold due to the COVID-19 pandemic. At the time of interruption 145 patients were screened at the outpatient clinic of whom 102 patients (70.3%) were included in the study. Until now, only 55 patients (53.9%) completed the pre-operative questionnaire and postoperative data is barely available. With the highest intensity of the COVID-19 crisis behind us, regular healthcare, and hence the care for inguinal hernia patients, has reverted. We expect to present data on the construct validity and reliability of the application, short and long term compliance with the application, and patient satisfaction with the application at a later stage.

Conclusions

1. Lightweight mesh should be used in open (Lichtenstein) inguinal hernia repair. (Chapter 2)
2. Heavyweight mesh should be used in laparo-endoscopic inguinal hernia repair. (Chapter 3 and 4)
3. Young adults do not experience more chronic postoperative inguinal pain after TEP hernia repair. (Chapter 5)
4. Athletes with inguinal disruption, selected through a multidisciplinary work-up, benefit from TEP repair. (Chapter 6)
5. A previous laparo-endoscopic inguinal hernia mesh repair frequently complicates the execution of a radical prostatectomy and pelvic lymph node dissection. (Chapter 7)
6. Follow-up after TEP inguinal hernia surgery serves no clinical purpose. The purpose of follow-up is patient satisfaction and data registration for quality objectives. (Chapter 8)
7. The PINQ-PHONE is a valuable tool in TEP repair follow-up by telephone for recurrences. (Chapter 9)
8. The Inguinal Hernia Application can potentially substitute follow-up after inguinal hernia surgery by telephone or at the outpatient clinic. (Chapter 10)

Future perspectives

Preperitoneal inguinal hernia repairs provide advantages considering the nerves are (relatively) unaffected. In this thesis predominantly the TEP inguinal hernia repair was studied. Regardless of the outstanding results of TEP repairs by experienced surgeons, it is important to keep an open attitude towards possible advantages of other newly developed or evolving inguinal hernia repair techniques. Lately, multiple open preperitoneal mesh techniques were developed owing to technical and commercial considerations, such as the TIPP and TREPP techniques.[63, 64] The limited available data show these techniques appear to be comparable to the Lichtenstein technique regarding recurrences and might result in less postoperative pain and faster recovery.[3] As for the laparo-endoscopic preperitoneal repairs, these techniques are most likely strongly correlated to the experience of the surgeon. Therefore, it is important to prospectively register data of relatively new techniques in experienced centers. Research will have to determine if open preperitoneal techniques have comparable outcomes to laparo-endoscopic preperitoneal techniques or offer advantages like reduced costs or a shorter learning curve.

Randomized comparisons of good quality that compared lightweight- and heavyweight mesh for both open and laparo-endoscopic inguinal hernia repair were abundantly published with an overall impressive sample size. Going forward the focus should be on implementing lightweight mesh for open repairs, and heavyweight mesh for laparo-endoscopic repairs. Performing more RCTs is a waste of resources and finances that could be applied more meaningful. However, the importance of maintaining prospective registration databases should be emphasized for quality control and to address new techniques, approaches, or mesh characteristics.

The use of mesh in inguinal hernia repairs is undisputed considering the accomplished reduction of recurrences. For both open and laparo-endoscopic inguinal hernia surgery the recommended type of mesh is now clear. However, worldwide there is considerable public unrest and media attention about the complications and effects of various implants. As a result, a growing number of patients are no longer eager to receive a mesh repair. In resemblance to silicone breast implants, some patients allegedly report allergy-like complaints after inguinal mesh placement, suggesting 'Autoinflammatory/Autoimmunity Syndrome Induced by Adjuvants (ASIA)'.[65] Although strongly suggested in the media, there is no available evidence that suggests mesh implants can cause immunity-related complaints or reduced quality of life. However, considering the public unrest, it is important to adequately address this hypothesis.

TEP repair treatment was optimized for three specific patient populations in this thesis. It remains of importance to be critical to (contra-) indications for inguinal hernia surgery.

Evaluation of other specific patient populations could indicate they would benefit or should refrain from inguinal hernia surgery. Likewise, as for young adults in this thesis, other presumed contraindications for a laparo-endoscopic inguinal hernia repair or risk factors for the development of chronic pain could be based on outdated studies or open inguinal hernia repair. Further research is also warranted to determine the therapeutic strategy for patients with clinically occult inguinal hernias (an inguinal hernia present on ultrasonography, however not with anamnesis or physical examination) and groin pain. Groin pain is a frequent symptom with a broad differential diagnosis. It is questionable if the radiological presence of a clinically occult hernia is the cause of the groin pain. Presently, for unclear reasons, the clinically occult inguinal hernia often leads to surgical repair. Currently, a multicenter randomized controlled non-inferiority trial (EFFECT-trial) with 1-year follow-up is ongoing that compares TEP repair and a watchful waiting approach (physiotherapy, rest and/or painkillers).[66] Surgical treatment with the associated risks and costs can be withheld if watchful waiting proves to be not inferior to TEP repair.

Inguinal Hernia Application

The Inguinal Hernia Application has the potential to substitute follow-up at the outpatient clinic or by telephone to reduce the workload and improve cost-efficiency and patient satisfaction. The use of mobile phones to measure inguinal hernia surgery outcomes is appealing since they are portable, easy-accessible, and fast, resulting in high compliance to follow-up. In 2019, 92.2% of the Dutch population older than 12 years had access to internet on a mobile phone.[67] Currently, the study to determine the reliability and validity of the Inguinal Hernia Application in patients undergoing endoscopic TEP repair is on hold. However, assuming the application will prove reliable, the next step towards implementing this application on a larger scale will be performing a large prospective trial with the aim of determining cost-efficiency and feasibility compared to regular follow-up in other inguinal hernia centers. Although we need further research, it is conceivable that through reduced telephone and outpatient clinic consultations the application will prove to be the cost-efficient method of follow-up. Additionally, the reliability and compliance with long-term follow-up will have to be determined. We aim to analyze the gathered data of the first 2 years and incorporate the results in the care path of the application to further inform patients with actual data on a normal postoperative course in our center. The care path can be adjusted to provide accurate data for each individual participating center. Eventually, this application has the potential to be used nationally, or even internationally, to establish a uniform method of follow-up after inguinal hernia surgery and stimulate large-scale benchmarking and high-volume research.

