Improving TEP inguinal hernia repair

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Improving TEP inguinal hernia repair
PhD thesis, Utrecht University, The Netherlands

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Verbeteren van de uitkomsten van de TEP liesbreukcorrectie
(met een samenvatting in het Nederlands)

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te ‘s-Gravenhage

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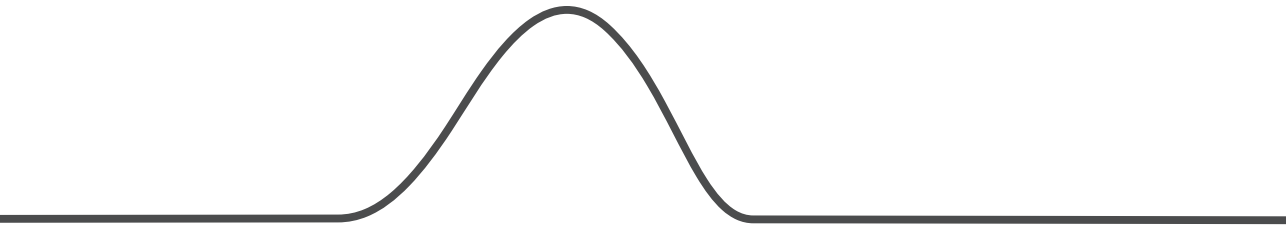
Table of contents

1

General introduction and thesis outline



General introduction

Inguinal hernias are commonly encountered with a lifetime occurrence of 27-45% in men and 3-6% in women.[1] Inguinal hernia repair is one of the oldest surgical procedures and the most frequently performed elective operation by general surgeons. Worldwide, 20 million inguinal hernias are operated on annually, with approximately 30.000 procedures in the Netherlands.[1,2] Since inguinal hernia is a common condition, improvements in treatment will have an enduring impact.

The first inguinal hernia repairs were done during the end of the sixteenth century. Subsequently, many hernia repair principles have been introduced throughout history.[3]
In the 19th century, the Italian surgeon Bassini introduced a new surgical concept, which was based on enforcement of the weakened posterior wall by suturing the fascial structures bordering the hernia defect.[4] The discovery of posterior wall involvement was very important and is still the foundation for modern hernia surgery techniques. However, the tension created by primary closing the defect was disadvantageous and frequently led to recurrences and (chronic) pain.

In 1958, prosthetic material was introduced by the American surgeon Usher.[5] Synthetic polypropylene mesh devices facilitated covering the defect instead of closing it, hereby avoiding tension formation. Utilisation of this new method resulted in a tremendous decrease in recurrence rates.[6-9] The tension-free anterior mesh repair developed by the American surgeon Lichtenstein (1964) became the gold standard and is nowadays still the most frequently used open repair technique.[10-13]

Once a substantial reduction in recurrences was achieved, the main outcome of interest following inguinal hernia surgery shifted from preventing recurrences towards reducing (chronic) postoperative pain. It is known that intraoperative inguinal nerve injury and the mesh-induced inflammatory response and subsequent fibrosis play an important role in the development of chronic pain.[14-18]

A major advantage of laparoscopic techniques over open surgery is the ability to approach the hernia defect from posterior, hereby avoiding direct contact with the inguinal nerves. The laparoscopic approach of the inguinal canal was first introduced in 1982 by the South African surgeon Ger and in 1991 the first endoscopic hernia repair was conducted in the Netherlands.[19,20] It gained popularity due to multiple advantages; a significant reduction in acute and chronic postoperative pain, less impairment of inguinal sensibility, a lower risk of wound infection, shorter hospital stay, a faster return to daily activities and higher levels of patient satisfaction were demonstrated.[21-32]

Today, many surgeons favour preperitoneal endoscopic approaches. There are two endoscopic repair methods in inguinal hernia surgery, both involving mesh placement in the preperitoneal space on the posterior side of the hernia defect. The techniques differ in the access used to reach the preperitoneal space. In totally extraperitoneal (TEP) repair, the preperitoneal space is entered directly. The hernia is visualized from within this plane and a preperitoneal mesh is placed, leaving the intra-abdominal cavity untouched. In trans-abdominal preperitoneal (TAPP) repair a laparoscopy is performed and visualization of the hernia takes place from within the abdominal space, after which the peritoneum is opened and the mesh is placed in the preperitoneal plane. Both techniques are commonly used and have comparable outcomes, so that the preferred endoscopic technique is mainly dependent on the skills, experience and education of the surgeon.[3,33] For the TEP technique in particular, a relatively long learning curve has been described.[3,8,34]

Centralization of care in high-volume centers has proven to be effective for many surgical procedures. Regular operating theater teams can decrease room turnover, preparation and procedure time and thereby increase daily patient volumes.[3,35] Favourable outcomes of laparoscopic hernia repair procedures have been reported for specialized hernia centers with high patient volumes.[3,36,37]

All studies described in this thesis are established and performed in a high-volume TEP hernia center in the Netherlands. This institution has been founded in 2005 and ever since, the number of TEP inguinal hernia procedures per year has increased. At this point, five experienced hernia surgeons perform approximately 1200 TEP procedures annually. Such large numbers of procedures provide room for assessment of specific issues. Up till now, the data generated from our hernia clinic have facilitated optimization of selection criteria for the TEP procedure, evaluation of specific patient populations undergoing TEP hernia repair and assessment of (adverse) outcomes of this technique.

Thesis outline

This thesis zooms in on specific aspects of inguinal hernia diagnostics and indications for TEP inguinal hernia repair. In addition, outcomes of TEP inguinal hernia surgery are addressed.

Inguinal hernia is a primarily clinical diagnosis that is established after history and physical examination in 95% of cases. A classical hernia presents as a reducible groin swelling, increasing with the Valsalva manoeuvre. Only in case of equivocal findings additional imaging in the form of ultrasound is indicated. In our center patients who underwent ultrasound upon request by the general practitioner are frequently encountered. In **Chapter 2** the extent of

this particular patient group presenting at the surgical outpatient clinic and the influence of the ultrasound requested in primary care on surgical decision-making are assessed.

In the subset of patients with groin complaints in whom clinical symptoms of an inguinal hernia are absent while a hernia is diagnosed upon radiological examination, this hernia is referred to as clinically occult. No specific therapeutic approach for this type of hernias is formulated in the current hernia guidelines and until now the radiological diagnosis of an inguinal hernia often leads to surgical intervention. However, it remains unclear if surgery is the best option in this group as it can be debated if this radiological hernia is the cause of groin pain in all cases or an alternative pain cause may be present, and if the radiological findings are correct. **Chapter 3** describes the rationale and design of a multicenter randomized controlled trial comparing a watchful waiting policy to TEP repair in patients with a clinically occult inguinal hernia.

A group of patients who might particularly benefit from TEP inguinal hernia surgery involves athletes with chronic groin pain originating from inguinal disruption. It has been hypothesized that the etiology of these chronic groin complaints lies in a weakened inguinal floor. Therefore, endoscopic TEP repair with mesh placement strengthening the inguinal floor might pose a solution for this problem. In **Chapter 4,** three-month- as well as long-term outcomes of a prospective study on TEP repair in athletes with inguinal disruption in whom conservative approaches had failed are presented.

In open anterior inguinal hernia repair, lightweight mesh has shown to be superior compared to heavyweight mesh in terms of postoperative pain. A randomized controlled trial (TULP-trial) was designed to assess the outcomes of lightweight (Ultrapro®) and heavyweight mesh (Prolene®) in endoscopic TEP inguinal hernia repair. The beneficial effects of the lightweight mesh in open repair could not be confirmed for TEP hernia repair, yet the use of lightweight mesh yielded a more than three-fold higher recurrence rate compared to heavyweight mesh after two years of follow-up. In **Chapter 5** five-year recurrence rates of this randomized controlled trial are reported.

Even though reported recurrence rates after endoscopic TEP inguinal hernia repair are low, recurrences still occur. Identifying possible patterns or causes of recurrence might further facilitate prevention and elimination of recurrences. Assessment of the nature of these recurrences is most reliable in a high-volume setting where the influence of surgical inexperience or an incomplete learning curve for TEP repair is eliminated. In **Chapter 6** results of an 11-year analysis of all groins reoperated for recurrence-like complaints after TEP repair are reported.

A feared complication of endoscopic TEP surgery is male infertility, since the mesh is placed in close contact with the spermatic cord in the preperitoneal space. Hypothetically, mesh-induced inflammation and fibrosis, or direct iatrogenic damage, could affect the spermatic cord structures, thereby possibly impairing fertility. Rare but potentially harmful complications reported after inguinal hernia repair are ischemic orchitis, testicular atrophy or obstructive azoospermia. In **Chapter 7** the six-month results of a prospective study assessing male fertility parameters in patients who underwent bilateral TEP repair are described.

The single visit pathway, offering diagnostic work-up and surgical treatment on the same day, has proven to be efficient and cost-effective for TEP inguinal hernia repair. However, the impact and benefits of single visit TEP repair might reach further than the known cost savings within the hospital. **Chapter 8** reports the results of a cost-analysis comparing single visit and regular TEP repair in an employed healthy population from both a hospital and societal point of view.

Aims of this thesis

1. To evaluate the utilization and influence of groin ultrasound for suspicion of inguinal hernia requested by the general practitioner in patients referred to the hernia surgeon.

2. To describe the rationale and design of a multicenter randomized controlled trial comparing a watchful waiting approach to endoscopic TEP inguinal repair in patients with groin pain and a clinically occult inguinal hernia.

3. To evaluate the outcomes of endoscopic TEP repair in athletes with inguinal disruption, selected through a multidisciplinary, systematic work-up.

4. To determine recurrence rates five years after endoscopic TEP inguinal hernia repair with either use of lightweight or heavyweight mesh.

5. To provide an 11-year analysis evaluating the characteristics of all groins re-operated for “recurrence-like” complaints after TEP inguinal hernia repair.

6. To assess fertility after bilateral endoscopic TEP inguinal hernia repair in male patients.

7. To provide a cost-analysis comparing single-visit TEP inguinal hernia repair to TEP inguinal hernia repair through the regular pathway.

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2

Groin ultrasound for diagnosing inguinal hernia in primary care

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Submitted

Abstract

Background

Inguinal hernias are primarily clinical diagnoses. In case of equivocal findings on physical examination, imaging may be required. The aim of this study was to evaluate the utilization and influence of groin ultrasound requested by general practitioners in patients referred to the surgical outpatient clinic.

Methods

All adult patients that underwent groin ultrasound for suspicion of inguinal hernia upon request of their general practitioner (GP) that were referred to the surgical outpatient department of a Dutch hernia clinic between July 2016 and July 2017, were studied retrospectively. Outcomes of ultrasound and clinical assessment were compared. In case of a discrepancy between ultrasound and clinical findings, influence of ultrasound on surgical decision-making was assessed.

Results

In 361 out of 1371 patients (26%), groin ultrasound was performed through the GP, involving 399 groins. Findings of 374 ultrasounds (94%) were positive for inguinal hernia and 25 ultrasounds were negative (6%). On physical examination, in 316 groins (79%) a clinically apparent inguinal hernia was reported and in 69 groins (17%) no hernia could be objectified. In 14 groins (4%) the diagnosis was inconclusive. Discrepancy between ultrasound and physical examination existed in 58 groins (15%). In this group 14 cases (24%) were (surgically) treated based on ultrasound outcomes.

Conclusion

Groin ultrasound was performed upon request of the GP in 26% of all referred patients, of which 79% had an inguinal hernia upon physical examination. In case of discrepancy between ultrasound and physical examination outcomes, (surgical) treatment was based on physical examination in 76%.

Background

Inguinal hernia is a frequently seen condition, and in many patients elective repair is performed. Approximately 95% of inguinal hernias can be diagnosed by physical examination, based on the classical presentation of a reducible groin swelling with a positive cough impulse (Valsalva manoeuvre), sometimes accompanied with pain.[1,2] Anamnestic history of groin swelling can contribute to the diagnosis as well. Only in case of vague groin swelling and diagnostic uncertainty, poor localization of swelling, intermittent swelling not present at time of physical examination or obscure groin complaints without swelling, imaging may be required.[2]

In case of equivocal clinical findings ultrasound is the first recommended imaging modality in the current guidelines for hernia surgery.[2,3] Advantages of ultrasound are its dynamic character without ionizing radiation, the ability to directly correlate physical examination to imaging findings and relatively low costs.[4-6] Disadvantages are intra-observer variety and intra-observer accuracy.[7]

When a patient presents with groin complaints in primary care, ultrasound is frequently requested before referring to a surgical specialist. Given that an inguinal hernia can be easily diagnosed clinically in the greatest part of patients, it is questionable whether all requested imaging would be necessary to obtain the correct diagnosis and to decide whether patients should be referred for possible surgical treatment.

The aim of this study was to evaluate the utilization and influence of groin ultrasound requested by the general practitioner (GP) in patients with (suspicion of) an inguinal hernia referred to the surgical outpatient department.

Methods

A retrospective observational analysis using a prospectively maintained database was performed in a hernia clinic specialized in endoscopic totally extraperitoneal (TEP) hernia repair in the Netherlands.

All adult patients referred to the surgical outpatient department between July 2016 and July 2017 who underwent groin ultrasound for suspicion of inguinal hernia upon request of the GP in advance were identified. Performance of ultrasound was not restricted to a particular radiologist or this hernia clinic. As long as the ultrasound outcome was documented in the referral letter or radiology report the patient was eligible for analysis. Patients referred by other specialists or with an ultrasound requested by any specialist other than the GP, were excluded.

Patient characteristics (age, sex, body mass index (BMI) and American Society of Anesthesiologists (ASA) classification), outcomes of clinical assessment, ultrasound outcomes and, if applicable, intraoperative findings were registered. Outcomes of history and physical examination were divided into positive, negative or inconclusive" for inguinal hernia. In case of a reported observable swelling or a palpable mass during the Valsalva manoeuvre, groins were scored positive. In case of incomplete or unspecified documentation, clinical assessment was still taken into account and scored positive, negative, or inconclusive but with the distinction that this could be based on the documented conclusion solely. Ultrasound outcomes were divided into positive or negative for inguinal hernia, based on the referral letter documenting the ultrasound outcome or the radiology report.

Evaluation of groin ultrasound was carried out by comparing ultrasound outcomes with clinical assessment and, if applicable, with subsequent perioperative findings of TEP inguinal hernia repair. Perioperative findings were obtained from the operative reports and divided into "positive" or "negative" for inguinal hernia.

In case of discrepant findings between ultrasound and clinical assessment, the influence of ultrasound and physical examination on decision-making of the surgeon was compared.

Results

During the study period, 1371 patients were referred to the surgical outpatient clinic for suspicion of an inguinal hernia. A total of 361 patients (26%) underwent ultrasound before visiting the surgical outpatient department, involving 399 groins (*table 1)*. Eighty-six percent of patients were male and 14% were female. The median age of the study population was 55 years (interquartile range (IQR) 43 – 66 years).

As regards ultrasound outcomes, 374 groins (94%) were scored positive for an inguinal hernia and 25 groins were scored negative (6%) (*figure 1)*. Upon physical examination by the surgeon 316 groins (79%) were reported positive for an inguinal hernia; in 264 of these cases (84%) an observable swelling or a palpable ma ss during the Valsalva manoeuvre was reported, representing 66% of all 399 groins. In 52 groins reported positive for inguinal hernia on clinical assessment (16%) solely the surgical conclusion in the medical record was positive. A total of 69 groins (17%) were scored negative for an inguinal hernia on clinical assessment and in 14 groins (4%) the surgeon doubted if an inguinal hernia was present.

Table 1. Patient characteristics (n=361, 399 groins)

Sex, n (%)	
Male	312 (86.4)
Female	49 (13.6)
Age (years)	55.0 (43.0-65.5)
BMI (kg/m^2)	24.8 (22.7-27.5)
ASA-classification, n (%)	
I	187 (51.8)
II	141 (39.0)
III	32 (8.9)
IV	1 (0.3)
Ultrasound , n (%)	
Unilateral	323 (89.5)
Bilateral	38 (10.5)
Location of alleged hernia per groin, n (%)	
Left	174 (43.6)
Right	225 (56.4)

Continuous data are presented as median (Interquartile range) BMI: Body Mass Index, ASA: American Society of Anesthesiologists

Figure 1. Interrelation between ultrasound and physical examination and number of cases in which was proceeded to hernia repair (n=399)

	Ultrasound +	**Ultrasound -**
Physical examination +	**309 (77.4)**	**7 (1.7)**
Hernia Repair	*272 (88.0)*	*7 (100.0)*
Physical examination –	**51 (12.8)**	**18 (4.5)**
Hernia Repair	*14 (27.5)*	*3 (16.7)*
Physical examination +/-	**14 (3.5)**	**-**
Hernia Repair	*9 (64.3)*	**-**

Values are reported as n (%) +: positive,-:negative, +/-: inconclusive

A discrepancy between outcomes of ultrasound and physical examination was present in 58 groins (15%), of which 21 groins underwent inguinal hernia surgery (36%). In seven groins with discrepant findings (12%) physical examination was positive, contrary to a negative ultrasound. All seven groins underwent hernia repair based on physical examination and an inguinal hernia was found perioperatively in all cases. In 51 groins with discrepant findings (88%) ultrasound was positive, contrary to a negative physical examination. Fourteen of these groins (27%) underwent hernia repair and an inguinal hernia was found perioperatively in 12 cases (86%). In the remaining 37 groins, an expectative policy was applied based on physical examination. In fourteen groins (4%) ultrasound was positive, but findings upon physical

examination were inconclusive. Nine of these groins underwent hernia repair and an inguinal hernia was found perioperatively in all groins.

In 18 groins both ultrasound and physical examination were scored negative. Three of these groins were operated due to a strong wish of the patients. In one patient an inguinal hernia was found perioperatively.

Discussion

Even though inguinal hernia is a predominantly clinical diagnosis, this study demonstrates that approximately one quarter of newly referred patients with suspicion of an inguinal hernia to the surgical outpatient department of a Dutch hernia clinic underwent ultrasound in advance. In nearly 80% of these patients a clinically apparent inguinal hernia was found upon surgical assessment, implying that in this subset of patients ultrasound may have been unnecessarily performed. These results point out that ultrasound diagnostics in patients with clinically apparent inguinal hernias are redundantly requested in primary care.

Ultrasound and physical examination conducted by the surgeon yielded discrepant results in 15% of cases, in which surgical treatment was based on interpretation of clinical findings in 76% of cases and based on interpretation of ultrasound findings in only 24%. All patients in whom ultrasound was negative yet physical examination positive underwent surgical treatment. In all cases a hernia was found intraoperatively, confirming a high accuracy of physical examination. Of patients with a negative clinical examination yet positive ultrasound only 27% underwent surgery, which demonstrates that a positive ultrasound finding alone is in the majority of cases not sufficient for proceeding to surgery. In 86% of operated cases in which physical examination was negative yet ultrasound positive for an inguinal hernia, a hernia was found intraoperatively. Even though in the great majority of these patients the hernia was confirmed during surgery, it is important to realize that ultrasound does not accurately predict the presence of an inguinal hernia in all cases.

A study performed by Kim et al. investigated the utilisation of ultrasound for suspicion of inguinal hernias as well.[8] This study evaluated all ultrasound examinations, either requested through primary or secondary care, performed in patients seen at the surgical outpatient department for clinical suspicion of an inguinal hernia. In this study, 267 ultrasounds were conducted of which 105 (39%) were positive for an inguinal hernia on physical examination by the surgeon. Although this percentage is considerably lower than the 66-79% described in this study, it still represents significant overuse of diagnostic ultrasound and supports the results of this study. A possible explanation for the lower numbers of both positive physical

examination and positive ultrasound findings in this study may be that approximately two third of ultrasound examinations were requested by the surgeon. Logically, a lower number of clinically evident hernias seen by the surgeon in this study would then be expected.