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Liesbreuk
Liesstreek
Lichtenstein
Zenuwen
Abdominale
Prostatectomie
Patiënten
Buikwand
TEP
TSA
TAPP
RCT
Mat
Protrusie
Vaten
Chronische
Liespijn
Epigastrische
Lichtgewicht
Operaties
Volwassenen
Liesbreukchirurgie
Zwaargewicht

Summary in Dutch|Nederlandse samenvatting

Nederlandse samenvatting

Een liesbreuk is een protrusie van abdominale inhoud door een defect in de buikwand in de liesstreek. Een liesbreuk wordt geclassificeerd als direct, mediaal van de epigastrische vaten; indirect, lateraal van de epigastrische vaten en door de interne opening van het lieskanaal; of femoraal, onder het ligamentum inguinale en door het femorale kanaal. Een liesbreuk komt gedurende het leven bij 27-43% van de mannen voor en bij 3-6% van de vrouwen. Een liesbreukoperatie is de meest uitgevoerde electieve chirurgische interventie met jaarlijks meer dan 20 miljoen operaties wereldwijd en ongeveer 30.000 in Nederland. Daarom is het optimaliseren van liesbreukchirurgie van verreikende betekenis voor chirurgen en patiënten over de hele wereld.

Een afwachtend beleid kan worden overwogen bij patiënten met een asymptomatische of minimaal symptomatische liesbreuk, omdat het risico op liesbreuk geassocieerde spoedgevallen laag is. Echter zijn of worden de meeste liesbreuken symptomatisch en dienen geopereerd te worden. De juiste operatietechniek moet worden gekozen op basis van de liesbreuk- en patiëntkarakteristieken, en is afhankelijk van de beschikbare middelen en expertise van de chirurg. Een liesbreukoperatie waarbij een synthetische mat wordt geplaatst is de gouden standaard voor zowel open als laparo-endoscopische technieken, aangezien het risico op een recidief aanzienlijk wordt gereduceerd door het plaatsen van een mat. Wereldwijd wordt de Lichtenstein operatie, een open anterieure techniek, het meest verricht. Echter, indien expertise en middelen voorhanden zijn, hebben laparo-endoscopische preperitoneale hersteltechnieken aanzienlijke voordelen: minder perioperatieve complicaties, kortere ziekenhuisopnames, een sneller postoperatief herstel en een snellere hervatting van dagelijkse activiteiten, werk en sport. Laparo-endoscopische technieken zijn de totaal extraperitoneale (TEP) en de transabdominale preperitoneale (TAPP) liesbreukoperatie. Deze technieken hebben vergelijkbare resultaten.

Het doel van dit proefschrift was niet alleen het blootleggen van problemen of gebrek aan consensus, maar met name het bieden van pragmatische oplossingen en aanbevelingen om de zorg voor liesbreukpatiënten te optimaliseren. Dit proefschrift heeft zich geconcentreerd op drie belangrijke en controversiële aspecten van de hedendaagse behandeling van patiënten met een liesbreuk: het juiste type mat voor laparo-endoscopische en open liesbreukchirurgie, het optimaliseren van het gebruik van de TEP liesbreukoperatie voor specifieke patiëntenpopulaties, en het optimaliseren van follow-up na liesbreukchirurgie. De onderzoeksresultaten uit dit proefschrift zijn verkregen in een groot TEP expertisecentrum.

Optimaliseren van het gebruik van matten

Sinds de introductie van synthetische matten is het recidiefpercentage na liesbreukchirurgie dusdanig gereduceerd dat het gebruik van een mat onomstreden is. De geplaatste mat

induceert een ontstekingsreactie en vervolgens fibrosering die essentieel is voor goede fixatie van de mat. Echter, overdadige fibrose kan bijdragen aan chronische pijn en het voelen zitten van het lichaamsvreemde materiaal (matgevoel). Het wordt verondersteld dat de ernst van de ontstekingsreactie gecorreleerd is aan de hoeveelheid synthetisch materiaal en de grootte van de poriën van de mat. Zodoende werden lichtgewicht matten met grotere poriën en minder materiaal ontwikkeld met als doel het verminderen van chronische pijn en matgevoel na een liesbreukoperatie. Daarentegen zijn mogelijk recidiefpercentages hoger bij het gebruik van een lichtgewicht mat. Sinds 2004 is uitvoerig wetenschappelijk onderzoek verricht naar het gebruik van reguliere zwaargewicht of lichtgewicht matten. De goede resultaten volgens eerdere systematische reviews hebben nog niet geleid tot een implementatie van lichtgewicht matten voor open liesbreukchirurgie. Gezien het gebrek aan implementatie werden overdadig veel aanvullende gerandomiseerde studies met controlegroep (randomized controlled trial; RCT) uitgevoerd en gepubliceerd. Dit heeft geleid tot 21 RCTs voor open (Lichtenstein) liesbreukchirurgie. In **Hoofdstuk 2** worden meer dan 4.500 patiënten die open liesbreukchirurgie hebben ondergaan geanalyseerd in een systematische review met meta-analyse. Er wordt geconcludeerd dat het gebruik van een lichtgewicht mat chronische pijn en matgevoel significant vermindert, terwijl recidieven niet vaker voorkomen. Een vergelijking tussen zwaargewicht of lichtgewicht matten voor verschillende type liesbreuken (direct of indirect) of de grootte van het defect was niet van invloed op het recidiefrisico. Conform eerdere systematische reviews wordt daarom voor open anterieure liesbreukchirurgie een lichtgewicht mat geadviseerd. Er werd een trial sequential analysis (TSA) uitgevoerd om de indicatie voor aanvullende RCTs te bepalen, en indien mogelijk een einde te maken aan de discussie over het gebruik van een lichtgewicht of zwaargewicht mat. De TSA laat zien dat er voldoende bewijs is geleverd voor de uitkomsten chronische pijn en matgevoel. Voor de uitkomst recidieven blijkt nog onvoldoende bewijs beschikbaar vanwege de lage incidentie, echter zijn de benodigde data niet binnen een realistisch bereik. De focus moet daarom liggen op de implementatie van lichtgewicht matten voor open liesbreukchirurgie.

Voor laparo-endoscopische liesbreukchirurgie zijn de voordelen van een lichtgewicht mat minder duidelijk. Laparo-endoscopische liesbreukchirurgie is geassocieerd met minder vroeg postoperatieve en chronische pijn in vergelijking met open liesbreukchirurgie. Dit is waarschijnlijk doordat de mat in de preperitoneale ruimte wordt geplaatst zonder direct contact met de zenuwen. Dit in tegenstelling tot de Lichtenstein operatie waarbij de mat tussen de spierlagen en aangrenzend aan de drie zenuwen in de lies wordt geplaatst (zie Hoofdstuk 1 – figuur 2 en 3). Daarom is het onduidelijk of voor laparo-endoscopische liesbreukchirurgie het type mat van invloed is, en zo ja, of chronische pijn en matgevoel afneemt bij het gebruik van een lichtgewicht mat zoals bij de Lichtenstein operatie. Een studie met een adequate follow-up duur of steekproefomvang om deze vraag te beantwoorden ontbreekt. In **Hoofdstuk 3** worden de langetermijnresultaten (5 jaar na TEP operatie) met

betrekking tot recidieven beschreven van een RCT (TULP-studie) die lichtgewicht (Ultrapro®) en zwaargewicht (Prolene®) matten vergelijkt onder 950 patiënten. Het risico op het ontwikkelen van een recidief is significant hoger wanneer een lichtgewicht mat (3.8%) wordt gebruikt ten opzichte van een zwaargewicht mat (1.1%). Een lichtgewicht mat lijkt vooral nadelig te zijn bij directe liesbreuken, aangezien 92% van de patiënten die een recidief ontwikkelde na een directe liesbreukoperatie een lichtgewicht mat had gekregen. Op eerdere follow-up momenten werd reeds aangetoond dat een lichtgewicht mat resulteerde in een hogere incidentie van chronische pijn en geen verschil in matgevoel. Gebaseerd op deze uitkomsten moet het gebruik van een lichtgewicht mat bij laparo-endoscopische liesbreukchirurgie ontmoedigd worden. De TULP-studie levert de grootste bijdrage aan deze vraagstelling in de huidige literatuur, echter zijn de uitkomsten in de literatuur wisselend en kan daarom alleen op basis van de TULP-studie niet een (definitieve) aanbeveling worden gedaan. Voornamelijk voor de uitkomst chronische pijn laten meerdere RCTs voordelen zien van een lichtgewicht mat. Bovendien laten de meeste RCTs geen significant voordeel van een zwaargewicht mat zien op het gebied van recidieven. In **Hoofdstuk 4** worden in een systematische review en meta-analyse meer dan 2.900 patiënten geanalyseerd uit RCTs die lichtgewicht en zwaargewicht matten vergelijken voor laparo-endoscopische liesbreukchirurgie, inclusief de TULP-studie. Een zwaargewicht mat heeft de voorkeur boven een lichtgewicht mat voor laparo-endoscopische correctie van directe en grote liesbreuken. Voor indirecte liesbreuken wordt geen verschil in uitkomsten gedetecteerd. Het risico op het ontwikkelen van een recidief is significant verhoogd en meer dan verdubbeld bij het gebruik van een lichtgewicht mat, met name voor niet-gefixeerde matten bij directe liesbreuken. Tevens is het gebruik van een zwaargewicht mat aanbevolen voor grote liesbreuk defecten, ondanks de relatief beperkt beschikbare data in de literatuur. Chronische pijn en matgevoel worden niet beïnvloed door het gebruik van een lichtgewicht of zwaargewicht mat. De TSA laat zien dat er voldoende bewijs is voor de uitkomst recidieven. Daarentegen blijkt er onvoldoende bewijs beschikbaar voor de uitkomst chronische pijn vanwege de aangetroffen heterogeniteit in de analyse. Echter is de benodigde data niet binnen een realistisch bereik. De focus moet daarom liggen op de implementatie van zwaargewicht matten voor laparo-endoscopische liesbreukchirurgie.

Dit proefschrift maakt een einde aan een discussie die al bijna twee decennia wordt gevoerd over het gebruik van lichtgewicht of zwaargewicht matten in de liesbreukchirurgie. Open (Lichtenstein) liesbreukchirurgie kan worden geoptimaliseerd door het gebruik van een lichtgewicht mat. Laparo-endoscopische liesbreukchirurgie kan worden geoptimaliseerd door het gebruik van een zwaargewicht mat. Het is essentieel aan de implementatie van deze uitkomsten te werken.

Optimaliseren van de TEP liesbreukoperatie voor specifieke patiëntenpopulaties

De behandeling van liesbreukpatiënten dient te worden afgestemd op de karakteristieken van de patiënt en de liesbreuk. Voor de meeste specifieke patiëntenpopulaties is de behandelstrategie duidelijk. Bijvoorbeeld vrouwelijke liesbreukpatiënten dienen laparo-endoscopisch geopereerd te worden zodat peroperatief een adequaat overzicht wordt verkregen en geen femorale liesbreuken worden gemist, bij ouderen met (pulmonale) comorbiditeiten dient een open procedure onder lokale anesthesie overwogen te worden, en bij patiënten met een recidief liesbreuk dient een anterieure en posterieure benadering afgewisseld te worden. Er zijn daarentegen meerdere specifieke patiëntenpopulaties voor wie de behandelstrategie of work-up inadequaat of onduidelijk is. Dit proefschrift heeft als doel om de behandeling voor drie specifieke patiëntenpopulaties te optimaliseren: jonge liesbreukpatiënten, atleten met inguinal disruption en liesbreukpatiënten die tevens in de work-up zitten voor een radicale prostatectomie.