The study by Kim et al. showed discrepant findings between physical examination and ultrasound in 30% of the population.[8] In this study, however, one proceeded to surgery in only 13% of cases in which ultrasound was negative and physical examination positive. In case of positive ultrasound and negative clinical examination 30% of patients were operated. Findings of the studies performed by Light et al. and Bradley et al. ,that examined the accuracy of ultrasound in diagnosing clinically inapparent inguinal hernias, yielded higher percentages of surgical treatment in patients with negative clinical findings and positive ultrasound, of respectively 70% and 95%. [9,10]

To our knowledge, this is the first study focusing solely on ultrasound for suspicion of inguinal hernia requested in primary care. Since all consecutive 1371 patients that newly presented at the surgical outpatient department of a hernia clinic within a year were screened and analyzed, we think the numbers reported in our study provide an accurate representation of the general patient population with inguinal complaints at the surgical outpatient clinic.

Due to its retrospective character, this study has some limitations. Physical examinations were not extensively reported in all cases and must therefore be interpreted with some caution. In 52 cases with clinical findings reported positive for an inguinal hernia (16%), only the conclusion was noted as such but the actual findings upon physical examination (clinically detectable bulge, Valsalva manoeuvre) were not reported. In these cases we cannot be as sure of a truly clinically detectable inguinal hernia as in the extensively documented cases. Another important consideration for the groins positively scored for an inguinal hernia on clinical assessment, is that there might be a possibility that the surgeon was influenced by the ultrasound results if they were already reported in the referral letter before the patient was clinically assessed. Also, it does not become entirely clear in all patients how decisions regarding proceeding or not proceeding to operative repair were made. Apart from ultrasound and physical examination, other reasons (eg. strong wish of the patient) could not be extracted in all cases.

Another limitation of this study is that intra-observer variety and intra-observer accuracy between different radiologists might have played a role. Although the inclusion of every ultrasound, regardless of where it was performed, reflects daily clinical practice, the lack of an uniform judgment of ultrasound examinations might not make their results fully comparable. Lastly, no information could be obtained about the patients in whom the GP requested an

ultrasound for suspicion of inguinal hernia that were not referred to the surgical outpatient department, since ultrasound was negative. Additional information about the number of cases in which performing ultrasound prevented unnecessary referral to the surgeon and costs would have provided even more insight.

There may be several explanations why ultrasound diagnostics for suspicion of inguinal hernias are frequently requested in primary care. Firstly, not all GPs may be capable of clinically diagnosing an inguinal hernia and may ask for an ultrasound in case of any inguinal complaints relatively soon. A second consideration may be that when GPs do suspect an inguinal hernia, US is requested for confirmation of their clinical suspicion before referral to the surgeon. Also, GPs might be scared of patients developing an incarcerated hernia might they have missed the diagnosis of an inguinal hernia previously, and therefore perform ultrasound to confirm or exclude the diagnosis of an inguinal hernia. However, the risk of an inguinal hernia becoming incarcerated is as low as less than 3% per year.[2] In the female population, clinically diagnosing an inguinal hernia is presumably even more difficult for the GP, most likely caused by the relatively high numbers of femoral hernias in women. This assumption is confirmed by the finding of a relatively high percentage of women that underwent ultrasound through primary care in this study.

The current total healthcare costs are high and expanding, and much effort is invested to control increasing costs.[11] This warrants careful evaluation of the utilisation and cost aspects of health care resources. Since radiology departments often enable GPs to refer patients for ultrasound examination directly without prior referral to secondary care, it is important that GPs become aware of the current groin ultrasound overdiagnostics and their accompanying costs.

However, as not all inguinal hernias are clinically apparent and a certain difference in experience and clinical skills in diagnosing inguinal hernias between GPs and surgeons can be expected, it remains logical that GPs request groin ultrasound in particular cases. Moreover, ultrasound diagnostics are expected to be cheaper and more efficient compared to surgical referral of all unclear or doubtful cases, since most patients with negative findings for inguinal hernia on groin ultrasound, which is expected to cost less than surgical referall, will not be seen by the surgeon and costs and time will be saved.

Even though a difference in expertise between the GP and the surgeon exists, it is of high importance GPs are adequately schooled and instructed in performing adequate physical examination for the diagnosis of inguinal hernia, the clinical signs of an inguinal hernia and the indications for additional imaging. We recommend performing physical examination

with the patient in standing position, in which it is likely that the swelling can already be seen in most cases. Only when doubt exists after inspection and performance of the Valsalva manoeuvre in this position, palpation of the inguinal canal is necessary. In case no swelling can be seen or palpated, an incarcerated hernia can reliably be excluded. In case the GP has a reasonable suspicion of an inguinal hernia after physical examination, direct surgical referral is advisable. With regard to performance of additional imaging, it is important GPs are aware that imaging is not necessary for diagnosis confirmation when a clinically apparent hernia is present, and that in case of abcense of or doubt about clinical signs of an inguinal hernia the ultrasound diagnosis of an inguinal hernia may not always be correct or related to the complaints the patient is experiencing.

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3

Effectiveness of endoscopic totally extraperitoneal (TEP) hernia correction for clinically occult inguinal hernia (EFFECT): study protocol for a randomized controlled trial

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Abstract

Background

Groin pain is a frequent complaint in surgical practice with an inguinal hernia being at the top of the differential diagnosis. The majority of inguinal hernias can be diagnosed clinically. However, patients with groin pain without signs of an inguinal hernia on anamnesis or physical examination provide a diagnostic challenge. If ultrasonography shows a hernia that could not be detected clinically, this entity is called a clinically occult hernia. It is debatable if this radiological hernia is the cause of complaints in all patients with inguinal pain. The objective of this study is to assess whether watchful waiting is non-inferior to endoscopic total extraperitoneal (TEP) inguinal repair in patients with a clinically occult inguinal hernia.

Methods

The EFFECT study is a multicenter non-blinded randomized controlled non-inferiority trial. Adult patients with unilateral groin pain and a clinically occult inguinal hernia are eligible to participate in this study. A total of 160 participants will be included and randomized to TEP inguinal hernia repair or a watchful waiting approach. The primary outcome of this study is pain reduction 3 months after treatment, measured by the Numeric Rating Scale (NRS). Secondary outcomes are quality of life, cost-effectiveness, patient satisfaction and crossover rate. Eight surgical centers will take part in the study. Participants will be followed-up for one year.

Discussion

This is the first large randomized controlled trial comparing treatments for patients with groin pain and a clinically occult inguinal hernia. To date, there are no interventional studies on the effect of surgery or a watchful waiting approach in terms of pain or quality of life in this subset of patients. A trial comparing the outcomes of the two approaches in patients with a clinically occult inguinal hernia is urgently needed to provide data facilitating the choice between the two treatment options. If watchful waiting is not inferior to surgical repair, costs of surgical repair may be saved.

Trial registration

The study protocol (NL61730.100.17) is approved by the Medical Ethics Committee (MEC-U) of the Diakonessenhuis, Utrecht, The Netherlands. The study was registered at the Netherlands Trial Registry (www.trialregister.nl, NTR6835) on November 13, 2017.

Background

Groin pain is a frequent complaint in surgical practice, that encompasses a large number of possible aetiologies. A well-known cause of groin pain is an inguinal hernia. Elective inguinal hernia correction is the most commonly performed operation worldwide with an estimated 30.000 procedures in the Netherlands annually.[1]

In the majority of cases, an inguinal hernia can be diagnosed clinically. A classical hernia presents as a reducible groin swelling with a positive cough impulse, with or without the presence of discomfort. However, patients with groin pain without signs of an inguinal hernia on anamnesis or physical examination provide a diagnostic challenge.

For patients with groin pain in whom no swelling can be identified, current guidelines advise ultrasonography of the groin, followed by MRI if ultrasonography is inconclusive.[2,3] When additional imaging shows a hernia that could not be detected clinically, this entity is called a clinically occult hernia. The current guidelines do not provide a specific therapeutic approach for these type of hernias, and for unclear reasons the radiologic presence of a clinically occult inguinal hernia often leads to surgical intervention.[2,3] -

However, it is debatable if in all cases a symptomatic inguinal hernia truly exists or whether the hernia on additional imaging is an incidental finding with an alternative cause for the pain complaints. The radiologic finding might even be false-positive in some cases. Considering this, it is likely that not in all patients with a clinically occult hernia a surgical procedure is justified, and it is possible that (chronic) pain complaints persist or increase after surgery. This consideration is important for adequate patient information and avoidance of unnecessary surgical interventions.

The incidence of groin pain in combination with a clinically occult inguinal hernia is not well described in literature. A prospectively registered database kept in the Hernia Clinic of the Diakonessenhuis (Diakonessenhuis Utrecht/Zeist, the Netherlands) shows inguinal pain without symptoms of an inguinal hernia on physical examination or anamnesis but presence of an inguinal hernia on ultrasonography in 9.5% of patients.

Up till now, there are no studies performed specifically focussing on the course of pain and quality of life after correction of a (clinically) occult inguinal hernia or a watchful waiting approach. A trial comparing the outcomes of the two approaches in patients with a clinically occult inguinal hernia is urgently needed.

Methods

Objective

The objective of this study is to assess if watchful waiting is non-inferior to endoscopic total extraperitoneal (TEP) inguinal repair in patients with a clinically occult inguinal hernia.

Study design

The EFFECT trial is designed as a non-blinded, randomized controlled non-inferiority trial comparing surgical treatment by TEP hernia repair to watchful waiting in patients with a clinically occult groin hernia. This study is conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. The independent ethics committee of the Diakonessenhuis Utrecht (MEC-U) has approved this study protocol (protocol number NL61730.100.17. Eight Dutch centers participate in this study: Diakonessenhuis Utrecht/Zeist, Meander Medical Center Amersfoort, Onze Lieve Vrouwe Gasthuis (OLVG) Amsterdam, Maasstad Hospital Rotterdam, Maxima Medical Center (MMC) Veldhoven, Elkerliek Hospital Helmond, Rode Kruis Hospital (RKZ) Beverwijk, Treant Care Group Hoogeveen.

Patient recruitment started on December 29th 2017. Written informed consent will be obtained from all participants by the study coordinator. Inclusion will take up to a maximum of 2.5 years and participants will be followed-up for 1 year in total. The total duration of the study will be 3.5 years. All study participants will be asked to fill out written questionnaires at different timepoints (baseline, 1.5, 3, 6 and 12 months) and will be scheduled for physical examination by experienced hernia surgeons at two additional timepoints at the surgical outpatient clinic for the purpose of this study. Participants can withdraw from the study at any time, for any reason.

Randomization, collection and storage of study data will take place through an uniform electronic case report form (eCRF). Clinical trial monitoring will be conducted by an independent monitor.

A SPIRIT figure for this study protocol is provided in figure 1.

Participants

Adult patients with groin pain and a clinically occult inguinal hernia are eligible to participate in this study.

All patients presenting to the outpatient clinics of participating centers are physically examined by experienced hernia surgeons and screened for trial eligibility (*figure 2*). Patients will be informed and included at the surgical outpatient department at one of the participating centers.

Figure 1. Content for the schedule of enrolment, interventions and assessments according to the SPIRIT statement

	STUDY PERIOD					
	Enrolment	**Allocation**	**Post-allocation**			**Close-out**
TIMEPOINT	*Before treatment*	0	*1.5 months*	*3 months*	*6 months*	*12 months*
ENROLMENT:						
Physical examination	X			X		X
Eligibility screen	X					
Informed consent	X					
Randomization	X					
X-ray & MRI pelvis		X				
INTERVENTIONS:						
TEP		X				
Watchful waiting						
ASSESSMENTS:						
Age	X					
Gender	X					
BMI	X					
ASA classification	X					
Smoking	X					
Side of complaints	X					
Duration of complaints	X					
Previous hernia on contralateral side	X					
*Presence of hernia**		X				
*Hernia type**		X				
*Lipoma**		X				
*Duration of surgery**		X				
*Conversion**		X				
*Complications**		X				
Pain	X		X	X	X	X
Quality of life	X		X	X	X	X
*Patient diary***						
Medical consumption			X	X	X	X
Productivity			X	X	X	X
Patient satisfaction			X			X
Complications						

BMI: Body Mass Index, ASA: American Society of Anesthesiologists * In case of randomization to totally extraperitoneal (TEP) hernia repair ** Patient diary regarding physiotherapy and use of painkillers

Each subject must meet the following inclusion criteria:
- Age ≥ 18 years
- Unilateral groin pain
- No features of an inguinal hernia on anamnesis (no visible or palpable groin swelling)
- No features of an inguinal hernia on physical examination (no visible or palpable groin swelling and a negative Valsalva manoeuvre)
- Radiological diagnosis of an inguinal hernia on ultrasonography

A potential subject who meets any of the following criteria, will be excluded from participation:
- Previous inguinal hernia on the symptomatic side
- Previous surgery in inguinal region of the symptomatic side
- BMI ≥ 40
- ASA classification > III
- Factors that complicate follow-up by means of questionnaires (eg. Language barrier, psychiatric disorders)
- Unwillingness to undergo surgery

Randomization

After informed consent is obtained, the study coordinator will directly randomize patients to either TEP repair or a watchful waiting approach by means of an online random treatment generator, stratified by center.
The surgeon, patient and coordinating researcher are not blinded for the allocated treatment.

Baseline assessment

At baseline, all participants are asked to fill out electronic questionnaires. Also, all participants will undergo X-ray and MRI of the pelvis, to be able to assess baseline comparability of the groups in a later stage. The surgeon will be blinded to the outcomes of these investigations and they do not influence treatment. Only in rare severe cases (eg. a tumour or fracture) radiologists are instructed to contact the treating physician.

Intervention

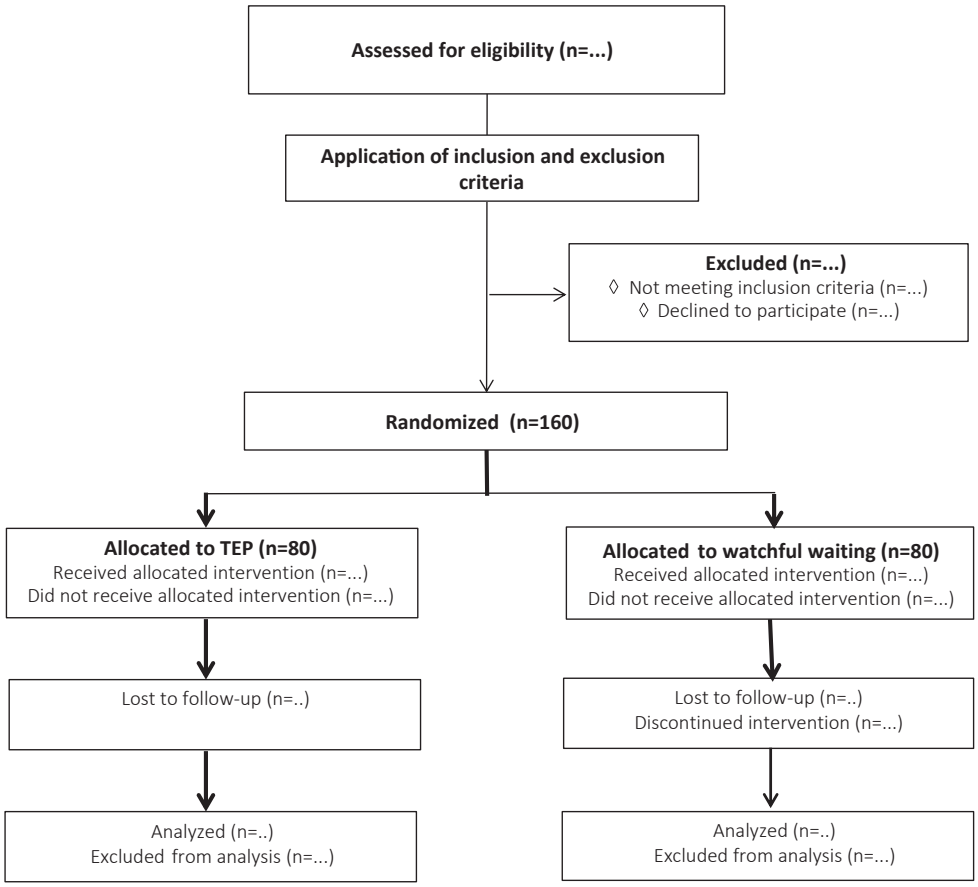
Patients will be randomized to TEP inguinal hernia repair or a watchful waiting approach.

TEP inguinal hernia repair

The patients randomized to an operative treatment will undergo endoscopic total extra-peritoneal (TEP) inguinal hernia repair. This procedure will be standardized according to current guidelines in all participating centers.[2,3]

A preperitoneal synthetic mesh will be placed in a standardized manner. Peroperative findings (presence of an inguinal hernia, classification of inguinal hernia according to the European Hernia Society (EHS) hernia classification, presence of a lipoma) and peroperative complications are recorded in the operation chart.[2,3]

Figure 2. Study flowchart



TEP: totally extraperitoneal hernia repair

Operative procedure

After induction of general anesthesia, a subumbilical incision is made. The anterior rectus sheath is divided transversely to expose the rectus muscle, which is retracted laterally. A 10 mm trocart is inserted into the preperitoneal space after which the preperitoneal space is created digitally (or with a balloon) and insufflated. A 5-mm trocart is placed at midline between

umbilicus and symphysis, after which the pubic bone and cavum Retzii are dissected. Below the level of the epigastric vessels lateral dissection takes place, and a second 5-mm trocart is placed laterally. (Another option is placement of the second 5 mm trocart in the midline, below the first 5 mm trocart). A possible lateral hernia sac is dissected with identification of the vas deferens and vessels. A possible medial of femoral hernia is reduced. The peritoneum is dissected cranially. Possible lipoma's are identified and reduced or resected. A synthetic mesh is introduced and positioned against the anterior abdominal wall, covering the internal ring, the femoral canal and the medial space. Next, under endoscopic sight the preperitoneal space is desufflated, and all trocarts are removed. The rectus sheath is closed with vicryl, the dermis is closed with monocryl.

Postoperative care

Patients are discharged at the day of surgery, unless complications prohobit early discharge. Participants are advised to avoid strenuous physical activity during the first postoperative week.

Surgical quality control

A selected number of trained surgeons will perform TEP hernia repair. Hereby we maintain quality of the operations and minimize differences in success rates. Surgeons in the participating centers have completed their learning curve are sufficiently experienced (>250 procedures per individual surgeon) for TEP inguinal hernia repair.

Watchful waiting

Surgical correction by TEP will be compared to a watchful waiting approach. Patients in this study arm will be treated with rest, pain killers and optional physical- and/or physiotherapy. It is expected that the patients in this group will present with a variety of complaints and will not experience the same (intensity of) complaints, therefore we cannot standardize the treatment in this study arm. Intensity and frequency of this treatment will depend on amount of complaints the individual patient is experiencing and is expected to differ between patients. The decision to offer physiotherapy will be in the hands of the treating physician, who will decide if he or she suspects the kind of complaints where physical- and/or physiotherapy will be of help.

Outcomes

The primary outcome will be pain reduction after 3 months, measured in rest and during physical activity. The first pain score is obtained at baseline. The first three questions of the validated EuraHS Quality of Life (EuraHS-QoL) reflect intensity of pain on an 11-point numeric

rating scale (NRS) (0-10 where 0 reflects “no pain” and 10 reflects “the worst possible pain).[4] Patients rank the intensity of their pain on this scale in rest (specified as lying down) and during physical activity (defined as walking, cycling or practicing sports). The third question is the amount of pain felt during the last week, so insight is also provided in the most recent pain the patient experienced. Follow-up pain levels are determined at three additional time points (1.5, 6 and 12 months) as secondary outcome parameters.