Met de indrukwekkende afname van recidieven werd chronisch postoperatieve liespijn de meest voorkomende invaliderende complicatie na liesbreukchirurgie. In de literatuur worden risicofactoren voor het ontwikkelen van chronisch postoperatieve liespijn beschreven: jonge leeftijd, vrouwelijk geslacht, hoog preoperatief pijn niveau, hoog vroeg postoperatief pijn niveau, open liesbreukoperatie en een recidief liesbreuk. Hieruit voortvloeiend wordt vanuit de richtlijn een voorstel gedaan om liesbreukchirurgie zonder mat te onderzoeken bij jong volwassenen met als doel het verminderen van chronische pijn. Echter zijn de meeste studies die jonge leeftijd als een risicofactor omschrijven verouderd en gebaseerd op open liesbreukchirurgie. Aangezien laparo-endoscopische liesbreuktechnieken minder chronische pijn veroorzaken dan open liesbreukoperaties is het onduidelijk of jonge leeftijd dan ook geassocieerd is met chronische pijn. **Hoofdstuk 5** laat zien dat jong volwassenen (18-30 jaar) in vergelijking met oudere volwassenen (≥31 jaar) niet meer chronische pijn ervaren na TEP liesbreukchirurgie in een expertisecentrum. Tevens laat een subgroep analyse van leeftijdscategorieën van 10 jaar geen leeftijd geassocieerde risicofactor voor het ontwikkelen van chronische pijn zien. Bovendien wordt in de literatuur beschreven dat het risico op het ontwikkelen van een recidief toeneemt bij liesbreukoperaties zonder mat bij jong volwassenen. De TEP operatie met mat is daarom een gepaste behandeling voor jong volwassenen.

Adequate behandeling blijft ook een uitdaging voor atleten met chronisch liespijn. Vaak zijn de klachten gerelateerd aan de adductoren of andere musculotendinogene oorzaken die conservatief behandeld kunnen worden. Frequent blijft de onderliggende pathologie echter onduidelijk en is er geen eenduidige behandeling die bij alle patiënten verlichting van symptomen geeft. Wanneer de pathologie onduidelijk blijft kunnen de symptomen geclassificeerd worden als ‘inguinal disruption. ‘Inguinal disruption’ wordt gediagnosticeerd per exclusionem en gedefinieerd als chronische liespijn waarbij andere verklarende pathologie

uitgesloten is. Veel atleten, zowel amateur als professioneel, kunnen hier klachten van ervaren. Er is voortdurend discussie over welke anatomische structuren aangedaan zouden zijn bij 'inguinal disruption'. Vaak gaat het om meerdere aangedane structuren waardoor de verwarring alleen maar toeneemt. De meest geaccepteerde theorie is een (combinatie van een) zwakte van de achterwand en een verstoring van de aanhechtingen van de adductor of rectus abdominis spieren op het os pubis. De fascia transversalis of overliggende spieren en fascie zouden kunnen verzwakken door de onevenredig tegengestelde krachten van de sterke adductoren bij een gefixeerde onderste extremiteit en de relatief zwakke lage buikspieren. Deze tegengestelde krachten leiden vooral tot klachten bij sporters die snel moet wenden en keren. Gezien de vermoedelijke zwakte van de achterwand als oorzaak van de klachten zou het versterken van de achterwand door middel van een TEP operatie met mat een oplossing kunnen zijn. In **Hoofdstuk 6** laten we zien dat atleten met 'inguinal disruption', die geselecteerd worden door een multidisciplinaire work-up, baat hebben bij de TEP liesbreukoperatie. De atleten laten verbetering in fysiek functioneren, reductie van pijn en een snelle hervatting van volledige sportactiviteit zien na de TEP operatie. Op 3 maanden postoperatief was de mediane pijnscore significant gedaald van NRS 8 preoperatief naar NRS 4, en de maximale intensiteit van sport significant toegenomen van 40% preoperatief naar 95%. Bij lange termijn follow-up (mediaan 19 maanden) was 62% van de atleten pijnvrij en kon 72% van de atleten weer met de maximale intensiteit sporten. De nadruk van de gunstige resultaten in deze studie ligt op het zorgvuldig selecteren van patiënten die het meest waarschijnlijk profiteren van het verstevigen van de achterwand door middel van een TEP operatie door het betrekken van een multidisciplinair team van een sportarts, een radioloog en een liesbreuk chirurg.

Met de toegenomen ervaring van liesbreukchirurgen en door de ontwikkelingen in de liesbreukchirurgie is de indicatiestelling voor een TEP operatie uitgebreid. Zo worden tegenwoordig TEP operaties verricht na eerdere abdominale chirurgie of bij patiënten met reponibele scrotaalbreuken. Desondanks blijft een TEP gecontra-indiceerd bij patiënten met een veranderd preperitoneaal anatomisch gebied, zoals bij patiënten met een dissectie of radiotherapie van de iliacale lymfeklieren of een radicale prostatectomie in de voorgeschiedenis. Andersom is het voor te stellen dat chirurgen meer rekening zouden moeten houden met de invloed die eerdere liesbreukinterventies hebben op daaropvolgende preperitoneale ingrepen door andere chirurgische specialismes, zeker indien de daaropvolgende indicatie meer levensbedreigend is. In dit kader is het optimaliseren van de work-up en behandeling nodig voor patiënten die een liesbreuk hebben en een radicale prostatectomie dienen te ondergaan vanwege een prostaatcarcinoom. Zowel prostaatkanker als liesbreuken hebben een hoge incidentie gedurende de levensloop van mannen en worden toenemend gediagnosticeerd met de leeftijd. Daarom komt het veelvuldig voor dat patiënten met een liesbreuk in een latere fase ook een radicale prostatectomie zullen ondergaan. Een eerdere laparo-endoscopische liesbreuk operatie met het plaatsen van een mat kan een radicale prostatectomie en lymfeklierdissectie