Secondary outcomes include quality of life, cost-effectiveness, patient satisfaction and crossover rate. Quality of life will be assessed by the validated EuraHS-QoL and Euro Quality of Life-5D-5L (EQ5D-5L) questionnaires at baseline, and 1.5, 3, 6 and 12 months postoperatively.[5] Cost-effectiveness will be based on all resources used within and outside the hospital and productivity loss for both groups of patients. The acquired data will consist of all health care professional visits, hospitalizations, imaging, biochemical investigations and surgery. Health care use will be monitored through the medical consumption questionnaire (MCQ), a generic instrument for measuring health care use and calculating medical costs, at 1.5 ,3, 6 and 12 months after treatment.[6] Participants in both treatment groups will be given a patient diary where the use of painkillers and (optional) treatment with physiotherapy will be registered the first 6 weeks after treatment. Productivity will be measured through the productivity cost questionnaire (PCQ), a standardized instrument for measuring and valuing productivity losses, at 1.5,3,6 and 12 months after treatment.[7] We aim to calculate total costs per patient in every group. We aim to calculate cost-effectiveness ratios to indicate the total costs per additional unit of effect, cost per quality-adjusted life year (QALY).
Patient satisfaction will be measured at 3 and 12 months after treatment. The measuring instrument for the outcome parameter patient satisfaction is a self-designed 11-point scale ranging from 0 (“no satisfaction) to 10 (“total satisfaction”).
The crossover rate will reflect the percentage of patients initially assigned to the watchful waiting group that cross over to surgical treatment.

Other study parameters include baseline characteristics (gender, age, American Society of Anesthesiologists (ASA) classification, body mass index (BMI), smoking, medication, side of complaints, duration of complaints, previous inguinal hernia on contralateral side), peri-operative outcomes (presence of a hernia, hernia type, presence of lipoma, duration of surgery, conversion, complications) and postoperative complications. Also, the percentage of clinically occult hernias in the watchful waiting group that develop into clinically overt inguinal hernias will be assessed.

Sample size calculation

The sample size determination is based on the assumption that a watchful waiting approach is non-inferior to a TEP inguinal hernia correction; from this assumption there is no expected difference between the difference scores of both groups. No consensus exists concerning a minimal clinically relevant difference on the NRS, though previously published literature describes a difference of one point.[8] We used three quarters of a point (0.75) on the NRS scale as an equivalence margin, using the NRS as a continuous variable. Expected variance in the primary outcome was estimated from a prospectively collected database containing 919 patients at the Diakonessenhuis; a standard deviation of 2.3 was found for the difference scores, and a correlation of 0.8 was found between pre-treatment pain and change in pain scores. To be able to detect an equivalence margin of 0.75 on change on the NRS scale between the groups, with a power of 90% and a 1-sided alpha of 0.025, a sample size of 199 patients in each arm is required. Because we will correct for baseline pain intensity, an analysis of covariance (ANCOVA) correction was used, resulting in 72 patients per arm.[9] Taking a loss-to-follow-up of 10% into account, the total sample size should contain at least 160 patients with 80 patients per arm.

Statistical analysis

Primary outcome measure

The primary outcome measure is the difference in pain intensity (NRS during rest/physical activity) 3 months after treatment compared to baseline. Difference scores of the NRS (posttest minus pretest) will be used in both treatment groups. The NRS score will be used as a continuous variable. For comparison of difference scores an analysis of covariance (ANCOVA) will be used, in which the estimated difference in pain scores will be corrected for the pain intensity at baseline.

Secondary / other study parameter(s)

Continuous secondary outcomes 3 months after treatment will be analysed similarly to the primary outcome, with an ANCOVA on the difference correcting for baseline score. Outcome measures at 1.5,3,6 and 12 months will be analysed using linear mixed effects models to adjust for repeated measurements within individuals. Contrasts will be used to investigate differences between the study arms at the post-treatment time points.

The primary analysis of outcome parameters is an intention-to-treat analysis. Primary and secondary outcomes 3 months after treatment will also be evaluated only for the patients who remained in the arm to which they were randomized (per protocol analysis).

Data will be analysed by means of IBM SPSS Statistics version 23 or higher (SPSS, Chicago, III, USA).

Discussion

This is the first randomized controlled trial comparing surgery to a watchful waiting approach in the specific subset of patients with a clinically occult inguinal hernia.

The current guidelines provide no clear advise on the treatment of the particular subset of patients that has a clinically occult inguinal hernia.[2,3] To date, we could find no intervention studies on the effect of surgery or a watchful waiting approach in terms of pain or quality of life in patients with a clinically occult groin hernia. Up till now, all the studies performed on clinically occult inguinal hernias were diagnostic and aimed to determine the diagnostic value for the diagnosis of occult hernia of imaging modalities in patients with groin pain and no findings of an inguinal hernia on physical examination.[10-22]

A trial comparing the outcomes of the two approaches in patients with a clinically occult groin hernia is urgently needed to provide data facilitating the choice between the two treatment options. With this trial we aim to determine which treatment strategy is the most (cost-) effective for this particular subset of patients. If watchful waiting is non-inferior to surgical repair, costs of surgical repair and complications may be saved.

Current status

The study was opened to recruitment in December 2017. Recruitment is ongoing. The duration of the study period will be 3.5 years.

Ethics approval and consent to participate

The indepent Medical Ethics committee of the Diakonessenhuis Utrecht approved the trial protocol (NL61730.100.17) and the study is registered in the Netherlands Trial Registry (www.trialregister.nl,NTR6835). Informed consent will be obtained from all participants by the study coordinator.

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4

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

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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.

Background

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, hipjoint 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 analysed 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

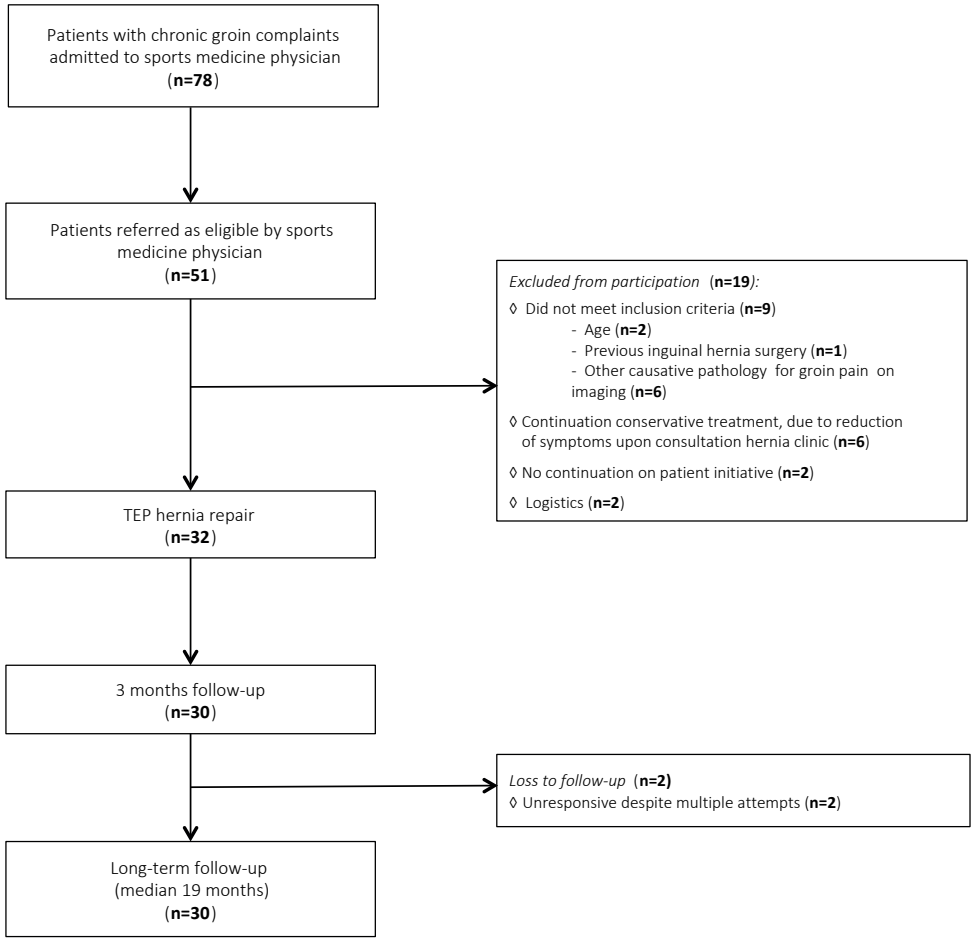
Thirty-two male athletes (median age 22 years) were included in our study *(figure 1, table 1)*. The majority of participants (68%) were soccer players *(figure 2)*. At physical examination, tenderness by palpation at the inguinal canal region was found in 97% of patients, and 46.7% of these patients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

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)	12.0 (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

Figure 1. Flowchart patient inclusion and follow-up

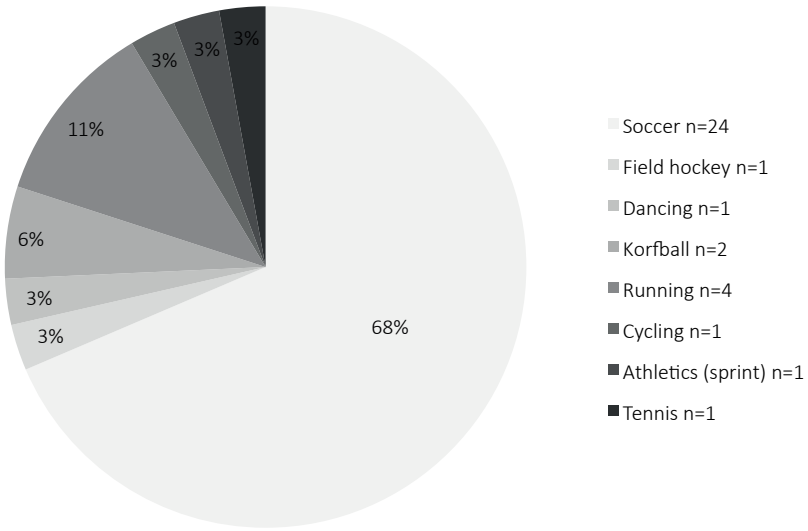


TEP: totally extraperitoneal

One or both radiologists observed abnormalities in 19 patients (59%) on MRI *(table 2)*.

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.

Figure 2. Distribution of sports type



The number of patients exceeds the sample size, since multiple patients participated in 2 sports.

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.

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)

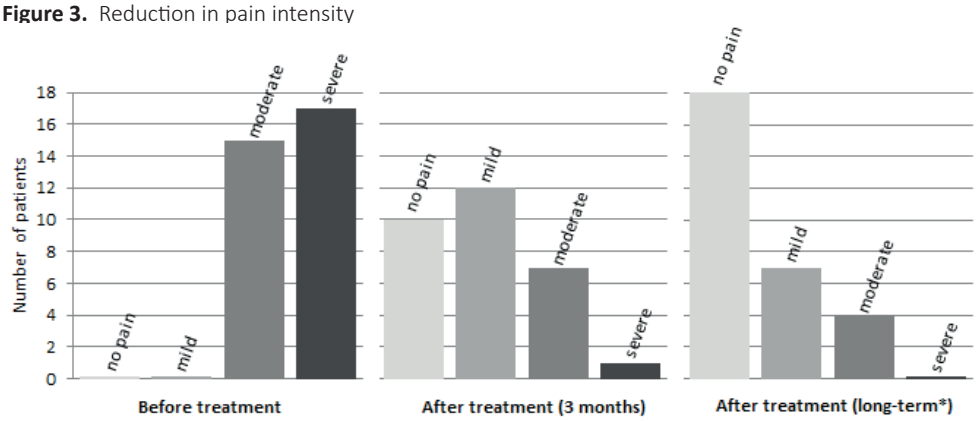
The number of patients exceeds the sample size, since multiple patients had oedema of the pubic bone and musculotendinous findings.

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

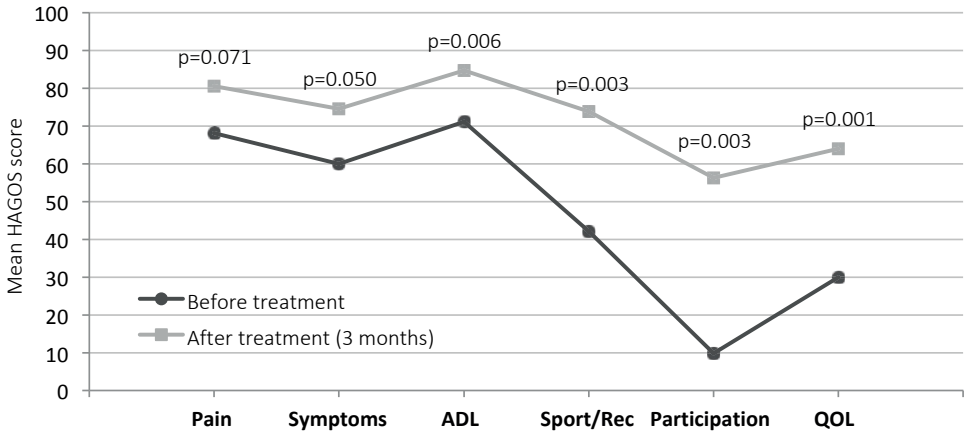
Resumption of sports

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.

Figure 4. Physical functioning



ADL: Activities of daily living, Rec: Recreation, QOL: Quality of life

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 recognisable 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 laparascopic 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 standardised 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 categorise 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 centres 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 practise 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 randomised controlled trials comparing different surgical treatment techniques are needed.

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5

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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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 anaesthesia, 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: 55g/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: 80g/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.

Figure 1. PINQ PHONE questionnaire

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?

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).

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

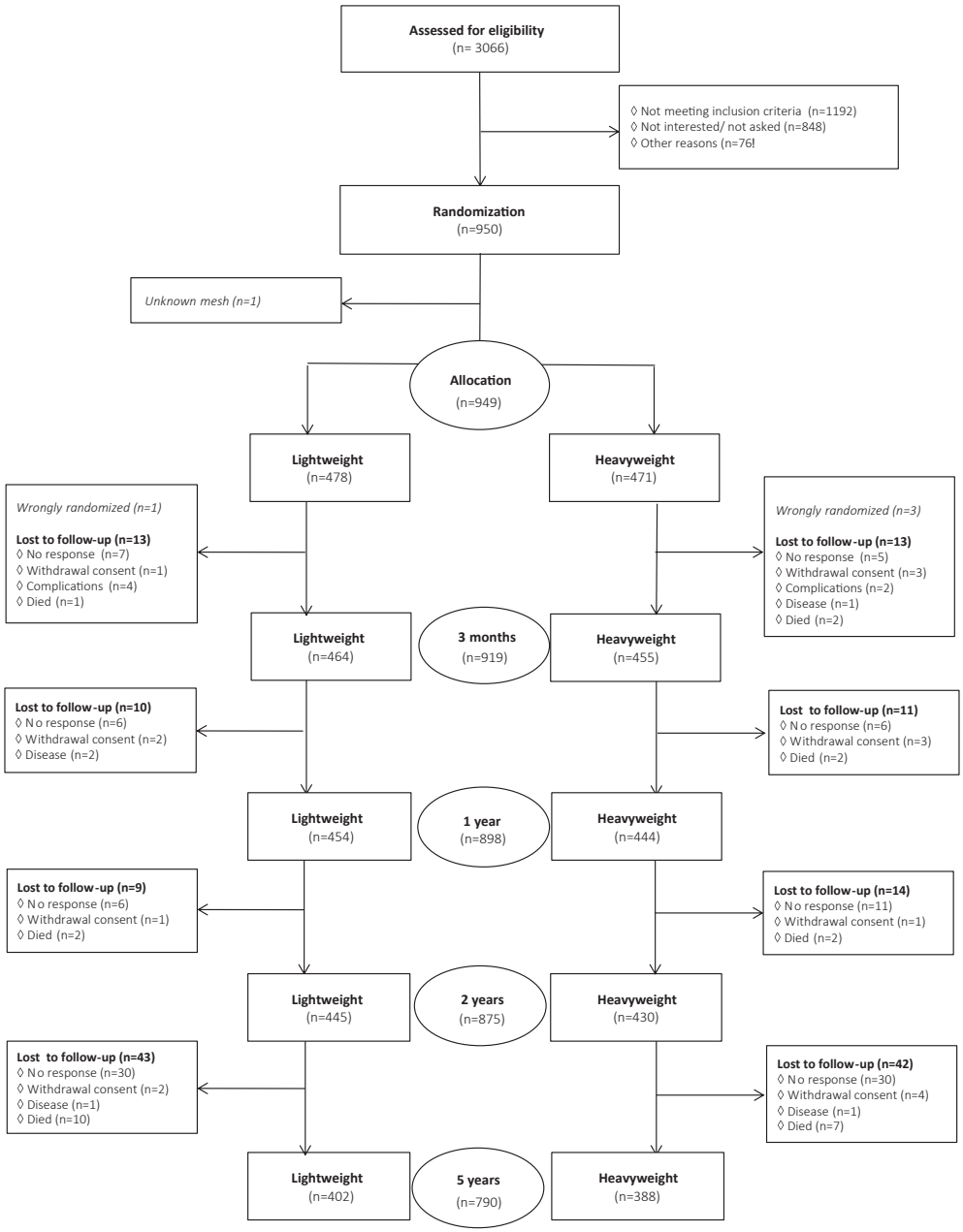
Initially, 949 patients were succesfully randomized to TEP hernia repair with lightweight or heavyweight mesh (*figure 2)*. At 5 years of follow-up, we were able to assess the presence of recurrence in 790 patients, who comprise 90.3 % of the 2-year follow-up group and reflect a 83.2% five-year follow-up 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.

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 (%)			0.15
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

Figure 2. Flowchart



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.

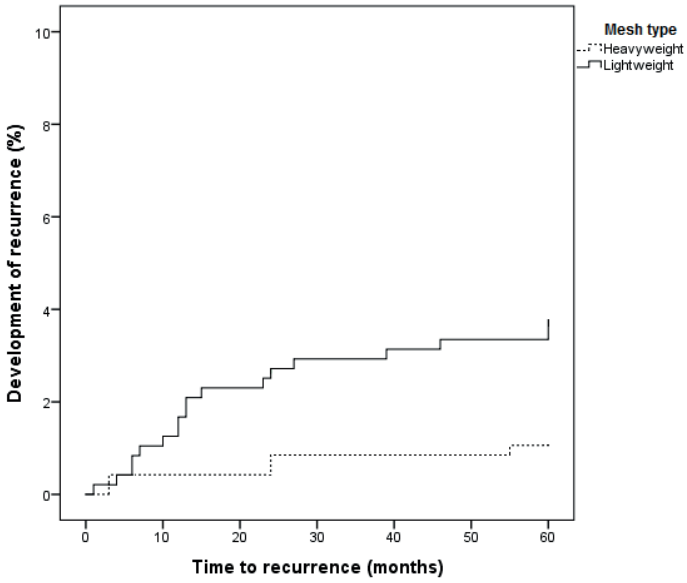
Table 2. Recurrence rates at different time points

	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

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.

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)*.

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



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).

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 organised 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 centre is a high-volume hernia clinic performing 1100 TEP inguinal hernia repairs annually, with all operating sugeons 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 centre 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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6

An 11-year analysis of reoperated groins after endoscopic totally extraperitoneal (TEP) inguinal hernia repair in a high volume hernia center

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Abstract

Background

Developments in inguinal hernia surgery have substantially lowered recurrence rates, yet recurrences remain an important outcome parameter of inguinal hernia repair. The aim of this study was to analyze the characteristics of all reoperated groins after endoscopic totally extraperitoneal (TEP) inguinal hernia repair in a high-volume hernia clinic in the Netherlands.

Methods

All groins with recurrence-like symptoms reoperated after previous TEP inguinal hernia repair between January 2006 and December 2016 were analyzed. Patient characteristics, imaging findings, primary hernia type, time to recurrence and recurrence type were assessed.