compliceren door ontstane verklevingen, de obstruerende positie van de mat en de verandering van anatomische vlakken. De beschikbare studies met patiëntendata over de veiligheid en uitvoerbaarheid van een radicale prostatectomie na eerdere liesbreukchirurgie zijn van zwakke kwaliteit en variëren enorm in bevindingen en aanbevelingen. Bovendien zijn alle uitgevoerde studies beschreven vanuit een urologisch perspectief. Gezien het tekort aan harde data om conclusies te trekken is de professionele mening en ervaring van urologen een noodzakelijke toevoeging aan de voortdurende discussie. In **Hoofdstuk 7** beschrijven urologen hun ervaring met het uitvoeren van een radicale prostatectomie na een voorgaande laparo-endoscopische liesbreukoperatie met mat. De urologen rapporteren dat de ingreep technisch lastiger is en dat dit frequent leidt tot afgebroken radicale prostatectomiën, lastige lymfeklierdissecties, aanvullende interventies vanwege het verwijderen van de mat of liesbreuk recidieven, en toegenomen zorgkosten. In de literatuur wordt, gebaseerd op de schaars beschikbare patiëntendata, geconcludeerd dat een radicale prostatectomie na eerdere liesbreukchirurgie uitvoerbaar en veilig is. Er worden echter meerdere ingrijpende complicaties aangekaart die nu worden onderbouwd door de ervaring van urologen: liesbreuk recidieven, het mogelijk afbreken van de radicale prostatectomie, noodzaak tot verwijderen van de mat en een minder adequate lymfeklierdissectie. Vooral een inadequate lymfeklierdissectie is onomstreden en is tevens klinisch het meest belangrijk aangezien dit kan leiden tot een slechtere stadiëring en onderbehandeling van het prostaatcarcinoom. Het verdient aanbeveling dat chirurgen zich meer bewust zijn van de invloed die een laparo-endoscopische liesbreukoperatie met mat in deze patiëntenpopulatie kan hebben. Door meer bewustwording en indien nodig heroverweging van de operatietechniek kan voorkomen worden dat urologen gecompliceerde radicale prostatectomiën moeten uitvoeren. Een liesbreukoperatie dient te worden uitgesteld in het geval van een aanstaande radicale prostatectomie waarbij het de voorkeur heeft gelijktijdig een radicale prostatectomie en liesbreuk operatie uit te voeren. Als alternatief kan een Lichtenstein operatie worden uitgevoerd zonder de geassocieerde problemen voor urologen.

Follow-up na liesbreuk chirurgie

Het uitvoeren van follow-up na interventies of ter opvolging van ingezet beleid is standaard in de huidige organisatie van gezondheidszorg. Om gezondheidszorgpatronen te optimaliseren is het noodzakelijk af en toe met een kritische blik ‘van buiten naar binnen’ te kijken om te voorkomen dat er een starheid ontstaat die de ontwikkeling van een dynamische organisatie en ondernemersmentaliteit in de weg staat. In onze huidige maatschappij met continue toenemende gezondheidszorgkosten en een beperkte begroting staat kosten-efficiëntie hoog op de agenda. De optimalisatie van liesbreukchirurgie kan zich niet langer alleen op klinische uitkomsten concentreren.

Follow-up na liesbreukchirurgie wordt uitgevoerd met een patiëntgerelateerd doel, in onderzoeksverband en om data te registreren voor interne kwaliteitscontrole en

benchmarking. Vele studies hebben zich geconcentreerd op de klinische uitkomsten na liesbreukchirurgie, met name in onderzoeksverband. Het doel en de noodzaak van follow-up na liesbreukchirurgie is daarentegen gebaseerd op aannames en wordt nauwelijks ter discussie gesteld. Uiteraard dient reguliere follow-up na liesbreukchirurgie anders georganiseerd te worden dan in onderzoeksverband, echter is een duidelijk advies niet voorhanden. In **Hoofdstuk 8** worden de efficiëntie en het doel van reguliere follow-up na TEP liesbreukchirurgie geëvalueerd en de waardering door patiënten voor follow-up onderzocht. Ten aanzien van het patiëntgerelateerde doel van follow-up blijkt dat de grote meerderheid van de patiënten zelf postoperatieve klachten of complicaties meldt. Follow-up op 1 jaar postoperatief, in aanvulling op 6 weken follow-up, levert bij maar 3% van de patiënten nieuwe klinische informatie op. Momenteel wordt op vaste momenten follow-up verricht, maar logischerwijs ontstaan de klachten bij patiënten niet in lijn met deze geplande momenten. Daarom dient follow-up na liesbreukchirurgie geen klinisch doel. Patiënten blijken wel waarde te hechten aan een follow-up moment in het algemeen en 92% van de patiënten prefereert telefonische follow-up ten opzichte van een polikliniek afspraak. Follow-up kan dus geoptimaliseerd worden door postoperatief een eenmalig telefonisch controle moment te plannen met als doel patiënttevredenheid en het registreren van data. We adviseren dit op 3 maanden na de operatie te doen, zodat de uitkomst chronische pijn adequaat kan worden geregistreerd.

In deze follow-up methodologie ontbreekt echter de kwaliteitscontrole voor recidieven na liesbreukchirurgie. Om waarheidsgetrouw recidiefpercentages te onderzoeken moet follow-up ten minste 2 jaar zijn. Tot op heden is de algehele opinie dat patiënten routinematig op de polikliniek onderzocht moeten worden om een recidief vast te stellen. Deze methodologie, met als enige doel het registreren van data, is patiënt onvriendelijk, tijdrovend voor patiënten en chirurgen, en duur. Bovendien verschijnen veel patiënten niet op de polikliniek voor follow-up. In 2014 is de Post-INguinal-repair-Questionnaire by telephone (PINQ-PHONE) ontwikkeld en gevalideerd als een follow-up methode voor het detecteren van recidieven. Het ontbreekt echter aan gedegen implementatie van deze vragenlijst met als gevolg dat de PINQ-PHONE niet voor klinische studies is gebruikt. In **Hoofdstuk 9** delen we onze ervaring met de PINQ-PHONE in een grote RCT. De studie laat zien dat de PINQ-PHONE een simpele, praktische en gebruiksvriendelijke telefonische vragenlijst is om liesbreuk recidieven vast te stellen. Op deze manier wordt een poliklinische controle voorkomen bij 93% van de patiënten. De PINQ-PHONE werd aangepast op basis van de verzamelde data en de ervaring van de onderzoekers zodat nog minder patiënten de polikliniek hoeven te bezoeken en alle recidieven nog altijd veilig worden gedetecteerd. Met name in een prospectieve klinische studie met vereiste follow-up voor alle patiënten is de PINQ-PHONE waardevol. Voor het beantwoorden van onderzoekshypotheses wordt het belang van prospectieve registratiedatabases in vergelijking met klinische studies steeds

meer erkend. De aangepaste PINQ-PHONE dient geïmplementeerd te worden in dergelijke registraties met als doel het onderzoeken van liesbreukchirurgie uitkomsten.

Het gebruik van een smartphone en tablet applicatie voor follow-up na liesbreukchirurgie kan huidige follow-up beperkingen wegnemen. Dataregistratie dor middel van een dergelijke innovatieve applicatie levert uniforme en nauwkeurige patiënt gerapporteerde uitkomsten (PROMs) op en kan tevens worden gebruikt voor grootschalig benchmarken met naar verwachting een verlaging van de zorgkosten en werkdruk. In **Hoofdstuk 10** introduceren we de Liesbreuk App waarin de geprefereerde vragenlijsten voor follow-up na liesbreukchirurgie zijn opgenomen. In dit hoofdstuk beschrijven we het studieprotocol voor het valideren en het bepalen van de betrouwbaarheid van deze applicatie in vergelijking met reeds gevalideerde vragenlijsten voor follow-up na liesbreukchrirurgie bij patiënten die een TEP liesbreukoperatie ondergaan. Momenteel is de studie onderbroken vanwege de COVID-19 pandemie. We verwachten in een later stadium data te kunnen presenteren over patiënttevredenheid met de applicatie en de constructvaliditeit en betrouwbaarheid van de applicatie. De Liesbreuk App kan mogelijk de werkdruk verlagen door telefonische of poliklinische follow-up na liesbreukchirurgie te vervangen, en kostenefficiëntie en patiënttevredenheid verbeteren. Uiteindelijk heeft deze applicatie de potentie om nationaal of zelfs internationaal te worden gebruikt om een uniforme methode van follow-up na liesbreukchirurgie tot stand te brengen ter stimulans van grootschalig benchmarken en grootschalig liesbreukonderzoek.

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Acknowledgements | Dankwoord

Dit proefschrift is tot stand gekomen met dank aan vele mensen die hebben bijgedragen aan mijn pomotietraject. Een aantal mensen wil ik graag in het bijzonder bedanken.

Geachte prof. dr. I.H.M. Borel Rinkes, beste Inne. De samenwerking in de afrondende fase van mijn proefschrift heb ik als zeer prettig ervaren. Bedankt voor de doelgerichte samenwerking, heldere communicatie en de verfrissend kritische blik. Het enthousiasme en de humor die u meebracht naar ieder overleg heeft als een bron van motivatie gewerkt.

Dr. J.P.J. Burgmans, geachte copromotor, beste Ine. Waar moet ik beginnen... Ik weet zeker dat menig arts-onderzoeker enorm jaloers zou zijn op de manier waarop wij samen dit proefschrift hebben neergezet: daadkrachtig (soms een tikkeltje kort door de bocht), efficiënt en uiteraard doelmatig. Ik heb dit traject dan ook als een prachtige samenwerking ervaren. De lijntjes waren kort, ons wekelijkse overleg bracht continue nieuwe ideeën of belichtte verfrissende invalshoeken, en wanneer we er samen niet uitkwamen wist je ons te omgeven door de juiste personen. Het was nooit saai, en er was veel ruimte voor gezelligheid, humor en filosoferen over liesbreuken en het leven. Met name de congressen in San Francisco, Las Vegas en Hamburg met de vele etentjes, borrels, casino's, Cirque du Soleil en potjes Rikken voelden bijna als vakanties en zal ik nooit vergeten. Je bent een inspirerend persoon!

Dr. E.J.M.M. Verleisdonk, geachte copromotor, beste Egbert Jan. Toen ik je 4 jaar geleden mailde voor een semi-arts stage had ik niet verwacht dat dit er allemaal uit voort zou komen. Bedankt voor je enthousiasme, het in de gaten houden van de grote lijnen, de goede inhoudelijke gesprekken en levenslessen op borrels en het onvoorwaardelijke vertrouwen in de financiën van onze onderzoeksgroep. In Las Vegas heeft niemand kunnen zien dat het geld eigenlijk op was!

Geachte leden van de beoordelingscommissie, bestaande uit prof. dr. F.J.G. Backx, prof. dr. L.M.O. de Kort, dr. R.K.J. Simmermacher, prof. dr. I.Q. Molenaar en prof. dr. F. Berrevoet. Bedankt voor het lezen, beoordelen van mijn proefschrift en plaatsnemen in de commissie.

Dr. T. van Dalen, beste Thijs. Bedankt dat je zo betrokken was als opleider in mijn ANIOS jaar. Je deur stond altijd open voor overleg over het combineren van onderzoek en mijn eerste klinische baan. Bedankt voor je open en niet-sturende gesprekken aangaande de beroepskeuze die in het verschiet lag.

Dr. G.J. Clevers, dr. P.H.P. Davids en dr. M. Avci, beste liesbreukchirurgen, beste Geert Jan, Paul en Murat. Zonder de door jullie geopereerde liesbreuk patiënten zou er geen proefschrift zijn. De kwaliteit en efficiëntie van het liesbreukcentrum Nederland is onomstreden, met name

door jullie inzet, expertise en ambitie. De door jullie geleverde data resulteert in alweer het 6de liesbreukchirurgie proefschrift dat ons bescheiden perifere centrum voortbrengt.