Results

A total of 137 groins were reoperated in 130 patients. The median age at the TEP procedure was 55 years (interquartile range (IQR) 45-64 years). Fifty-seven groins were initially part of a bilateral procedure (42%). Median time until recurrence was 9 months (IQR 4-26 months). Reoperation findings were a hernia recurrence in 76%, an isolated lipoma in 18%, and no recurrence or lipoma in 6%. The majority of hernias recurred at their initial site (70%), of which the greatest part involved direct hernias. Isolated lipomas were more frequently seen after indirect hernia repair.

Conclusion

Inguinal hernia recurrences were still observed in this high-volume hernia clinic. Recurrences were most frequently seen at their initial hernia site, the majority involving direct hernias. Isolated lipomas presenting as a pseudo-recurrence were most frequently seen after correction of indirect hernias. In accordance with the current guidelines, reducing recurrence rates can be achieved by mesh fixation in bilateral, large and direct defects and by thoroughly reducing lipomas.

Background

Once inguinal hernia repair was accompanied by a substantial number of recurrences, yet recurrence rates decreased tremendously since mesh repair has become routine.[1-4] Consequently, follow-up after inguinal hernia repair focused less on recurrence and shifted towards postoperative pain. The posterior approach of the inguinal area with a preperitoneal position of mesh demonstrated a significant reduction in chronic pain compared to an anterior approach.[5] Therefore, the endoscopic totally extraperitoneal (TEP) inguinal hernia repair is widely used and by many surgeons considered the preferable preperitoneal technique.[6-11]

Conceptually, a retromuscular and preperitoneal position of mesh covering Fruchaud's triangle with overlap, should eliminate the risk of recurrence. However, recurrences after TEP inguinal hernia repair still develop and remain a clinical problem and an important outcome parameter of inguinal hernia surgery.[12-16]

It has been demonstrated that surgical skills and experience contribute to the recurrence risk after endoscopic inguinal hernia repair. Low long-term recurrence rates have been achieved in highly specialized centers, implying that volume may have a positive impact on recurrence rates.[17-20] Concerning the TEP technique in particular, recurrences have been associated with the learning curve of the individual surgeon.[6-11,21,22]

As we are still confronted with recurrences after primary TEP inguinal hernia repair, analyzing operative outcomes of recurrent hernias in a high-volume center specialized in TEP hernia repair with low recurrence rates may facilitate better understanding of their cause and may contribute to detecting patterns of recurrence and possible prevention of recurrence development. The objective of this study was to provide an 11-year analysis of all reoperated groins for recurrence-like symptoms in a high-volume hernia center in the Netherlands specialized in TEP inguinal hernia repair.

Methods

Study design

The characteristics of all groins with recurrence-like complaints that were reoperated between 2006 and 2017 in our hernia clinic were studied retrospectively.
During the study period, approximately 1000 patients were operated annually by TEP inguinal hernia repair by five experienced surgeons with extensive experience in this technique (>500 procedures per surgeon). Two- and five-year recurrence rates in this center are respectively 0.8% and 1.1%.[19,20]
Institutional Review Board approval was obtained for this study.

Patients

All patients reoperated for recurrence-like complaints between January 1, 2006 and December 31, 2016 after previous unilateral or bilateral TEP hernia repair in this hernia clinic were identified and screened for eligibility. All patients had undergone endoscopic TEP hernia repair under general anaesthesia in a day-case setting. Operative details of this technique have been described previously.[14] In all subjects a synthetic mesh (Prolene® or Ultrapro®, 10x15 cm) was placed preperitoneally over the hernia defect. Prolene® is the mesh standardly used in this center, but from 2010 until 2012 Prolene® mesh was compared to Ultrapro® mesh in a randomized controlled trial.[19,20] Mesh fixation was not routinely performed.

For evaluation of recurrence-like complaints after TEP repair, patients presented upon own initiative, through referral by their general practitioner or for follow-up regarding a randomized controlled trial conducted in this center.[19,20] Evaluation at the surgical outpatient department consisted of history taking, physical examination and, when deemed necessary, additional imaging by ultrasonography, MRI or CT. A recurrence was assumed in case of a typical history of an inguinal swelling, a clinically detectable bulge in the abdominal wall exacerbated by the Valsalva manoeuvre, or suspicion of a hernia recurrence on additional imaging. Decisions to reoperate were based on a clinical or radiological suspicion of a recurrent hernia, a clinical or radiological suspicion of an isolated lipoma assumed to cause the recurrence-like complaints, or in case of a strong wish of the patient. Clinical suspicion of a recurrence when radiological findings were negative for a recurrence was also an indication for reoperation. The following exclusion criteria were applied: Patients who were referred after TEP performed elsewhere, patients who presented with recurrence-like symptoms who underwent another type of hernia repair after the initial TEP or patients who were operated for suspicion of recurrence elsewhere.

Outcomes

Patient characteristics (age, sex, body mass index (BMI)), imaging findings and time to recurrence after TEP repair were registered. Imaging findings (ultrasound, MRI or CT) were divided into recurrence, no recurrence or an isolated lipoma. The date when a patient visited the outpatient clinic with recurrence-like complaints was used as a surrogate for date of recurrence. Time to recurrence was defined as the interval between the TEP procedure and the day of re-attendance at the outpatient clinic.

The following peroperative findings of initial TEP repairs and subsequent operations for recurrences were assessed: Operation date, type of procedure (only for reoperations), side (left/right/bilateral), presence of hernia, hernia type, presence of lipoma, type of mesh, fixation of mesh and duration of the operation. When assessing the type of recurrence

upon the second operation the following distinction was made: A protrusion through a weakness in the posterior wall of the inguinal canal (fascia transversalis) was classified as a direct recurrence, a protrusion through the deep inguinal ring (hernia sac or fatty tissue) was classified as an indirect recurrence, and solely fatty tissue not originating from the deep inguinal ring was classified as an isolated lipoma. The size of the hernia defect was not standardly reported in operation charts, but large initial defects were scored when reported as such by the operating surgeon.

Since several patients were bilaterally operated for recurrence, recurrence characteristics are presented for groins instead of patients.

Analysis

Statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). The cumulative percentage of recurrences was assessed by Kaplan Meier analysis.
For comparison of categorical variables, two-sided p-values were calculated from Pearson's chi-square and Fisher's exact test. For comparison of continuous (non-parametric) variables the Mann-Whitney U test was used.

Results

Between January 2006 and December 2016, 130 patients were seen at the outpatient clinic and reoperated for suspicion of 137 recurrent hernias after TEP hernia repair (*table 1)*. The majority of patients were male (96%) and the median age at the initial TEP procedure was 54.5 years (interquartile range (IQR) 44.8-63.6 years).

Primary TEP hernia repairs were performed between October 2001 and March 2016 (*table 2)*. Fifty-seven (42%) groins were part of a bilateral procedure. In 12 cases (9%) the initial TEP repair had been for a recurrent hernia after primary open repair, these cases thus present re-recurrences.

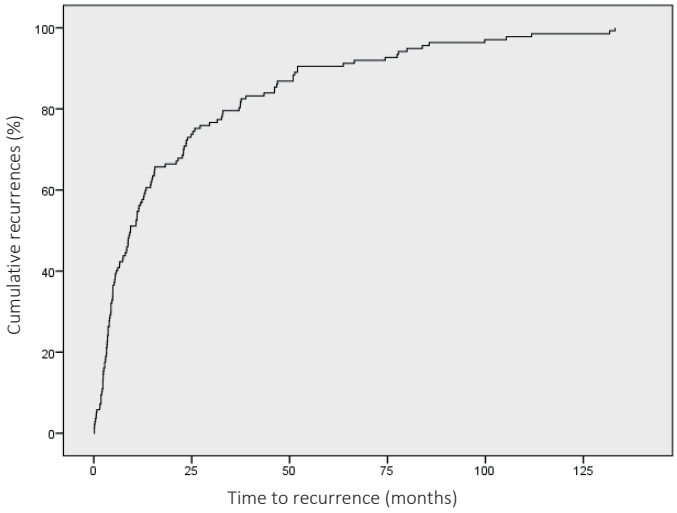
The median time to detection of recurrence was 9.4 months (IQR 3.6-25.5 months) with the two earliest detected recurrences four days after surgery and the latest detected recurrence 11 years after surgery. The majority of recurrences were diagnosed in the first two years after surgery. At three months postoperatively, 25 (18%) recurrences were diagnosed, increasing to 78 recurrences at one year postoperatively (57%) and 100 recurrences (73%) at two years postoperatively (*figure 1)*.

Table 1. Patient characteristics (n=130)

Sex, n (%)	
Male	125 (96)
Female	5 (4)
BMI (kg/m^2)	25.2 (23.2-27.8)
Age at initial TEP procedure (years)	54.5 (44.8-63.6)
Location of initial hernia, n (%)	
Unilateral	80 (62)
Bilateral	50 (38)
Median time to recurrence* (months)	9.4 (3.6-25.5)

Continuous data are presented as median (Interquartile range). BMI: Body Mass Index, TEP: totally extraperitoneal
* Displayed for total number of groins, since 7 patients developed a bilateral recurrence (n=137).

Figure 1. Cumulative percentage of recurrences



At the TEP procedures 123 Prolene® (90%) and 14 Ultrapro® (10%) meshes were used. During the initial procedures 68 direct, 63 indirect, four mixed and two femoral hernias were observed (*table 3)*. Mesh fixation was performed in seven groins (5%), six involved bilateral repairs (three direct and three indirect hernias) and one involved a large unilateral direct defect. An additional 10 primary large hernias (three direct and seven indirect defects) were described of which none were fixated.

The majority of patients were reoperated through an open anterior approach according to Lichtenstein (124 groins, 91%). In three early recurrences (four,four and five days after

surgery) two TEP procedures and a Stoppa procedure were executed. In seven patients (5%) an anterior approach without placement of mesh was performed.

Table 2. Operative characteristics of groins reoperated for clinical suspicion of recurrence (n=137)

Initial TEP procedure, **side** n (%)	
Unilateral, left	36 (26)
Unilateral, right	44 (32)
Bilateral, left	25 (18)
Bilateral, right	32 (24)
TEP procedure, **operation time** (minutes)	
Unilateral	22.5 (16.3-30.8)
Bilateral	31.0 (24.0-45.0)
Reoperation, **side** n (%)	
Unilateral, left	57 (42)
Unilateral, right	72 (52)
Bilateral, left	4 (3)
Bilateral, right	4 (3)
Reoperation, type of procedure n (%)	
Lichtenstein	124 (91)
TEP	2 (1)
Stoppa	1 (1)
Fabricius repair	2 (1)
Repair femoral hernia with preperitoneal mesh	1 (1)
Inguinal exploration, lipoma removal	6 (4)
Inguinal exploration, suturing small femoral defect	1 (1)

Continuous data are presented as median (Interquartile range). TEP: totally extraperitoneal

Table 3 demonstrates the correlation between the peroperative findings upon initial TEP repair and the operation for (suspected) recurrence. In all reoperated groins, 104 recurrences were found (76%) and in 33 cases no hernia could be objectified (24%). Twenty-five cases yielded an isolated lipoma (18%) and in eight patients no recurrence or lipoma was found (6%). The recurrent hernias described upon reoperation were direct in 65 cases (63%), indirect in 27 cases (26%), mixed in three cases (2%), femoral in three cases (2%) and in six groins the type of recurrence was not clearly specified (4%). Seventy-three hernias recurred at their initial site (46 direct to direct, 20 indirect to indirect, four mixed to direct, one direct to mixed and two indirect to mixed), representing 70% of recurrences and 53% of all reoperated groins. Initial direct defects recurred significantly more as direct or mixed hernias compared to to indirect defects recurring as indirect or mixed hernias (69% versus 35%, p=0.000).

Table 3. Correlation between peroperative findings upon initial TEP repair and reoperation (n=137)

Primary direct hernia, n (%)	**68 (50)**
Direct recurrence	46 (68)
Indirect recurrence	7 (10)
Mixed recurrence (direct and indirect)	1 (1)
Femoral recurrence	2 (3)
Recurrence, type unclear	4 (6)
No recurrence, only lipoma	4 (6)
No recurrence or lipoma	4 (6)
Primary indirect hernia, n (%)	**63 (46)**
Direct recurrence	15 (24)
Indirect recurrence	20 (32)
Mixed recurrence (direct and indirect)	2 (3)
Femoral recurrence	1 (2)
Recurrence, type unclear	2 (3)
No recurrence, only lipoma	19 (30)
No recurrence or lipoma	4 (6)
Primary mixed hernia, n (%)	**4 (3)**
Direct recurrence	4 (100)
Primary femoral hernia, n (%)	**2 (1)**
No recurrence, only lipoma	2 (100)

TEP: totally extraperitoneal

Nine out of eleven primary defects that were reported as large hernias recurred as the same type of hernia (82%) (four direct hernias, five indirect hernias) and four out of seven primary fixated hernias (57%) (three direct hernias, one indirect hernia) recurred at their initial site.
In 25 reoperated cases (18%) an isolated lipoma without a hernia recurrence was found (initially 19 indirect hernias, four direct hernias and two femoral hernias). Significantly more of these lipomas were seen after correction of indirect hernias in comparison to direct hernias (30% versus 6%, p=0.000).
Of the cases where no recurrence or lipoma was found, one patient had developed a hydrocele and in one patient bulging of the abdominal wall was observed. In five patients no abnormalities were found. One early assumed recurrence underwent a second TEP four days postoperatively; no recurrence but only hematoma was found.

When comparing time to recurrence for the true recurrent hernias compared to the findings of an isolated lipoma or no recurrence no significant differences were found (*table 4)*. Also, no significant difference in time to recurrence could be found for initially unilateral or bilateral hernias and different hernia types.

Table 4. Comparison of time to clinical diagnosis of recurrence, specified for operative details and hernia type (n=137)

	Time to recurrence (months)	***p-value***
Initial operation unilateral (n=80)	8.7 (3.3-23.4)	
Initial operation bilateral (n=57)	10.8 (4.3-41.9)	0.675
First recurrence (n=125)	9.2 (3.6-32.1)	
Re-recurrence (n=12)	10.2 (4.5-20.8)	0.783
Hernia recurrence (n=104)	9.0 (3.8-25.1)	
No hernia recurrence (n=33)	10.8 (3.4-48.5)	0.962
Primary direct hernia (n=68)	10.1 (3.6-30.1)	
Primary indirect hernia (n=63)*	10.8 (4.4-27.1)	0.933
Direct to direct hernia (n=47)	6.1 (3.4-24.8)	
Indirect to indirect hernia (n=22)**	8.1 (4.0-25.8)	0.860
Same hernia type[¥] (n=73)	6.6 (3.1-25.1)	
Different hernia type (n=25)***	11.5 (5.9-24.4)	0.354

Continuous data are presented as median (interquartile range). TEP: totally extraperitoneal
* The total of primary direct and indirect hernias adds up to 131 groins, since the remainder of hernias were primary mixed or femoral ** The total of direct to direct and indirect to indirect hernias adds up to 69 groins, since the remainder of hernias were primary mixed, femoral or recurred at a different site ***The total of same and different hernia types adds up to 98, since in 6 of recurrent hernias the herniatype was not specified peroperatively
[¥]direct to direct or mixed hernia, indirect to indirect or mixed hernia, mixed to direct or indirect hernia

Imaging was performed in 81 groins before reoperation (59%). Imaging findings and findings upon reoperation yielded similar results in 58 cases (72%). In 79 groins ultrasound was conducted; 65 of these ultrasounds were conclusive and diagnosed 56 hernias (peroperatively 41 recurrent hernias, 10 solitary lipomas and no recurrence or lipoma in five cases), three lipomas (peroperatively one recurrent hernia and two lipomas) and no abnormalities in six cases (peroperatively four hernia recurrences and no recurrence or lipoma in two cases). In ten cases ultrasound was inconclusive and followed by MRI; five hernias and five lipomas were diagnosed (peroperatively four hernia recurrences and six lipomas). In four cases ultrasound was inconclusive followed by CT; three hernias were diagnosed (peroperatively two recurrences and no recurrence or lipoma in one case), in one case no abnormalities were described (peroperatively a lipoma). In one case only CT was performed and a hernia was diagnosed (peroperatively a recurrent hernia) and in one case only MRI was performed and a lipoma was diagnosed (peroperatively a lipoma).

Discussion

This retrospective analysis of 137 groins with recurrence-like symptoms after TEP inguinal hernia repair demonstrated true recurrent hernias were present in more than three quarter

of cases. The majority of the recurrent hernias involved direct hernias after primary direct repair and developed in the first two years postoperatively. Patients presenting with large primary defects or undergoing bilateral TEP repair were at increased risk of developing a recurrence. Lipomas clinically mimicking hernia recurrences were present in nearly one fifth of reoperated groins.

Recurrence rates remain an important parameter in determining the clinical effectiveness of hernia surgery and represent a challenge for hernia surgeons. Even though currently reported recurrence rates after TEP inguinal hernia repair are low, auditing own outcomes by analyzing possible mechanisms of repair failure and recognition of causes of recurrence further facilitates prevention, elimination, and subsequent decrease of recurrences. Since this study was performed in a high-volume hernia clinic specialized in the TEP technique the influence of surgical inexperience or an uncompleted learning curve on development of recurrences after TEP repair allegedly was eliminated.

Recurrent hernias were present in 76% of all reoperated groins and the majority of recurrent hernias had developed at their initial hernia site (70%), of which the greatest part involved direct hernias. A non-absorbable mesh of adequate (chemical and physical) properties, size and overlap that is adapted to the underlying tissue and enables good ingrowth without dislocation should prevent recurrence.[4] A recurrence at the initial hernia site might be the consequence of failure in mesh positioning, mesh displacement or an inadequate mesh regarding the defect. Immediate or very early displacement might occur due to desufflation and removal of instruments, folding, lifting by hematoma or urinary retention. Late displacement may be caused by insufficient scar tissue ingrowth, mesh protrusion or mesh shrinkage due to contraction of fibrotic fibers.[4,23]

Similar to the findinges of this study, Lamb et al. and Felix et al. found that respectively 67% and 76% of hernia recurrences were the same type as the original hernia.[23,24] However, Lamb rapported on more reformation of indirect hernias.[23] A study using data from the Danish Hernia Database conducted by Burcharth et al. also found a significant correlation between development of the same type of primary and recurrent hernia, most frequently involving direct hernias.[15] Lamb et al. and Burcharth et al. both described that development of the same type of hernia occurred significantly earlier postoperative, a finding that could not be confirmed from the results of this analysis.[15,23]

In more than four fifth of patients in whom a primary large defect was reported hernias recurred as their initial type. This percentage was considerably lower in cases where mesh fixation was performed, even though it does not become entirely clear from this analysis if all

of the defects in the fixated cases were primary large. It is known that large defects increase the risk of development of the same type of hernia recurrence, with the currently used cut-off value for a large hernia defect of greater than 3 centimeter.[9,25]

Since the most frequently observed recurrences are direct to direct defects, with an increasing recurrence risk when the primary defect is large, one could consider (besides placement of tags) performing reduction of the dead space caused by the dilated transverse fascia in large direct hernia sacs as recommended in the recently updated guidelines for (endoscopic) hernia surgery.[9-11] However, described benefits of this method are mainly prevention of hematoma or seroma, and no clear correlation with prevention of recurrence is described so far.[10,11]

More than 40% of patients that presented with a recurrence initially underwent a bilateral procedure. Since approximately 16% of patients that undergo primary TEP repair in our hernia clinic present with primary bilateral hernias, these numbers imply that patients undergoing primary bilateral TEP hernia repair are at an increased risk of developing a recurrence.[22] Even though one could hypothesize that overlap of two meshes during bilateral TEP repair would decrease the chance on development of (direct) recurrence, this particular overlap of mesh may also prevent adequate fixation of mesh in the surrounding tissue. In case of bilateral repair, especially in larger patients, we would like to emphasize the importance of usage of an adequate mesh size and to consider the option of mesh fixation.

The greatest part of recurrences was diagnosed within two years after TEP hernia repair. Previous research that reported on time to development of hernia recurrence yielded similar results.[15,23,24,26] The studies performed by Lamb et al. and Liem et al. also state that the majority of hernia recurrences developed within the first two postoperative years after TEP inguinal hernia repair, as well as the randomized controlled trial conducted in this hernia clinic between 2010 and 2012.[19,20,23,26]

Isolated lipomas were found in 18% of cases and occurred more frequently after correction of indirect hernias. Herniation of retroperitoneal adipose tissue into the inguinal canal is a frequent intraoperative finding during TEP repair and reduction of only the hernia sac without appropriate treatment of this lipoma can lead to recurrence-like symptoms. Unawareness of this condition of persisting lipoma can result in placing the mesh posterior of herniated retroperitoneal fatty tissue during TEP repair.[27] This study demonstrated the incidence of isolated lipomas clinically mimicking recurrences was significantly higher after correction of indirect hernias. It is possible that these lipomas developed after the primary operation, but also likely that the isolated lipomas observed in this study represent ‘forgotten’ lipomas

overlooked at the initial repair. Previous studies have reported upon (untreated) lipomas causing a pseudo-recurrence as well.[24,27,28] Even though technically these isolated lipomas are no true recurrences, this finding is still clinically relevant since reoperation will still be required in cases where these lipomas cause (recurrence-like) complaints.

When looking at the procedures performed at reoperation, based on the intraoperative findings a greater number of patients received a mesh than would have been necessary. With regard to the 25 patients where only an isolated lipoma was found during the second procedure, 18 Lichtenstein procedures with placement of mesh, one Fabricius repair and six inguinal explorations with removal of lipoma were performed. The eight patients where no recurrence or lipoma was found all received a mesh at the second operation; seven patients underwent a Lichtenstein procedure and one patient underwent another TEP procedure. For the patients that solely presented with lipomas, strictly, only removal of this lipoma would have been necessary and for patients without recurrence or lipoma no additional operative actions would have been required after inspection. Placement of a mesh in these cases unnecessarily increased the chance of (chronic) pain complaints.

The role of imaging to overcome unnecessarily mesh placement or operation, remains unclear. In this study in nearly 60% of reoperated groins preoperative imaging was conducted, however in more than a quarter of cases preoperative imaging findings and findings upon reoperation were discrepant. Due to the retrospective character of this study, the indication for and relevance of the performed imaging did not become entirely clear in all cases. In some cases the radiological hernia was already clinically apparent, and the imaging seemed unnecessary. When imaging showed an isolated lipoma instead of a recurrence, in this study population there was still decided to reoperate. Also, not in all cases the radiological diagnosis was in line with the clinical suspicion, and in some cases decisions to reoperate were made irrespective of (negative) imaging findings. In the current guidelines clinical examination plus ultrasound is recommended most suitable for evaluating patients suspected of having recurrent groin hernias, if diagnostic doubts persist CT or MRI should be considered.[9] However, up to this point solely two studies of low quality have addressed this role of imaging for groin hernia recurrence.[29,30] In our opinion, further research needs to be done regarding this issue.

Strengths of this study are the performance of a long-term eleven-year analysis of all reoperated groins in a high-volume hernia clinic where extensive experience is present.

A limitation is the retrospective character of this analysis, as not for all patients all required information could be retrieved. In the operation reports of the initial TEP repairs no distinction was made in the type of lipoma (funicular or preperitoneal). Also, not for all groins the hernia

type was clearly specified upon reoperation. The size of the hernia defect was not standardly measured or reported, therefore primary large defects may have been missed or defects that actually measured less than three centimeters in diameter may have been wrongly classified as large in some cases. Due to the anterior approach that was used in the majority of reoperated cases possible reasons of recurrence (eg. mesh dislocation or shrinkage) were not possible to assess and therefore report. Another limitation of this study is that only the patients reoperated for their recurrence within our hernia clinic were analyzed. Literature points out true recurrence rates are difficult to obtain, and currently reoperation rates are used as a proxy for recurrence rates, under the assumption recurrences occur up to twice as common as reoperations.[16] Within the time frame of this study, more recurrences may have developed that have not presented at the outpatient clinic, were not reoperated or were possibly reoperated in another center. The characteristics of these possible recurrences remain unknown.

The recommendations regarding primary TEP repair and the operative procedure for recurrent hernias that could be formulated based on these study results are mainly in line with the current guidelines for (endoscopic) inguinal hernia repair.[7-11] In case of primary large direct and bilateral defects, mesh fixation should be considered. The entire hernia floor should be thoroughly inspected with mandatory performance of lipoma removal, in case of indirect hernias in particular, to minimalize overlooked hernias and/or lipomas at TEP repair. For recurrent hernias after previous posterior (TEP) inguinal hernia repair, an anterior approach is recommended, where it remains important to act on peroperative findings and to avoid unnecessary operative steps in case no true hernia recurrence is found.

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7

Bilateral endoscopic totally extraperitoneal (TEP) inguinal hernia repair does not impair male fertility

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Abstract

Background

Endoscopic totally extraperitoneal (TEP) hernia repair with polypropylene mesh has become a well-established technique. However, since the mesh is placed in close contact with the spermatic cord, mesh-induced inflammation may affect its structures, possibly resulting in impaired fertility. The aim of this observational prospective cohort study was to assess fertility after bilateral endoscopic TEP inguinal hernia repair in male patients.

Methods

Fifty-seven male patients (22-60 years old) with primary, reducible, bilateral inguinal hernias underwent elective bilateral endoscopic TEP hernia repair with use of polypropylene mesh. The primary outcome was testicular perfusion; secondary outcomes were testicular volume, endocrinological status, and semen quality. All patients were assessed preoperatively and 6 months postoperatively.

Results

Follow-up was completed in 44 patients. No statistically significant differences in measurements of testicular blood flow parameters or testicular volume were found. Postoperative LH levels were significantly higher [preoperative median 4.3 IU/L (IQR 3.4-5.3) versus postoperative median 5.0 IU/L (IQR 3.6-6.5), p=0.03]. Levels of inhibin B were significantly lower postoperatively [preoperative median 139.0 ng/L (IQR 106.5-183.0) versus postoperative median 27.0 ng/L (IQR 88.3-170.9), p=0.01]. No significant changes in FSH or testosterone levels were observed. There were no differences in semen quality.

Conclusion

Our data suggest that bilateral endoscopic TEP hernia repair with polypropylene mesh does not impair fertility, as no differences in testicular blood flow, testicular volume or semen quality were observed. Postoperative levels of LH and inhibin B differed significantly from preoperative measurements, yet no clinical relevance could be ascribed to these findings.

Background

Inguinal hernia repair is the most commonly performed general surgical procedure worldwide, with a lifetime risk of developing an inguinal hernia of 27% for men and 3% for women.[1] There has been a considerable reduction in recurrence rates since the introduction of tension-free mesh repair, which has now become standard practice.[2] Endoscopic totally extraperitoneal (TEP) hernia repair, based on the concept of strengthening the weak inguinal floor by reducing the sac and placing preperitoneal mesh, has become increasingly popular, since this approach provides faster recovery and lower incidence of postoperative (chronic) pain compared to open techniques.[3-5]

Hypothetically, mesh-induced fibrosis or direct iatrogenic damage may affect the structures of the spermatic cord and impair testicular function and fertility. Rare but potentially harmful complications that may occur after hernia surgery include ischemic orchitis, testicular atrophy, or obstructive azoospermia.[6] Several experimental animal studies and case reports have described patients with these complications after open hernia repair with implantation of polypropylene mesh.[7-10] A systematic review on male infertility following inguinal hernia repair was recently conducted; however, the majority of procedures were open (99.5%) and unilateral (>80%).[11] Men undergoing bilateral mesh hernia repair or unilateral hernia repair with pre-existing impairment of the contralateral testis are considered to be at greatest risk of fertility impairment, but relevant large and prospective clinical trials on endoscopic bilateral hernia repair are lacking.

The objective of this study was to evaluate the effect of endoscopic bilateral TEP inguinal hernia repair on male fertility by analyzing testicular perfusion and volume, semen analysis, and endocrinological status.

Methods

Patients

This observational, prospective study was conducted on male patients (22-60 years old) with primary bilateral inguinal hernias at the Department of Surgery in a high-volume hospital in the Netherlands specializing in the TEP technique for inguinal hernia repair (Diakonessenhuis Utrecht/Zeist). The aim of this study was to evaluate male fertility preoperatively and 6 months after bilateral TEP inguinal hernia surgery. The study was approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, The Netherlands) and the hospital's Ethics Board, and it was registered in the Netherlands National Trial Registry (NTR-2208). Written informed consent was obtained from all participants.

Patients eligible for inclusion were men of fertile age (18-60 years old) with primary, bilateral inguinal hernias who were scheduled for elective endoscopic Totally Extraperitoneal (TEP) hernia repair. Patients with an ASA classification >III, recurrent and/or femoral/scrotal hernias, a medical history of testicular pathology, pelvic surgery or radiotherapy, known fertility problems, co-morbidity associated with possible fertility problems and use of medication that might impair fertility were excluded from participation (*table 1)*. Participants were recruited at their first visit to the outpatient clinic and enrolled after signing informed consent. Preoperative patient data (age, medical history, smoking habit, and body mass index (BMI)) were obtained through measurements and a general questionnaire.

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• Male gender • Age ≥ 18 and ≤ 60 years • Primary, reducible inguinal hernias • Bilateral hernias • Eligible for TEP (and therefore for general anaesthesia)	• Female gender • Age ≥ 60 years • Period of high fever prior to semen analysis • Recurrent inguinal hernias • Unilateral hernias • Hydrocele and/or varicocele • Femoral or scrotal hernia • Incarcerated hernia • ASA classification ≥ III • Previous medical history of: - Testicular infarction - Testicular torsion - Cryptorchidism - Inguinal, scrotal, testicular or prostate surgery - Vasectomy - Radiotherapy of pelvic region - Diabetes Mellitus - Cystic Fibrosis - Fertility problems and/or treatment, erection disorders or (other) problems in sexual function - Use of gonadotropins - Use of anabolic steroids

Surgical procedure

Patients underwent simultaneous bilateral endoscopic TEP inguinal hernia repair with use of a double-mesh implantation technique. The procedure was performed under general anaesthesia. Two identical polypropylene meshes (Prolene, 10x15 cm) were positioned in a tension-free manner in the preperitoneal space. The mesh graft was not fixed to avoid possible entrapment neuralgia. Nyhus classification, operative time and intra-operative complications were recorded during surgery. Surgeons with extensive expertise in this procedure (>500 procedures per surgeon) performed all operations. The operation and perioperative care did not differ from those of patients not participating in the study.

Postoperative management and follow-up

Patients were discharged on the day of surgery, unless complications prohibited early discharge. Duration of hospital stay and postoperative complications were recorded. Patients were advised to take pain medication as needed (paracetamol, and if necessary, diclofenac) and to avoid strenuous physical activity (such as lifting and sports) during the first postoperative week. The routine follow-up schedule after TEP hernia repair in our centre was followed: patients were followed-up by telephone 6 weeks after surgery and were scheduled for an additional visit to the outpatient clinic in case of complaints. Six months postoperatively, all participants visited the outpatient clinic for assessment of fertility parameters.

Outcome measures

Male fertility parameters were assessed preoperatively on the day of surgery and 6 months postoperatively by means of bilateral scrotal ultrasonography, semen analysis, and biochemical analysis. The primary outcome of this study was testicular perfusion, and secondary outcome measures were testicular volume, semen quality, and serum endocrinological status.

Testicular perfusion and volume

Bilateral testicular perfusion and volume were determined by measuring the blood flow velocity (cm/s) by Color Doppler ultrasonography (CDUS) and Gray scale ultrasonography, respectively. Measurements were performed by experienced ultrasound technicians, who received specific instructions for the purpose of this study. The patient was placed in the supine position and the penis was held suprapubically.

For testicular perfusion, blood flow was measured at four different points: the inguinal and extratesticular-intrascrotal level of the testicular artery, the capsular arteries, and the intratesticular arteries. The parameters assessed were end diastolic velocity (EDV), peak systolic velocity (PSV), resistive index (RI), pulsatility index (PI), and acceleration time (ATA). To improve intraobserver reliability, each parameter was measured three different times and the mean value was calculated. Possible signs of distension of the epididymis and/or vas deferens, as well as formation of a thrombus in the pampiniform plexus, were also assessed.

To determine testicular volume, length, width and height were measured separately, and the ultrasonography device performed a volume calculation with these dimensions.

Semen analysis

For semen analysis, seminal volume (mL), sperm concentration (10^6 cells/mL), motility (% progression), VCM (volume x concentration x progressive motility), and pH were analyzed.

Semen was obtained in our hospital by means of masturbation after which the sample was analyzed within an hour. Patients were instructed to remain abstinent for 48-hours so that reliable semen samples could be obtained.

Biochemical analysis

Endocrinological status was assessed by determining serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH) and testosterone. Inhibin B serum level was also collected. Blood samples were obtained and analyzed in our hospital.

Statistical Analysis

Statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY). Differences in preoperative and postoperative fertility parameters were analyzed by means of the paired sample T-test (parametric data) or the Wilcoxon signed-rank test (non-parametric data). Comparison of preoperative and postoperative measurements of testicular perfusion and volume were done separately for the left and right testes. In case of a statistically significant difference in blood hormone levels, an additional calculation with the reference change value (RCV) formula was performed. The RCV formula incorporates analytical variation and intra-individual biological variation, and the difference in hormone level must exceed the RVC to be clinically significant [12]. A p-value <0.05 was considered statistically significant.

Results

Fifty-seven consecutive patients were recruited and operated on between March 2010 and March 2016 (*table 2)*. The median age of the study population was 51 years (range 22-60 years). One patient with a history of appendicitis complicated by abscess formation had multiple adhesions, leading to bladder perforation intraoperatively, which was managed conservatively with an indwelling catheter. Two patients were clinically diagnosed with a recurrent hernia and underwent an additional operation: one patient developed an early recurrence 5 days after surgery, the other 4 months after surgery. Two patients required an additional visit to the outpatient clinic due to pain. Ultrasonography showed postoperative hematomas in both patients, and the pain subsided with conservative treatment. No readmissions after discharge from the hospital were reported.

In total, 44 patients (78.6%) completed the follow-up period of 6 months. One patient was excluded since he was not able to obtain semen preoperatively. One patient who was only experiencing symptoms in the right inguinal region requested a change to unilateral intervention hours before surgery. Eight of the patients withdrew their consent, and 3 of the patients could not be reached for follow-up, despite multiple attempts by telephone and e-mail.

Table 2. Patient and treatment characteristics (n=57)

Age (years)	51.0 (42.0-56.2)
BMI (kg/m^2)	24.7 (23.0-27.3)
ASA classification (%)	
I	76.8
II	22.8
Smoking (%)	
No	82
Yes	18
Type of hernia (%)	
Left, medial	53.6
Left, lateral	46.4
Right, medial	49.1
Right, lateral	50.9
Operation time (min)	28.0 (24.5-31.5)
Intraoperative complications (%)	
Bladder injury	1.8
Conversion rate (%)	0
Postoperative complications (%)	
Hematoma	3.6
Recurrence	3.6

Continuous data are presented as median (interquartile range).

Testicular perfusion and volume

There were no significant changes in PSV, EDV, RI, PI and AT between pre- and postoperative measurements of testicular perfusion at all levels of both sides (*table 3)*. There was an increase in the PSV and EDV of the left intratesticular arteries from preoperative to postoperative assessment that trended towards significance. A thrombus in the right-sided pampiniform plexus was observed in 1 patient preoperatively and 3 patients postoperatively. None of the patients had a thrombus in the left pampiniform plaxus on preoperative assessment; postoperatively, this finding was present in 3 patients.

Analysis of bilateral testicular volume showed no significant differences between pre- and postoperative measurements.

Table 3. Testicular perfusion and volume (n=44)

	Preoperative		*Postoperative*		*p value*	
	Left	**Right**	**Left**	**Right**	**Left**	**Right**
Perfusion testicular artery (ing)						
PSV (cm/s)	15.5 (10.1-22.4)	15.9 (11.1-24.8)	15.5 (10.1-21.4)	14.4 (9.8-19.9)	0.80	0.52
EDV (cm/s)	2.3 (1.8-3.0)	2.4 (1.7-3.4)	2.0 (2.0-3.7)	2.5 (1.6-3.4)	0.12	0.51
RI	0.8 (0.7-0.9)	0.8 (0.8-0.9)	0.8 (0.8-0.9)	0.8 (0.7-0.9)	0.09	0.52
PI	2.2 (1.5-2.8)	2.6 (2.0-3.3)	2.4 (1.9-2.8)	2.5 (1.8-3.1)	0.97	0.78
AT (ms)	131.1 (76.3-248.7)	162.0 (6.,3-238.8)	150.0 (83.0-217.0)	140.0 (80.0-213.0)	0.83	0.85
Perfusion testicular artery (scrt)						
PSV (cm/s)	12.2 (9.0-14.5)	10.6 (8.7-14.7)	11.1 (8.6-16.3)	11.8 (8.3-14.4)	0.68	0.89
EDV (cm/s)	2.5 (1.8-3.5)	2.3 (1.7-3.4)	2.4 (1.7-3.6)	2.6 (2.0-3.7)	0.76	0.36
RI	0.8 (0.7-0.8)	0.8 (0.7-0.8)	0.8 (0.7-0.8)	0.8 (0.7-0.8)	0.67	0.62
PI	1.9 (1.6-2.2)	1.8 (1.4-2.2)	1.8 (1.5-2.6)	1.9(1.4-2.5)	0.88	0.34
AT (ms)	79.0 (57.0-123.6)	80.0 (48.0-122.0)	86.0 (56.4-137.0)	76.3 (49.8-123.2)	0.93	0.23
Perfusion intracapsular arteries						
PSV (cm/s)	9.4 (7.5-13.0)	9.2 (6.6-10.7)	9.1 (6.8-11.2)	10.0 (7.0-12.6)	0.28	0.51
EDV (cm/s)	3.1 (1.9-4.1)	3.0 (1.9-3.5)	2.9 (1.9-4.0)	3.0 (1.9-3.9)	0.87	0.38
RI	0.7 (0.6-0.7)	0.7 (0.6-0.7)	0.7 (0.6-0.7)	0.7 (0.6-0.7)	0.68	0.84
PI	1.4 (1.0-1.7)	1.4 (1.1-1.8)	1.4 (1.1-1.6)	1.3 (1.1-1.8)	0.31	0.39
AT (ms)	53.0 (36.2-78.0)	47.3 (29.3-71.4)	49.1 (36.5-72.7)	52.3 (32.7-88.6)	0.26	0.73
Perfusion intratesticular arteries						
PSV (cm/s)	6.7 (5.0-8.8)	5.6 (4.0-8.0)	7.7 (4.8-11.3)	6.1 (4.6-10.2)	0.07	0.11
EDV (cm/s)	2.5 (1.8-3.4)	2.4 (1.3-3.0)	3.1 (2.1-4.2)	2.4 (1.8-3.3)	0.05	0.28
RI	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.86	0.49
PI	1.0 (0.8-1.4)	1.1 (0.8-1.5)	1.1 (0.9-1.3)	1.1 (0.8-1.3)	0.62	0.37
AT (ms)	31.1 (17.7-43.1)	24.0 (14.0-31.3)	34.5(25.1-52.0)	25.9 (19.3-45.0)	0.12	0.44
Testicular volume (mL)	15.5 (11.8-18.8)	16.5 (12.8-19.8)	15.4 (11.9-18.6)	17.4 (12.9-20.3)	0.14	0.95

Data are displayed as median (interquartile range). ing: inguinal level, scrt: scrotal level, PSV: peak systolic velocity, EDV: end diastolic velocity, RI: resistive index, PI: pulsatility index, AT: acceleration time

Endocrinological status

Comparison of blood hormone values revealed higher LH levels postoperatively with a median value of 5.0 IU/L (IQR 3.6-6.5) compared to 4.3 IU/L (IQR 3.4-5.3) (*table 4)*. Both measurements were within the LH reference range of 1.3-13.0 IU/L. There were no significant differences in FSH or testosterone levels. Levels of inhibin B were significantly lower postoperatively with a preoperative median of 139.0 ng/L (IQR 106.5-183.0) versus a postoperative median of 127.0 ng/L (IQR 88.3-170.9); however, both measurements were within the reference range (<400ng/L).