Geachte dr. van Hessen, beste Vanessa, beste Coen. Samen begonnen we aan dit avontuur. Van begin af aan mijn partner in crime, met als aftrap het decoreren van onze onderzoekskamer met planten en kunstvoorwerpen vanuit de rest van het ziekenhuis. Al snel gingen we als Jut en Juul door het Diak en vroeg Hassan of ik ziek was als je alleen in het busje stapte. Het was een eer om als fan van het eerste uur betrokken te zijn bij alle muziek die je produceert. Het trekken aan ons dode paard, was heel wat makkelijker met SACO ter ondersteuning. Als hoofd van je promo(tie)team zou een kleine share van de inkomsten inmiddels niet meer dan terecht zijn lijkt me. Vervolgens moesten we om en om alleen de kar trekken toen ik een jaar als ANIOS chirurgie ging werken tussendoor. Inmiddels zijn wij alweer opgevolgd, ben jij gepromoveerd en is het voor mij ook bijna een afgerond hoofdstuk. Enorm gefeliciteerd met jouw prachtige proefschrift! Bedankt voor de mooie tijd! Ik hoop je nog lang te kennen en wens je veel succes in je verdere carrière als collega huisarts!

Geachte dr. Roos, beste Marleen. Enorm bedankt voor de groundwork waarop Coen en ik verder konden bouwen. Het spijt ons, ik weet dat ik ook namens Coen spreek, dat de EFFECT-studie niet het succes is geworden waar we allemaal op hoopten. We hebben ons uiterste best gedaan. Daar staan gelukkig de vele stukken die ik met jou heb mogen schrijven en die in succesvolle journals terecht zijn gekomen tegenover. Ik heb veel van je geleerd in de beginfase van dit PhD traject, eerst als wetenschappelijke stage student en daarna in de samenwerking bij meerdere studies. Als toekomstig collega kom ik nog wel vaker voor een paar wijze lessen aankloppen. Bedankt voor alles!

Geachte dr. T.J. Aufenacker, beste Theo. Bedankt voor je scherpe oog, kritische blik, en het delen van je ervaring met het schrijven van een systematic review. Ik zal ons overleg in een Van Der Valk hotel langs de snelweg tot in de late avonduren niet snel vergeten.

Geachte dr. J.S. Boschman, beste Julitta. Bedankt voor je input bij hoofdstuk 2 en 4. Jouw ervaring met statistiek en het opzetten van een systematic review was belangrijk voor het tot stand komen van dit proefschrift.

Beste Niels Bax, onze samenwerking was kort en krachtig. Het was mooi om te zien hoe je leergierig en vol enthousiasme bereidt was het stokje over te nemen! Bedankt voor al je hulp. Ik weet dat je een mooi traject wacht als je besluit mijn opvolger te worden! Heel veel succes met waar je ook toe besluit.

Alle overige co-auteurs, bedankt voor jullie bijdrage aan de hoofdstukken van dit proefschrift.

Beste Atie, bedankt voor de dagelijkse gezelligheid op het secretariaat in Zeist en hulp bij praktische zaken. De faxmachine is ondergewaardeerd en moet men opnieuw een kans geven!

Beste dames van de poli chirurgie in Zeist. Bedankt voor jullie heldere communicatie naar patiënten over onderzoek en meedenken over de praktische uitvoerbaarheid van patiënt informatie gesprekken. En nee, niet alles is inmiddels uitgezocht… En ja, waarschijnlijk binnenkort alweer een studie…

Dr. C. Orelio, beste Claudia. Bedankt voor je adviezen en hulp bij statistiek wanneer YouTube geen uitkomst meer bood.

Beste Bastiaan en Julia, mijn mede-onderzoekers van de chirurgie. Helaas liepen we elkaar door al die verschillende werkplekken meer mis dan ons lief was. Desalniettemin, bedankt voor de gezellige lunches, praatjes op de gang en het delen van overwinningen en frustraties.

Overige chirurgen en arts-assistenten van de chirurgie van het Diakonessenhuis. Bedankt voor jullie interesse in mijn onderzoek en het leerzame en bovenal gezellige jaar in de kliniek. Het Diakonessenhuis is door jullie een fijne leeromgeving en een warm bad. Verander niets! De zomer- en winteruitjes, het 175-jaar Diak feest, het eindejaarsdiner, de BBQ's bij Dennis, en al die vrijdag middag- en afscheidsborrels zal ik gaan missen…

Beste vrienden van vroeger, beste Yves, Martijn, Koen, Casper, Joël, Dennis en Jonathan. Bedankt voor jullie vriendschap! Bedankt voor de eindeloze initiatieven die hebben gezorgd voor de nodige afleiding. Jullie zijn allemaal legends. In het bijzonder wil ik uiteraard mijn paranimfen Yves Bodar en Koen de Wilde bedanken, mijn vrienden van vroeger met wie ik samen aan de studie Geneeskunde begon.

Beste heren van JC Molotov. Sinds 2010 hebben we ongelofelijk veel meegemaakt. Eerst intens en frequent, nu met een sterke basis. Bedankt voor jullie betrokkenheid, jullie vriendschap en geduld wanneer het alweer over Geneeskunde ging. Ik kan niet wachten op het volgende lustrum.

Waarde Cambrinianen, dat Groningen nog steeds als thuiskomen voelt komt door jullie. Een sporadische vrijdagavond meepakken is nog altijd een goede uitlaatklep. Mijn lichting en de lichtingen om mij heen, enorm bedankt voor een prachtige studententijd! Tot bij koningsdag, een vrijdagavond of een van de weekenden!

Beste oud-huisgenoten in Groningen en Utrecht. Bedankt voor jullie vriendschap. Opdat we elkaar nog maar vaak mogen blijven zien!

Beste Theo, Saffiya, Sainey, Jordi, May en Gertie, de familie wordt maar groter en groter! Bedankt voor jullie gezelligheid, en voor wat jullie betekenen voor mij en mijn familieleden!