Semen quality

We did not find statistically significant differences in semen volume, concentration, motility, VCM, or pH after bilateral TEP inguinal hernia repair (*Table 4)*.

Table 4. Endocrinological status and semen analysis (n=44)

	Preoperative	***Postoperative***	***p value***
Endocrinological status			
LH (IU/L)	4.3 (3.4-5.3)	5.0 (3.6-6.5)	0.03
FSH (IU/L)	5.0 (3.5-7.1)	5.0 (3.3-7.0)	0.99
Testosterone (nmol/L)	15.1 (11.9-19.9)	14.7 (10.4-19.4)	0.14
Inhibin B (pg/mL)	139.0 (106.5-183.0)	127.0 (88.3-17.,9)	0.01
Semen quality			
Volume (mL)	3.0 (2.0-3.5)	3.0 (1.7-4.0)	0.74
Concentration (10^6 cells/mL)	49.0 (22.3-90.3)	39.0 (11.8-82.3)	0.21
Motility (% progression)	41.5 (24.5-58.0)	42.0 (26.3-59.3)	0.86
VCM (10^6)	51.5 (20.0-133.0)	28.5 (14.3-121.3)	0.29
pH (mol/L)	7.7 (7.5-8.0)	7.7 (7.5-7.7)	0.87

Data are presented as median (IQR). LH: luteïnizing hormone, FSH: follicle-stimulating hormone, VCM: volume x concentration x progressive motility

Discussion

The present study shows no impairment of fertility 6 months after bilateral endoscopic TEP inguinal hernia repair. Polypropylene, the biomaterial most commonly used in mesh hernia repair, has good mechanical stability and induces an acute inflammatory reaction followed by a chronic foreign body fibroblastic reaction, which is essential for optimal fixation and incorporation of the biomaterial in the abdominal wall.[13] During the TEP procedure, the mesh is placed in close contact with the vas deferens, testicular vessels, autonomic nerves, and fascia. Injuries to the vas deferens and/or spermatic vessels may be a result of direct

iatrogenic injury by dissection of the preperitoneal space, or delayed obstruction caused by scar tissue from the mesh-induced inflammatory tissue response, which is part of the normal healing process .[9,14]

We did not observe significant differences in testicular perfusion or volume 6 months after bilateral mesh hernia repair. Blood supply through the spermatic vessels was assessed in this study using CDUS, a well-documented procedure for investigating testicular vascularization and perfusion.[15] Due to interdependence of flow within an arterial network, we measured the blood flow on testicular, intracapsular and intratesticular levels to avoid false normal results from partial measurements. On CDUS measurements, the RI and PI are used for interpretation of vascular resistance and tissue perfusion. When testicular perfusion is disrupted, a decrease in end diastolic pressure and an increase in RI and PI can be seen, with an elevated RI suggestive of ischemia.[16] While we did not find significant changes in blood flow parameters for left and right testicular perfusion, we did observe a trend towards significance in higher PSV and EDV values of the left intratesticular arteries. However, RI and PI ratios calculated from the PSV and EDV were not significantly different, so we did not regard these differences as clinically relevant.

Since the start of our study, several other studies have investigated the effect of endoscopic mesh hernia repair on testicular perfusion and volume.[17-23] Results of these studies may be divided into early postoperative (1-7 days after surgery) and late postoperative (3 months-3 years after surgery) categories. With respect to early postoperative results of testicular perfusion, Stula et al. demonstrated an increase in PSV at the testicular, capsular and intratesticular level, and higher RI and PI ratios of the intratesticular artery 2 days after laparoscopic TAPP hernia repair, which normalized in the late postoperative period after 5 months.[17] While not statistically significant, Lal et al. demonstrated a trend of increased RI of testicular, capsular and intratesticular arteries 1 day after laparoscopic TEP repair, which then decreased to preoperative values 7 days after surgery.[18] Ersin et al. noticed a significant decrease in RI of capsular and intratesticular arteries and an increase in PSV and EDV of the capsular artery on postoperative day 1 that normalized 1 week after the operation.[19] In summary, the findings of these studies suggest only a transient change in testicular perfusion in the early postoperative period. The results might be influenced by hypervascularity and edema of the testes and epididymis, as these are known to occur in the early postoperative period. Thus, the short term effects on perfusion appear to be a result of the operation itself rather than the fibroblastic tissue response, which would be expected to have more long term effects. In concordance with our study, the studies that assessed testicular perfusion between 3 months and 3 years after mesh hernia repair did not find clinically relevant changes in testicular blood supply.[20-23]

Since interruption of the testicular blood supply may result in testicular atrophy, testicular volume was also taken into account, and we found no significant differences in our study population. Akbulut et al. found a significant decrease in testicular volume after TEP hernia repair; however, postoperative testicular volume remained within normal limits, and this finding was not considered as testicular atrophy.[24] This study did not assess testicular perfusion.

Thrombosis of the pampiniform plexus may result from overzealous dissection of the cord or excessive use of cauterization intraoperatively, or from pressure exerted by a large hematoma in the groin postoperatively, but might also be the result of pressure from a large hematoma in the groin postoperatively.[25] Pampiniform plexus thrombosis may cause venous outflow obstruction and testicular infarction. Although a few patients had plexus pampiniformis thrombi on scrotal ultrasound, we did not observe testicular infarction in our study population. In our opinion, it is more likely that these thrombi are the result of postoperative hematoma or are not even related to the surgical intervention.

Six months postoperatively, significantly higher blood levels of LH and lower blood levels of Inhibin B were found. LH, also called interstitial cell-stimulating hormone in males, stimulates secretion of the steroid hormone testosterone by Leydig cells.[24] High levels of LH could indicate testicular dysfunction due to decreased testosterone production. In the case of low testosterone, hypothalamic secretion of GnRH and hypophysic secretion of LH and FSH would be stimulated to increase spermatogenesis. However, FSH was not increased in our study. Furthermore, when applying the reference change value (RCV) for LH, which takes biological and analytic variations between separate measurements into account, LH levels did not increase significantly. Inhibin B, secreted by the Sertoli cells, inhibits production of FSH, thereby leading to decreased spermatogenesis. However, levels of FSH did not differ significantly, and the RCV volume showed that the decrease in inhibin B was not significant. Taking these factors into consideration, we did not regard the isolated higher levels of LH and decreased levels of inhibin B as clinically relevant. Our findings on LH, FSH, and testosterone levels are in line with other studies that analyzed blood hormone levels after endoscopic inguinal hernia repair and did not find significant changes in endocrinological parameters in the early postoperative to 6 months postoperative period.[18,22,24] Inhibin B has, to our knowledge, not been investigated in this context before.

Semen analysis can be used as a parameter for seminal tract patency or obstruction. No significant differences in semen volume, concentration, motility, or pH were found after TEP hernia repair. Several other studies performed semen analysis after endoscopic inguinal hernia repair.[17,21-22,26] Only the study conducted by Peeters et al. found a significant decrease

in one of the parameters assessed in semen.[21] In this trial, where quality of life and fertility analysis after laparoscopic inguinal hernia repair were compared between patients who received a lightweight (Vypro II, TiMesh) versus a heavyweight (Marlex) mesh, sperm motility was decreased at 1-year follow-up in the lightweight group. This decrease in sperm motility could not be confirmed in a long-term follow-up of 3 years.[23] The clinical relevance of this isolated decreased sperm motility is not entirely clear, as fertility depends on several factors and all other sperm parameters remained within normal limits.

To our knowledge, this study represents the first clinical prospective trial assessing testicular perfusion and volume, endocrinological status, and semen quality after endoscopic TEP inguinal hernia repair in a human patient population comprised solely of bilateral hernia repairs. This study design ensured that a healthy contralateral side did not positively influence our results. More than 80 percent of studies that have been performed on male fertility after inguinal hernia repair consisted of unilateral repairs.[11] Studies involving bilateral inguinal hernia repairs often had mixed populations of uni- and bilateral hernias, did not involve TEP hernia repair, had relatively small numbers of patients, or measured different outcome parameters. Since we are an expertise TEP hernia center, our patient population involved only bilateral TEP hernia repairs, making our results not applicable to other frequently performed preperitoneal techniques. However, since clinical outcomes of laparoendoscopic techniques are similar, we do not expect differences in fertility outcomes between TEP and TAPP. In open preperitoneal operations such as TIPP and TREPP mesh placement and possible damage to the vas are theoretically comparable with laparo-endoscopic techniques. However, longterm outcomes of these techniques have not been studied thoroughly and there is insufficient evidence to recommend these techniques for primary (bilateral) inguinal hernia repair. With regard to frequently performed open techniques with anterior mesh placement (Lichtenstein), we would like to recommend performing a study similar to ours. Even though studies evaluating fertility after Lichtenstein repair demonstrated good results with low rates of infertility-related complications, no prospective study had a patient population consisting of bilateral inguinal hernia repairs only.[11]

A limitation of this study is the relatively small sample size and the high percentage of loss-to-follow-up. Participant enrollment was slow due to the fact that many patients had been previously sterilized or were not willing to participate due to the study needs (two times scrotal ultrasonography and collection of semen, additional visit to the hospital after surgery) , therefore we closed the study prematurely after 6 years. However, the sample size that we initially calculated (76 patients) was based on 2 studies with very small patient numbers.[27] Also, the size of our patient population is comparable to the previously mentioned studies that assessed fertility.

In this study, we did not assess early postoperative effects on fertility, therefore we may have missed significant changes in early testicular perfusion, endocrinologal status, or sperm quality that have been shown in other studies. However, we regard the long term outcomes as clinically relevant, since the early postoperative effects can be attributed to the impact of the surgical intervention itself and its natural postoperative course.

Since it is assumed the mesh-related inflammatory reaction subsides after 6 months, we deliberately chose our follow-up period at this time point.[28] After this time interval it is not likely to expect any decrease of perfusion or other late delayed complications impairing fertility. This is in accordance with the long-term follow-up study of Peeters et al., where no significant changes in testicular volume or flow and no other fertility-related complications were reported until 3 years after TEP inguinal hernia repair.[23]

In conclusion, the available data suggest that there are no clinically relevant long-term effects of endoscopic bilateral TEP hernia repair on fertility. Based on our current results, we think bilateral TEP inguinal hernia repair can be safely performed in men of fertile age.

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8

One-stop routing for surgical interventions; a cost-analysis of endoscopic inguinal hernia repair

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Submitted

Abstract

Background

Single-visit (SV) totally extraperitoneal (TEP) inguinal hernia repair is an efficient service without impairment of safety or complication rate. Data on the economic impact of this approach are rare. The aim of this study was to compare the costs between the SV TEP and the regular TEP in an employed healthy population from a hospital and societal point of view.

Methods

Retrospectively collected hospital costs and prospectively collected societal costs were obtained from patients treated between July 2016 and January 2018. Outcome measures consisted of all documented institutional care, productivity loss and medical consumption.

Results

For analysing the hospital costs a total of 116 SV patients were matched to 116 regular patients. The hospital costs of a mean SV patient were €1148.80 compared to €1267.60 for a regular patient, with a mean difference of €118.80. Prospective analyses of 50 SV patients and 50 regular patients demonstrated higher societal costs for a mean regular patient (€2188.87) compared to a mean single visit patient (€1629.78). The mean total cost difference between a SV TEP repair and a regular TEP repair equalled €677.89 corresponding to a 19.6% decrease in costs.

Conclusion

This comprehensive cost-analysis showed that in an employed, healthy population, the SV TEP repair outprices the regular TEP repair, with savings of €678.00 per patient, reflecting a 19.6% decrease in costs. This routing is mainly interesting from a societal point of view as the difference is mainly impacted by a decrease in societal costs.

Background

In the current era where health care costs maintain to rise and the health-care budget is increasingly restricted, it is a challenge to attain maximal health benefit that is not only cost-effective, but also provides patient satisfaction.[1] In order to achieve this aim and reflect interest of society on all stakeholder groups, clinical pathways are integrated with increasing frequency.[2-4.] Given that groin hernia repair is one of the most commonly performed surgical procedures (more than 20 million worldwide and an estimated 28 000 procedures in the Netherlands annually[5]), a small improvement in care regarding hernia surgery can consequently lead to a big enhancement of health care outcomes.[6,7]

Nowadays several surgical specialties aim to achieve improvement for different surgical procedures, by combining the traditionally separate preoperative evaluation, diagnostics and subsequent operation into one single visit (one-stop shop).[8-12] The hernia clinic of the Diakonessenhuis Utrecht/Zeist provides a corresponding pathway for inguinal hernias and started to offer single-visit (SV) endoscopic totally extraperitoneal (TEP) hernia repair since 2010. Results of a recently conducted study have demonstrated that this service appears to be a suitable option, with a high level of patient satisfaction and without impairment of safety or complication rate.[13]

Reducing health care costs through accelerating treatment, minimalizing hospital visits, and providing a rapid return to work has a strong intuitive appeal, however studies on the actual impact of this approach on reducing total health care costs have never been published. The aim of this study was to widen the current knowledge of economic impact by assessing the costs of SV endoscopic TEP hernia repair compared to regular TEP hernia repair. In order to provide a comprehensive view, both hospital costs and costs outside the hospital (societal costs; consisting of productivity loss and medical consumption) were assessed.

Methods

Study design

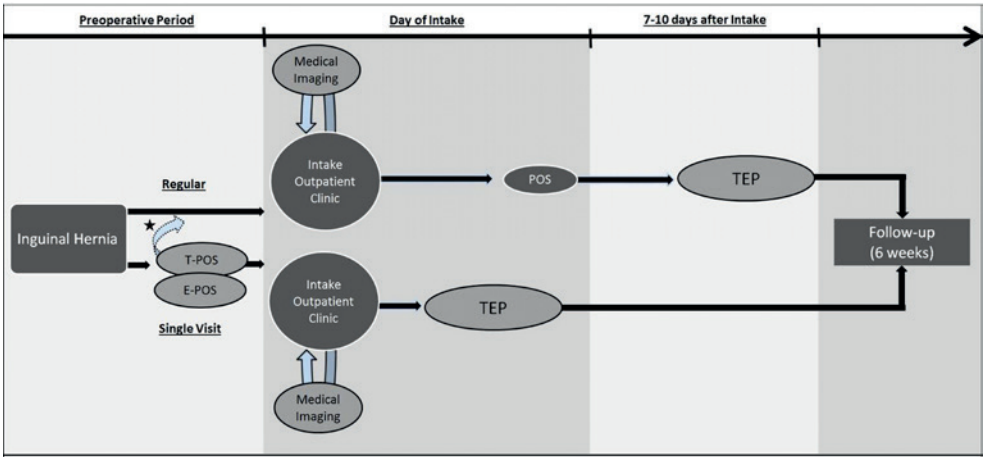
The study was carried out in the Hernia Clinic of the Diakonessenhuis Zeist, a high-volume hernia center focusing on TEP inguinal hernia repair. In this center over 1200 procedures are performed annually, of which up to 15% involve SV repair.

This cost-analysis compared SV TEP hernia repair to regular TEP hernia repair and consisted of two analyses. In a retrospective analysis of patients treated between July 2016 and May 2017, the hospital costs were compared. In a prospective analysis of patients treated between July 2017 and January 2018, societal costs were compared.

Single-visit routing

Patients received information regarding the SV TEP repair through the website of the hernia clinic or through their general practitioner (GP). When the patient contacted the hernia clinic, a telephone preoperative screening (T-POS) assessing eligibility for SV TEP hernia repair was conducted by the department's secretary. After approval of eligibility for the SV procedure, patients filled out a questionnaire, which was sent to the anaesthesiology department as an electronic alternative for the pre-operative screening (E-POS). After the E-POS was approved, the surgical intake and TEP hernia repair were scheduled for the same day (*figure 1)*. Detailed data on the recruitment process and patient routing within the SV hernia clinic have been described previously.[13]

Figure 1. Timeline cost analysis



★Only if a patient appears to be not eligible based on pre-operative screening. T-POS: telephone preoperative screening (by the secretary), E-POS: electronic preoperative screening (by the physician assistant, POS: physical preoperative screening (anesthesiologi

Regular routing

Patients referred through their GP for a regular TEP, first had their surgical intake at the outpatient clinic. If the surgeon confirmed a groin hernia, the pre-operative screening (POS) was conducted on the same day. After approval the TEP was planned within 7-10 days (Figure 1).

Patients

The target population for this analysis consisted of employed men and women, aged between 18 and 65 years old with a primary unilateral inguinal hernia (*table 1*). For the hospital costs, all patients who underwent a single visit TEP between July 2016 and May

2017 were retrospectively identified and matched in terms of age, sex and BMI to patients who underwent a regular TEP procedure. As for the societal costs, patients who underwent a single visit TEP between July 2017 and January 2018 and all eligible patients who underwent a regular TEP repair in this period, were prospectively analysed.

Table 1. Eligibility Criteria Single Visit

Inclusion
- Age 18- 65 years
- Employed
- Primary unilateral inguinal hernia confirmed by GP
- ASA I or II
Exclusion
- Use of anticoagulans
- Diabetes mellitus (exception of good glycemic control)
- Cardial, pulmonary or other high risk disorders (ASA III/IV)
- Employed in animal husbandry (high risk MRSA)
- Foreign hospitalization in the last 3 months

GP:General Practitioner, ASA:American Society of Anesthesiologists, MRSA:methicillin-resistant Staphylococcus Aureus

Surgical procedure

The applied surgical technique in all patients was the endoscopic TEP repair with implantation of a polypropylene mesh (Prolene®, 10x15cm). Procedures were performed under general anaesthesia. Fixation of mesh was not routinely performed. Further surgical details on the TEP repair have been described in previous literature.[14] Procedures were carried out by five experienced surgeons specialised in TEP hernia repair (>1000 procedures per surgeon).The operation and the perioperative care were standardized and did not differ between the SV and the regular group.

Postoperative management and follow-up

There was no difference in postoperative management between the two cohorts compared. Discharge took place on the day of surgery, unless complications prohibited early discharge. At discharge, patients were advised to take pain medication during the first days and abstain from strenuous physical exercise during the first week. Follow-up took place by telephone, 6 weeks after surgery, according to a fixed schedule. In case of physical complaints an additional visit to the outpatient clinic was planned.

Outcome measures

The primary outcomes of this study were hospital costs and societal costs. The costs were valued, using a top-down approach in which all relevant cost components were identified and valued for the average patient by separating out costs from a comprehensive resource such as annual accounts.[15]

Hospital costs

To obtain standardized hospital cost estimates, the Dutch Manual for Costing was used for all documented care according to the International Classification of Diseases (ICD-10).[16] The costs of an inpatient day included both direct costs (e.g. nursing costs and medical materials) and indirect costs (e.g. accommodation and overheads). For some specific SV costs, such as the T-POS and E-POS, no ICD-10 codes were assigned or no reference price was available. Hence it was necessary to calculate these costs based on the average time it took for a secretary (15 minutes) or physician assistant (5 minutes) to screen a patient. Furthermore, there was no reference price for the TEP hernia repair, therefore we took the published price of a recent study in a setting comparable to ours.[17] The costs for medical staff members were calculated by multiplying the mean operative time of 20.3 minutes (as described in a previous publication[13]) with the standardized patient-related hourly wage of a Dutch medical specialist.[16] Costs in euros per item are shown in table 2.