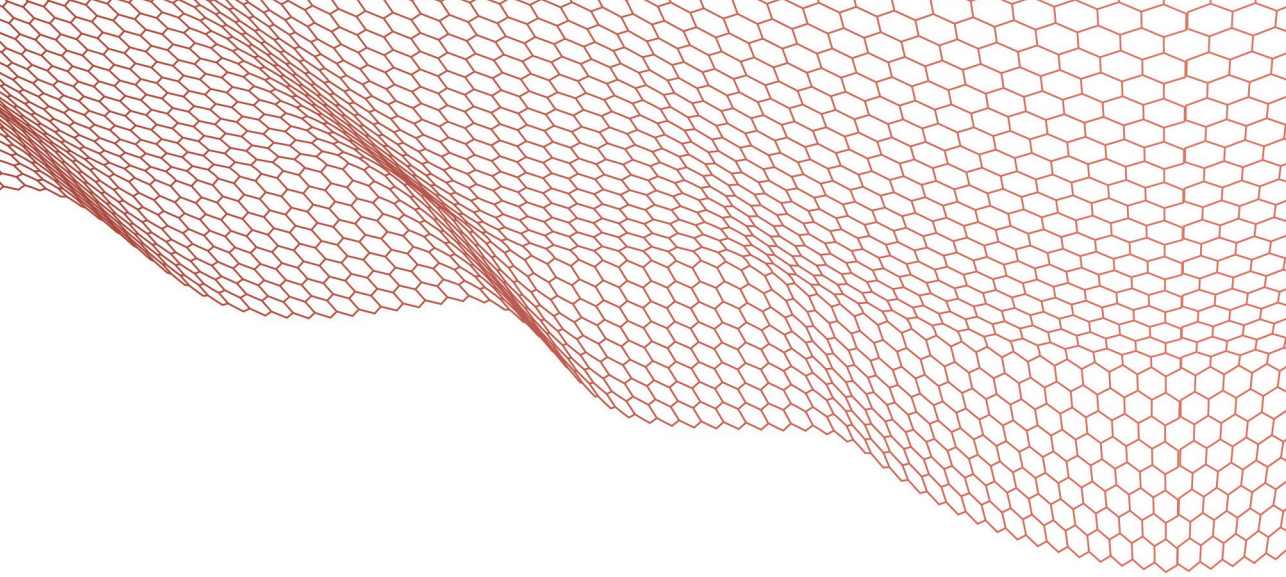
Lieve schoonfamilie Rodijk, de Rodiekies. Bedankt voor jullie nimmer wijkende interesse en gezelligheid. De Twentse nuchterheid wordt erg gewaardeerd. Ik prijs me zeer gelukkig met een schoonfamilie zoals jullie!

Lieve pa en ma, Karsten en Renske, bedankt voor jullie liefde en onvoorwaardelijke steun. Bedankt voor alle mogelijkheden en de ruimte die jullie mij hebben gegeven om mijn eigen beslissingen te nemen. Nog altijd het grootste gedeelte van mijn leven heb ik met jullie doorgebracht, en door jullie ben ik geworden zoals ik ben. Ik heb altijd genoten van de reikwijdte tussen volledige ontspanning op de bank tot discussies op het scherpst van de snede!

Lieve Lyan, mijn leven zonder jou is ondenkbaar. Bedankt voor je eeuwige vrolijkheid, steun en liefde. Jouw bevlogenheid en enthousiasme werkt aanstekelijk, en jouw altruïsme is bewonderenswaardig. In dit traject hebben jouw eigen onderzoek worstelingen voor mij zeer relativerend gewerkt, bedankt daarvoor. Maar nu zijn we allebei de ‘s’ kwijt, en dat hebben we samen gedaan. Ik kan niet wachten op wat ons allemaal nog te wachten staat! Ik ben trots op ons!

Curriculum Vitae

Wouter Jesse Bakker was born on the 26th of January, 1992 in Utrecht, the Netherlands. He is the son of Cok Bakker and Linda Otterman, and lived in Zeist most of his youth. Following his graduation from the bilingual gymnasium at the Christelijk Lyceum Zeist, his interest in the medical profession motivated him to start his medical studies at the University of Groningen in 2010.

He received his propaedeutic in 2011, and his Bachelor of Medicine in 2014. Besides his studies, he worked part-time for 4 years at the emergency general practitioners station, organized a summerschool on oncology, participated in multiple medical committees, and was an active member of the student association Vindicat Atque Polit and the association M.H.D. Cambrinus. For his Master programme in Medicine he fulfilled a year of internships at both the University Medical Centre Groningen and the Deventer Hospital, and a 2 months internship at the emergency- and surgery department of Stanger Hospital in South-Africa. He completed his Master degree with a final year of inguinal hernia surgery research and a specialized internship with the surgery and urology department of the Diakonessenhuis hospital in Utrecht/Zeist. Due to his continuing involvement with inguinal hernia surgery research, his interest in the future perspectives of the totally-extraperitoneal (TEP) inguinal hernia repair, and the efficiency of specialized hernia centers increased. Immediately after his graduation in March 2018, Wouter was offered a PhD program at the Hernia Clinic of the Diakonessenhuis Zeist under the supervision of dr. J.P.J. Burgmans and dr. E.J.M.M. Verleisdonk, in cooperation with the University Medical Centre Utrecht (prof. dr. I.H.M. Borel Rinkes). While working on his PhD, Wouter worked as a surgical resident (not in training) at the Diakonessenhuis hospital in 2019, and as a posting by Medilead as a geriatric resident at multiple nursing homes of Rivas Zorggroep in 2020 and as psychiatry resident at a FACT team of Reinier van Arkel in 2021, and thereafter fulfilled his PhD at the end of 2021. During this period, he coordinated multiple prospective studies and a multicenter randomized controlled trial (EFFECT-trial) in 9 Dutch hospitals, collaborated on the Dutch hernia guidelines, and presented his research at multiple national and international congresses.

It is with a heavy heart that he abandons his surgical career, but his true interest lies with becoming a general practitioner because of the diversity of the patients, the career growth opportunities that it accompanies and the future perspectives of the general practitioner profession in the current Dutch healthcare system.