Table 2. Costs per item

Cost Item	Costs (€)
Intake	91,00
Groin ultrasound	80,00
POS	91,00
T-POS	5,65
E-POS	7,50
TEP repair	484,90
Wage Surgeon	39,00
Wage Anaesthesiologist	39,00
Inpatient Day	405,00
Telephone Consultation	17,00
Physical Consultation	91,00

POS: preoperative screening, T-POS: telephone preoperative Screening, E-POS: electronic preoperative screening, TEP = totally extraperitoneal

Societal costs

The societal costs were based on productivity and medical consumption. Two validated questionnaires were used; the productivity cost questionnaire (iPCQ) and the medical consumption questionnaire (iPMQ). Regarding productivity, lost workdays and underperformance were extracted until 6 weeks after surgery and converted to costs based on the average (male) Dutch wage of €37.90 an hour (net income 2017). Given that every patient of the regular cohort had an intake in the weeks before the operation, half a lost workday was added for every regular patient. Medical consumption, travel expenses, pharmaceutical consumption and additional consultations of primary and secondary care were all extracted until 6 weeks after surgery and translated into costs. To obtain travel expenses, we multiplied the average distance to the hospital (7 km) by the tax-free reimbursement of €0.19 per kilometre and added €3.00 parking costs, based on the average car parking charges at hospitals.[16] Pharmaceutical prices were based on current chain pharmacy cash pricing.[18] We took the average of the highest and lowest price. As for the additional consultations, a standardized consultation with a general practitioner was set at €33.00 with a standardized traveling distance of 1,1 km, which implies travel expenses of (2.2 x €0.19 =) €0.42.[16] Ambulance charges were set at €515.00. For some specific costs the reference price was unknown. In this case costs were estimated based on requested charges from health insurance companies and charges found on the internet. Thus, a consultation with a company doctor was set at €80.00, homeopathic care charges were set at €88.00 and blood tests in primary care setting were set at €9.15 (haemoglobin, white blood cells, C-reactive protein and erythrocyte sedimentation rate).

Results

Hospital costs

A total of 116 single visit patients were matched to 116 regular patients. The majority of patients in both groups were male (*table 3*). The median age, Body Mass Index (BMI) and American Society of Anesthesiologists (ASA) classification were similar between both groups.

The total hospital costs for the SV TEP group were €133260.80 whereas the total hospital costs for the regular TEP group were €147038.40, with a difference of €13777.60 (*table 4).* This equates to a mean SV TEP of €1148.80 (€1073.00 to €1586.00) and a mean regular TEP of €1267.60 (€1150.00 to €2 643.00) with a mean difference of €118.80 per patient, reflecting a 9.4% decrease in costs in favour of the SV analysis. The foremost causes of this decrease are the pre-operative screening, inpatient days and telephone consultations.

Table 3. Baseline characteristics of 232 retrospectively analysed patients (hospital costs)

	Single-visit (n=116)	**Regular** (n=116)
Male, n (%)	114 (98)	114 (98)
Age (years)	50 (40-57)	48 (42-55)
BMI (kg/m^2)	24 (23-27)	25 (23-26)
ASA, n (%)		
I	97 (84)	97 (84)
II	19 (16)	19 (16)
Smoking, n (%)		
Current smoker	17 (15)	23 (20)
Non-smoker	92 (81)	87 (76)
Ex-smoker	5 (4)	5 (4)
Occupation, n (%)		
Intense physical work	30 (27)	35 (30)
Light intensity work	33 (29)	23 (20)
Sedentary work	45 (40)	54 (47)
Different	5 (4)	2 (2)
Location of hernia, n (%)		
Unilateral (left)	51 (44)	55 (47)
Unilateral (right)	60 (52)	56 (48)
Bilateral	5 (4)	5 (4)
Hernia type, n (%)		
Lateral	87 (75)	85 (73)
Medial	17 (15)	24 (21)
Femoral	1 (1)	1 (1)
Medial (Bilateral)	4 (3)	3 (3)
Lateral (Bilateral)	1 (1)	1 (1)
Medial & Lateral	5 (4)	1 (1)
Lateral & Femoral	1 (1)	0 (0)

Continuous data are presented as median (interquartile range). BMI: body mass index; ASA:American Society of Anesthesiologists

Table 4. Uncomplicated and analysed hospital costs of a single-visit TEP and regular TEP

	Single-visit		Regular		Difference in analysed costs (Regular - SV)
	Uncomplicated costs	Analysed costs	Uncomplicated costs	Analysed costs	
Intake	€ 10.556,00	€ 10.556,00	€ 10.556,00	€ 10.556,00	€ 0,00
Ultrasound	€ 0,00	€ 80,00	€ 0,00	€ 480,00	€ 400,00
POS	€ 0,00	€ 0,00	€ 10.556	€ 10.556	€ 10.556
E-POS	€ 870,00	€ 870,00	€ 0,00	€ 0,00	-€ 870,00
T-POS	€ 655,40	€ 655,40	€ 0,00	€ 0,00	-€ 655,40
TEP repair	€ 56.248,40	€ 56.248,40	€ 56.248,40	€ 56.248,40	€ 0,00
Wage surgeon	€ 4.553,00	€ 4.553,00	€ 4.553,00	€ 4.553,00	€ 0,00
Wage anesthesiologist	€ 4.553,00	€ 4.553,00	€ 4.553,00	€ 4.553,00	€ 0,00
Inpatient day	€ 46.980,00	€ 52.650,00	€ 46.980,00	€ 55.890,00	€ 3.240,00
Blood test	€ 0,00	€ 65,00	€ 0,00	€ 265,00	€ 200,00
Telephone consultation	€ 1.972,00	€ 1.938,00	€ 1.972,00	€ 2.754,00	€ 816,00
Physical consultation	€ 0,00	€ 1.092,00	€ 0,00	€ 1.183,00	€ 91,00
Total costs	€ 126.387,80	€ 133.260,80	€ 135.418,40	€ 147.038,40	€ 13.777,60
Mean costs	€ 1.089,55	€ 1.148,80	€ 1.167,40	€ 1.267,60	€ 118,80

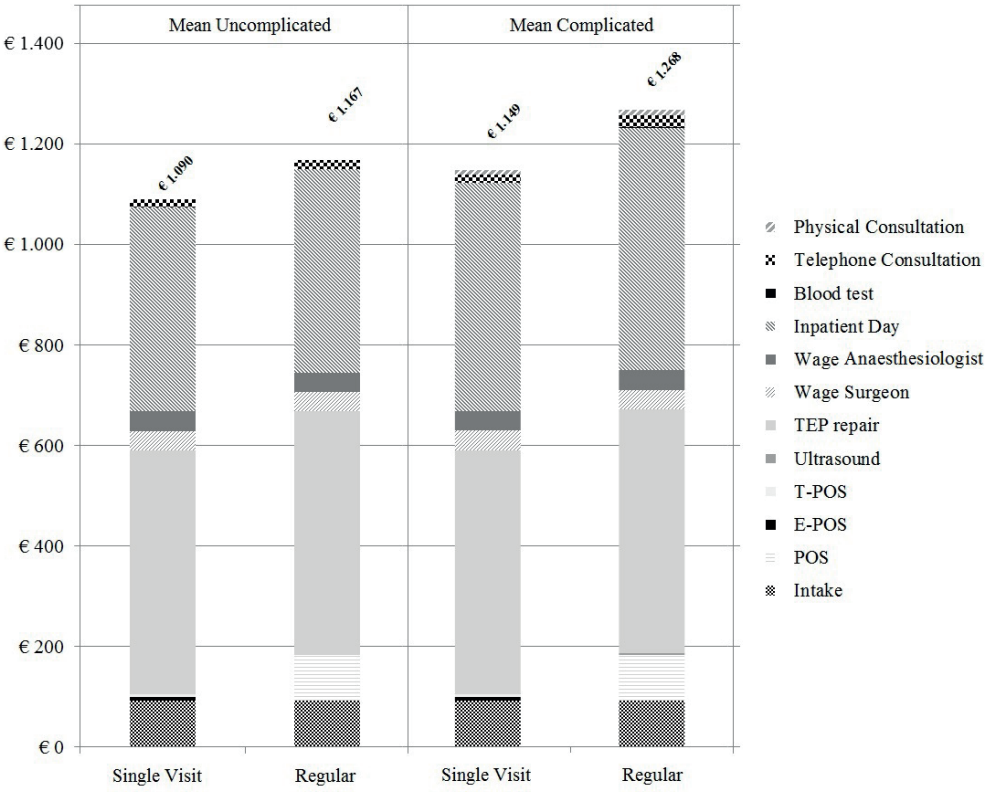
TEP: totally extraperitoneal, POS: preoperative screening, T-POS: telephone preoperative screening, E-POS: electronic preoperative screening, SV: single-visit

A standard SV TEP, without complications or extra consultations costed €1089.55 (*figure 2)*. The additional costs of the mean analysed SV TEP therefore equalled €59.25. A total of 31 patients (26.7%) made more hospital costs than the standard costs per SV patient, 73 patients (62.9%) were equal to the standard and in 12 patients (10.3%) less hospital costs were made (due to absence of follow-up by telephone after 6 weeks). A standard regular TEP, without complications or extra consultations costed €1167.40. The additional costs of the mean analysed regular TEP therefore equalled €100.20. A total of 47 patients (40.5%) made more hospital costs, 58 patients (50.0%) were equal to the standard and in 11 patients (9.5%) less hospital costs were made (due to absence of follow-up by telephone after 6 weeks).

Societal costs

A total of 50 eligible SV TEP patients were compared to 50 eligible regular TEP patients. The majority of patients in both groups were male (*table 5*). The median age, BMI and ASA were similar.

Figure 2. Mean institutional costs



TEP: totally extraperitoneal, T-POS: telephone preoperative screening, E-POS: electronic preoperative screening

Lost workdays and underproductivity

Twenty-seven patients (54%) in the single visit cohort indicated to have missed at least one day in the 6 weeks following the operation. This led to a total of 244 lost workdays including the day of operation, resulting in an amount of €73980.80. In the SV cohort, 14 patients (28%) reported 128 under-productive days, with a mean of 83% productivity. This equalled 22.2 lost workdays, resulting in an amount of €6731.04. In the regular cohort, 19 patients (38%) reported lost workdays after the operation, resulting in a total of 301 lost workdays (including day of operation & day of intake), which equalled an amount of €91263.20. A total of 130 under-productive days were reported by 14 patients (28%) in the regular group. With a mean productivity of 60%, this resulted in 52.2 lost workdays, equalling an amount of €15827.04.

Table 5. Baseline Characteristics of 100 prospectively analysed patients (costs outside hospital)

	Single-visit (n=50)	**Regular** (n=50)
Male, n (%)	49 (98)	46 (92)
Age (years)	53 (46-58)	57 (44-63)
BMI (kg/m^2)	24 (22-27)	24 (23-26)
ASA, n (%)		
I	39 (78)	22 (44)
II	11 (22)	28 (56)
Smoking, n (%)		
Current smoker	5 (10)	11 (22)
Non-smoker	41 (82)	33 (66)
Ex-smoker	4 (8)	6 (12)
Occupation, n (%)		
Intense physical work	12 (24)	14 (28)
Light intensity work	11 (22)	8 (16)
Sedentary work	27 (54)	28 (56)
Location of hernia, n (%)		
Unilateral (left)	16 (32)	17 (34)
Unilateral (right)	34 (68)	33 (66)
Bilateral	0 (0)	0 (0)
Hernia type, n (%)		
Lateral	40 (80)	32 (64)
Medial	6 (12)	10 (20)
Femoral	2 (4)	3 (6)
Medial & Lateral	2 (4)	5 (10)

Continuous data are presented as median (interquartile range), BMI: body mass index, ASA: American Society of Anesthesiologists

Travel costs

The total number of hospital visits (including intake and POS) for the SV cohort was 51 in contrast to 103 for the regular cohort. The corresponding unalloyed travel costs were €135.66 and €279.30 respectively. By adding the parking costs, this resulted in total travel costs of €282.66 for the SV group and €594.30 for the regular group.

Pharmaceutical consumption

Of the SV cohort 36 (72%) patients consumed medication in the 6 weeks following surgery. Of the regular cohort 35 patients (70%) used medication. The drugs consumed in response

to the inguinal hernia repair were paracetamol, non-steroidal anti-inflammatory drugs (NSAID's) in combination with proton-pump inhibitors and laxatives. Based on the current chain pharmacy cash pricing, a total amount of €73.20 was consumed by the single visit cohort and an amount of €77.80 by the regular cohort.

Additional consultations

Of the SV cohort 5 patients (10%) consulted their GP (€167.10), 1 patient (2%) consulted his company doctor (€88.00) and 1 patient (2%) had 2 homeopathy consultations (€160.00). As for the regular cohort, 13 patients (26%) consulted their GP (€434.46), 8 patients (16%) visited their company doctor (€704.00), 1 patient (2%) had his blood tested in primary care setting (€33.00) and 1 patient (2%) used an ambulance due to severe constipation (€515.00).

Mean societal costs

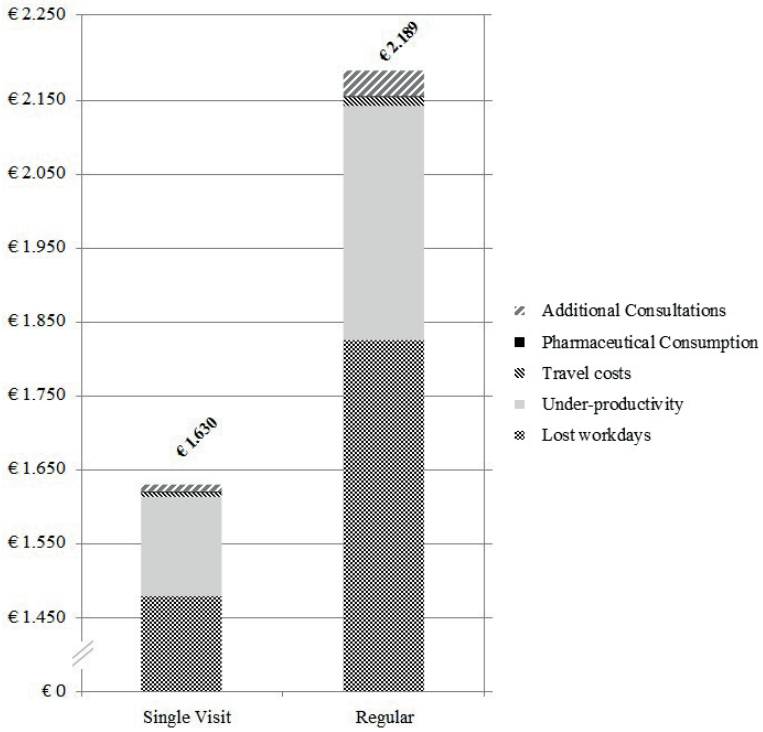
To sum up, the total societal costs were €81480.50 for the SV cohort and €109443.34 for the regular cohort. Hence, a mean SV patient costed €1629.78 (€307.53 to €9612.95) from a societal perspective whereas a regular patient costed €2188.98 (€459.13 to €7435.01) from this perspective (*table 6, figure 3*) with a difference of €559.20, reflecting a 25.5% decrease in costs in favour of the SV analysis.

Table 6. Analysed societal costs of a single-visit TEP and regular TEP

	Single-visit	Regular	Difference in analysed costs (Regular - SV)
	Costs (€)	Costs (€)	
Lost workdays	€ 73.980,80	€ 91.263,20	€ 17.282,40
Under-productivity	€ 6.731,04	€ 15.827,04	€ 9.096,00
Travel costs	€ 135,66	€ 279,30	€ 143,64
Parking costs	€ 153,00	€ 315,00	€ 162,00
Pharmaceutical consumption	€ 73,20	€ 77,80	€ 4,60
GP consultation	€ 167,10	€ 434,46	€ 267,36
Company doctor	€ 88,00	€ 704,00	€ 616,00
Homeopathy consultation	€ 160,00	€ 0,00	-€ 160,00
Blood test primary care	€ 0,00	€ 33,00	€ 33,00
Ambulance	€ 0,00	€ 515,00	€ 515,00
Total	€ 81.488,80	€ 109.448,80	€ 1.581,60
Mean	€ 1.629,78	€ 2.188,98	€ 559,20

TEP: totally extraperitoneal, GP: general practitioner, SV:single-visit

Figure 3. Mean societal costs



Total cost-analysis

By combining hospital and societal costs, a mean SV patient costed €2 778.58. From this same comprehensive point of view a regular patient costed €3 456.58. The mean difference between both pathways therefore equalled €678.00 which corresponded to a 19.6% decrease in costs in favour of the SV analysis.

Discussion

The aim of this study was to provide a comprehensive view on the cost savings of the SV routing and to widen the current knowledge of economic impact. In an employed, healthy population, SV TEP inguinal hernia repair results in a 19.6% decrease in costs and offers cost savings of €678.00 per patient. These study results demonstrate that the SV endoscopic inguinal hernia repair outprices the regular TEP inguinal hernia repair for employed healthy patients and makes it an interesting alternative for the common pathway. The biggest cost reduction can be achieved within the societal costs. To our knowledge, this is the first cost-analysis of single visit routing analysing both hospital and societal costs.

The mean difference in hospital costs was €118.80 per patient, reflecting a 9.4% decrease in costs in favour of the SV procedure. This correlates fairly well with previous publications and further supports the idea of increased accessibility along with boosting hospital related productivity. Several studies have demonstrated lower costs in the one-stage surgery compared to its regular counterpart, without impairment of safety or complication rate.[10-12,19] However, cost-items were not specified or poorly estimated. Olson et al, who compared the single visit paediatric ambulatory surgical procedures (SVS) with common surgery (CS), estimated that SVS had higher costs than common surgery (CS).[20] With a total hospital reimbursement of $810878 for the SVS group (n=90) and $776762 for the CS group (n=90), this equalled an increase of 4.4% and contrasts our findings. The explanation may be sought in the different patient population consisting of children and same-day cancellation rate, which was higher in SVS group due to incorrect diagnoses, need for further testing or ability to do the procedure in clinic rather than the operating room. This high cancellation rate did not apply for our clinic.[13] The main cause of lower hospital costs found in this study is the difference in POS between a regular (in hospital POS) and SV (T-POS and E-POS) procedure. Given that since 2005 the Dutch financing system gradually changed to a system with market competition, the findings can be of great interest for hospitals performing the TEP repair.[21] However, this alternative POS may even be extrapolated to all healthy patients (ASA I or II) with an operation on the horizon.

The inequality of hospital costs cannot only be explained by the pathway itself and its alternative POS but is also a result of the difference in physical consultations, inpatient days and telephone consultations. Given the fact that the surgical procedure, perioperative- and postoperative care were standardized and did not differ between the SV and the regular group, an explanation for the difference in health care consumption might be found in the patient characteristics or the personality type. This, however, applies even more to the patient and societal perspective and will be discussed later on.

Despite the fact that the difference in hospital costs between the SV and regular treatment is small, big cost savings can be achieved in high volume settings and by implementing this method in day-care surgery for other procedures.

From a societal point of view, the mean difference in costs was €559.20, reflecting a 25.5% decrease in costs in favour of SV TEP repair. This correlates with the findings of Olson et al, who found family cost savings of $188.00 for the SVS compared to CS, reflecting a 44.5% decrease in costs.[20] However, Olson et al. used the mean household income and the mean travel distance (which differed between groups) instead of standardised values, which may explain the bigger difference in costs.

The inequality of costs is mainly a result of the increased number of lost workdays and hospital visits, with the associated travel expenses. Given the one-stage surgery-routing of the single visit group, this seems to be a natural consequence. An extra hospital visit for the intake not only means additional travel expenses, but also additional (partially) lost workdays. However, the inequality exceeded our expectations. It seems that the SV-patient has a smaller demand for health care and consequently has a reduced number of lost workdays. In line with the difference in hospital costs, an explanation can be found in the patient characteristics and personality type. It is plausible that the SV pathway especially attracts those who are the "go-getter" type of patient. The patient type who has looked into the matter carefully, gets the possible advantages and disadvantages and is understanding in the face of adversity. It is not unlikely that the health consumption to some extent is built much more around intrinsic motivation than the actual need. Negative experiences, passivity, hostility and pessimism can all contribute to health care consumption and therefore can be related to various negative health outcomes, whereas optimistic control has a significant positive impact on various health indicators, although the existing literature is not conclusive on this subject. [22-25]

Another possible explanation that can justify the inequality is the difference in occupation between the two groups compared. The number of patients with intense physical work is higher in the regular group whereas the number of patients with light intensity work is lower. At discharge, patients were advised to abstain from strenuous physical exercise for the first week, which consequently applies more to patients with intense physical work. Given that work has long been associated with key components of mental health, it is also plausible that early return to work has a positive effect on recovery by distraction.[26] Hence, the negative effect of not working and sitting at home could have a wider impact on the regular group.

It is not inconceivable that a number of limitations could have influenced the study results. These limitations indicate the difficulty of collecting data on a comprehensive cost-analysis. The time horizon over which these costs were evaluated, was 6 weeks after surgery and started from the day of intake. Hence, medical consumption in the period before the intake was not taken into account. This underestimate of total health care costs is made deliberately, given the difficulties of retrospectively retrieving all medical records from GPs, other hospitals or paramedical care. In line with the personality types, one can expect a higher number of doubters and second opinions in the regular group, thus it is not unlikely this underestimation applies particularly to this group.

A general limitation of this cost-analysis is the high volume context. As the study is carried out at the Hernia Clinic of the Diakonessenhuis Zeist/Utrecht, the largest Dutch hernia center focusing on TEP repair, with a well-organised SV routing including experienced secretaries,

this might not be applicable for every hospital. The same goes for some of the hospital costs (e.g. the TEP repair), which are relatively low. Due to the differences between hospitals in costs of OR-time and inpatients days, one has to consider the results as a comprehensive estimation.

Another limitation of the prospective analysis, is the fact that we worked with a voluntary response sample. Not every applicable patient finished and returned their questionnaire, which may have led to a voluntary response bias, due to the fact that it probably oversamples patients who have strong opinions. Together with the small sample size, the voluntary responses may have also led to large costs spreads.

Despite the fact that this study found relatively small cost savings for hospitals, the SV routing can be of great interest for high volume hospitals performing the TEP repair and can be extrapolated to other commonly performed surgical procedures. By changing the pathway within a hospital, the effect outside the hospital will be considerably higher. Therefore both employers and employees will benefit most from changing the hospital patient routing with a 25.5% decrease in costs.

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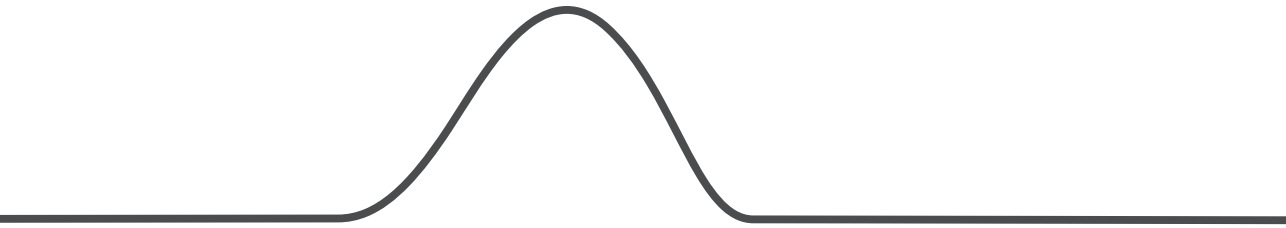
Summarizing discussion, conclusions and future perspectives



Discussion

Inguinal hernias are common phenomena, and surgical repair is frequently indicated. There is no single standardized approach applicable to all patients that develop an inguinal hernia, and the choice of repair method is dependent on patient-related factors, as well as surgeon experience and preference.[1] Mesh-based techniques are regarded as the gold standard, since they substantially lower the recurrence risk.[2-4] In the most recent guidelines, this recommendation is equally valid for the open anterior approach by Lichtenstein as for the minimally invasive totally extraperitoneal (TEP) and transabdominal preperitoneal (TAPP) endoscopic procedures.[1] However, endoscopic techniques with preperitoneal placement of mesh have shown considerable advantages over open repair methods and have become increasingly popular.[5-13]

When aiming at improving the TEP procedure, it is important to take the interests of all who are concerned into account. This implies not only focusing on the patient's point of view, but also looking at matters from the perspectives of surgeons, hospital and society.

In this thesis several aspects of TEP inguinal hernia repair are addressed, extending from diagnostics and indications for TEP hernia surgery to postoperative outcomes and costs.

In **Chapter 2** the utilization of groin ultrasound for suspicion of inguinal hernia requested in primary care was assessed. An apparent inguinal hernia with clear clinical features does not require further investigation. However, this analysis pointed out that overuse of groin ultrasound for this indication currently is present in primary care. Nearly a quarter of patients referred for an inguinal hernia underwent ultrasound before they were seen by a hernia surgeon. Since the great majority of hernias can be diagnosed clinically, this is far more than would be expected. In up to four fifth of patients in which ultrasound was conducted, the surgeon was able to diagnose a clinically apparent hernia upon physical examination. In case results of groin ultrasound and physical examination were contrasting, physical examination findings appeared to overpower ultrasound results in approximately three quarter of cases with regard to surgical treatment decisions. Naturally it cannot be expected that the clinical skills level of the general practitioner (GP) in diagnosing an inguinal hernia is as good as the skills level of a hernia surgeon working in a high volume hernia clinic. However, training GPs in physical examination of the groin region might reduce ultrasound use in a significant number of patients. Not many other studies have addressed this particular topic. There is one other study that specifically examined the utilization of groin ultrasound and its influence on proceeding to surgical repair, however this study combined ultrasound requests originating from both primary and secondary care.[14] Even though in this study the number of groins that underwent ultrasound despite of clinically apparent features (39%) was lower than

the numbers we found, it still represents overdiagnostics. In case the GP has a reasonable suspicion of a hernia causing inguinal complaints after physical examination, it would be advisable to refer directly to the surgeon without prior imaging for diagnosis confirmation. Current healthcare costs are expanding, and careful evaluation of the utilization and cost aspects of health care resources is warranted.

Over the past years, an increasing trend in health care efficiency has been observed, with expanding focus on tailored, cost-effective care. When surgical treatment is planned for a particular condition, sufficient prove of the effectiveness of this procedure must be present. In **Chapter 3** the study protocol of a randomized controlled trial (EFFECT-trial) designed to determine the therapeutic preference for patients with groin pain combined with a clinically occult inguinal hernia is presented. Studies concerning clinically occult hernias that have been conducted were mainly focused on the diagnostic value of imaging modalities.[15-19] Currently, a lacuna regarding the therapeutic approach for patients with groin pain and a clinically occult inguinal hernia exists in the guidelines.[1] Very recently, one retrospective study regarding this topic was published.[20] The results of this analysis showed that patients with a clinically occult hernia diagnosed by ultrasonography reported a high incidence of chronic pain after elective hernia repair and that patients with atypical groin pain prior to surgery were especially prone for chronic pain development. A prospective randomized trial comparing outcomes of watchful waiting and surgical (TEP) repair in patients with groin pain and clinically occult inguinal hernias is required, as dependent on the outcomes, possible unnecessary surgeries and costs may be saved.

In **Chapter 4**, outcomes of TEP repair in athletes with inguinal disruption were analysed. Many athletes suffer from chronic groin pain, often of multifactorial origin. Inguinal disruption is a diagnostic challenge, defined as chronic groin pain when other clear explanatory pathology is excluded.[21] When initial conservative treatment does not provide pain relief, surgery might reduce symptoms. The results of our prospective study demonstrate that athletes, selected through a systematic work-up by a multidisciplinary team of a sports medicine physician, radiologist and hernia surgeon benefit from reinforcing the posterior wall by TEP repair. After 3 months of follow-up, a significant decrease in pain was observed. At long-term follow-up, nearly two third of patients were totally pain-free. Three months after TEP repair, the maximum intensity at which sports could be performed increased significantly from 40% to 95%. At long-term follow-up, the great majority of patients was able to exercise with maximum intensity. Other studies that investigated TEP repair in athletes also reported beneficial results in terms of pain relief and sports resumption.[22-24] Nevertheless, there is an ongoing debate regarding the optimal surgical technique for inguinal disruption. Various explanations have been proposed for the suspected underlying nature of injury, and consequently widely

ranging repair techniques have been recommended. The most widely accepted pathogenesis of inguinal disruption supports the theory of a deficient posterior inguinal wall, endorsing the beneficial results of our analysis.[25-27] However, when assessing athletes with chronic groin pain for TEP repair one must remain aware the pain cause is often multifactorial and other pathology may co-exist. The athletes in whom a deficiency of the posterior wall is expected are most likely to benefit from TEP repair, and it is important to carefully select these athletes.

With the introduction of tension-free mesh repair and subsequent drop in recurrence rates the main focus in postoperative outcomes shifted towards chronic pain. It was hypothesized that the amount of synthetic mesh material correlated with the extent of fibrosis formation.[28,29] In order to diminish chronic pain, so-called lightweight meshes containing larger pores and therefore less material were developed. Animal studies indeed demonstrated a less extensive fibrotic response when lightweight mesh was used and in open anterior repair, application of lightweight mesh resulted in less pain and foreign body feeling.[28-31] However, the alleged benefits of lightweight mesh could not be confirmed for endoscopic inguinal hernia repair.[32] To gain more insight into the influence of the different mesh types, a large randomized controlled trial was designed and conducted in our hernia clinic.[33-35] Postoperative outcomes were studied in 950 patients, who were randomized to TEP hernia repair with either lightweight (Ultrapro®) or heavyweight (Prolene®) mesh. One- and two- year follow-up results of this study demonstrated a higher incidence of clinically relevant pain for lightweight mesh, however, it should be emphasized that the overall incidence of chronic pain was very low in both mesh subgroups. However, concern was raised regarding the significant difference between recurrence rates of lightweight and heavyweight mesh (2.7% versus 0.8%) at the two-year follow-up point. Moreover, little was known about follow-up of recurrences more than two years after endoscopic inguinal hernia repair in large samples of patients.[36]

In **Chapter 5** the long-term follow-up results of this trial with regard to recurrences are presented. Five years postoperatively, the validated PINQ-PHONE telephone questionnaire for detection of recurrences was carried out and when suspicion of possible recurrence development was raised, patients were examined clinically.[37] Lightweight meshes remained associated with a three- to fourfold higher recurrence rate of 3.8%, versus 1.1% after heavyweight mesh implantation. Most hernia recurrences occurred within the two-year postoperative period, and relatively few additional recurrences were detected after five years of follow-up. This analysis demonstrated that lightweight mesh seems mainly disadvantageous in direct defects since in 92% of recurrences after direct hernia repair lightweight mesh was used. This finding may not only result from intrinsic weakness and less adequate fixation of lightweight mesh, but also protrusion of mesh through the hernia defect may have occurred, presumably in the early postoperative period and most likely in large defects. Nevertheless, after correction for hernia type in multivariate analysis, lightweight mesh remained

independently associated with a higher recurrence rate. Based on our findings, there are no clear advantages of lightweight mesh over heavyweight mesh in TEP hernia repair and we would discourage use of this mesh for endoscopic hernia surgery.

Despite the implementation of tension-free mesh repair and introduction of endoscopic techniques providing a clear overview of the entire groin area, recurrences still develop. In order to provide insight into mechanisms of recurrence after TEP hernia repair an 11-year analysis of all reoperated groins with clinical or radiological recurrence-like symptoms in our hernia clinic was performed, of which the results are presented in **Chapter 6**. The high-volume setting with experienced surgeons allowed for critical evaluation with elimination of contribution of surgical inexperience or an uncompleted learning curve on recurrence development. Upon reoperation, recurrent hernias were confirmed in more than three quarter of groins, of which the majority were direct recurrences after primary direct hernia repair. If the primary defect was large, hernias recurred as the same type in 82% of cases. Recurrence development at the initial hernia site may be due to failure in mesh positioning, mesh displacement or mesh protrusion in case of large defects. Early postoperative displacement might be a direct postoperative effect, such as immediate displacement after desufflation and removal of instruments, or lifting of mesh by hematoma or urinary retention. Late displacement may be caused by insufficient fibrosis formation and therefore insufficient ingrowth of mesh, or either mesh protrusion or shrinkage due to contraction of fibrotic fibers. A lipoma mimicking a hernia recurrence was present in 18% of groins and occurred most frequently after correction of indirect hernias. It may be possible these lipomas developed after the primary operation, on the other hand they may also represent 'forgotten' lipomas that were overlooked at the initial repair. Our analysis also pointed out that patients undergoing bilateral TEP hernia repair are at increased risk of developing a recurrence. Results of this study are (mainly) in accordance with the most recent guidelines regarding endoscopic TEP inguinal hernia repair.[38,39] In case of primary large direct and bilateral defects, mesh fixation should be considered. Furthermore, the entire hernia floor should be inspected thoroughly with mandatory lipoma removal. For recurrence-like symptoms after TEP repair, the groin area should be explored by an anterior approach. Only in case of a true recurrent hernia, mesh repair is recommended.

During TEP inguinal hernia repair, the mesh is placed in close contact with the spermatic cord, containing the vas deferens, testicular vessels, pampiniform plexus, lymphatic vessels and nerves. Therefore, it was hypothesized that mesh-induced fibrosis or direct iatrogenic damage could affect the structures of the spermatic cord, hereby possibly impairing fertility. **Chapter 7** demonstrates the results of a prospective study assessing fertility parameters in male patients preoperatively and 6 months after bilateral TEP repair. No significant differences

in testicular perfusion, testicular volume or semen quality volume were observed. These findings are in line with other studies evaluating long-term fertility after hernia repair.[40-45] Even though biochemical analysis showed higher serum luteinising hormone (LH) levels and lower inhibin B levels postoperatively, both of these measurements were within reference levels and therefore not regarded as clinically relevant. Other studies evaluating endocrinological parameters after hernia repair did not demonstrate significant changes. To our knowledge, our analysis represents the first prospective trial assessing fertility in a human population solely consisting of bilateral hernia repairs. This study design ensured that the possible beneficial influence of a healthy, non-operated contralateral side on the results was prevented. As no clinically relevant long-term effects of bilateral TEP hernia repair on male fertility were demonstrated, in our opinion, this procedure can be safely performed in fertile men.

Since 2010 the single-visit pathway for TEP inguinal hernia repair is offered in our clinic, providing assessment and surgery in one-day. Previous research on this method demonstrated attendance and same-day surgery rates of respectively 99 and 96% and high levels of patient satisfaction.[46] Although it seemed very plausible that the single-visit method has a high potential of reducing health care costs since this acceleration of treatment minimalizes hospital visits and provides a more rapid return to work, an actual cost-comparison between the single-visit and the regular TEP pathway was not conducted yet. **Chapter 8** describes a cost-analysis comparing single-visit TEP inguinal hernia repair to TEP inguinal hernia repair through the regular pathway from both a hospital- and societal point of view. The results demonstrated that the single-visit procedure outprices the regular TEP procedure in employed, healthy patients. The total cost decrease in favour of the single-visit procedure was 18%, of which the great majority consisted of a reduction in societal costs. Inside the hospital, the cost decrease was mainly achieved by the telephone preoperative screening (POS) applied in the single-visit pathway instead of the physical POS consultations. Increased hospital visits in combination with more travel expenses and a bigger amount of lost workdays explained for the higher societal costs in the group of patients that underwent the TEP procedure following the regular pathway. The implementation of more efficient in-hospital care leading to a substantial decrease in societal costs is an interesting finding. Since inguinal hernia repair is the most frequently performed surgical procedure the single-visit routing will lead to substantial cost savings for hospitals, with presumably even bigger cost savings outside the hospital. We would recommend single-visit TEP repair in patients with inguinal hernias who are suitable for this pathway. Furthermore, it would be appealing to apply this pathway to other frequently performed surgical procedures as well, as by doing so a further minimization of costs would be expected.

Conclusions

1. In primary care, ultrasound diagnostics for the suspicion of inguinal hernia are redundantly requested, while surgeons rely more on physical examination findings in treatment decisions.

2. Watchful waiting may be non-inferior to TEP repair in case of groin pain and a clinically occult groin hernia, yet the optimal treatment strategy for these entities has to be determined.

3. Endoscopic TEP repair is beneficial in athletes with inguinal disruption if carefully selected through a systematic work-up by a multidisciplinary approach.

4. Application of Ultrapro® lightweight mesh in endoscopic TEP inguinal hernia repair leads to significantly more recurrence compared to application of Prolene® heavyweight mesh.

5. The majority of recurrence-like symptoms observed after endoscopic TEP inguinal hernia repair represent true recurrences, of which the greatest part involves direct hernias recurring as direct hernias.

6. Bilateral endoscopic TEP inguinal hernia repair does not impair male fertility.

7. Single-visit endoscopic TEP inguinal hernia repair is cost-effective compared to the regular TEP procedure from both a hospital and societal perspective, of which the reduction in societal costs is the most contributory.

Future perspectives

Even though many improvements in hernia repair techniques have been made over the past years, developments aiming to optimize inguinal hernia repair are still relevant. Surgical treatment of an inguinal hernia starts with diagnosing this condition. The diagnosis is sometimes obvious and already obtained in primary care by the GP, or can be confirmed in a later stage after referral to the surgeon. When investigating the use of ultrasound in primary care, it became clear that currently no Dutch guideline for GPs concerning instructions for diagnosis and subsequent treatment of inguinal hernias exists. To increase awareness about the optimal diagnostic and treatment pathways of inguinal hernias, we believe establishing such a guideline in collaboration with GPs will be beneficial. In these guidelines we aim to provide clear instructions on how to perform adequate physical examination when an inguinal hernia is suspected, and in which (rare) cases imaging would be advised before surgical referral.

Since groin pain can have a wide variety of possible causes, we cannot be completely sure that in all patients where a clinically occult hernia is diagnosed upon additional imaging their experienced pain is caused by this hernia. We often see atypical patterns of complaints in this patient population, which sometimes already suggest a different pathophysiology.

Findings of the EFFECT-trial will provide more insight into the influence of a watchful waiting approach compared to surgical intervention by TEP repair on groin complaints in patients with clinically occult inguinal hernias. In this randomized study, pain, quality of life and cost-effectiveness will be determined up to one year after treatment.

As previous studies have demonstrated that ultrasound is not 100% accurate in diagnosing occult inguinal hernias, one cannot be sure if all ultrasound diagnoses of inguinal hernias are correct.[18,19] We further hypothesized inguinal hernias only visible on ultrasound may also be present in healthy males without inguinal complaints. We aim to investigate this particular idea in a cohort of healthy males who are not experiencing groin pain. Would radiological hernias be present in a fair share of these males, these findings would support the theory that the finding of a clinically occult groin hernia could be coincidental in patients that actually suffer from an alternative cause of groin pain.

Chronic pain remains an important outcome parameter of hernia repair, and much effort is invested to lower pain levels following surgery. Chronic postoperative inguinal pain (CPIP) is defined as bothersome moderate pain that influences daily activities at least 3 months after surgery and decreases over time.[1] The current guidelines report young age as a risk factor for development of CPIP, however, no concrete boundaries regarding the definition of young

age are formulated.[1] The studies in which young age was determined a risk factor for chronic pain involved mainly open repairs, yet its influence on chronic pain after TEP has not been thoroughly investigated so far.[47-49] From the available evidence, it does not become entirely clear if all young adults with inguinal hernias would benefit from a repair involving mesh placement.[1] Further research comparing the incidence of CPIP in young adults compared to the older hernia population is required. Would a significantly higher incidence of CPIP be present in younger adults after TEP repair with mesh placement, it would be advisable to compare TEP repair to only hernia sac reduction in young adults with assessment of both CPIP as well as recurrence rates.

For assessment of five-year recurrence rates, the PINQ-PHONE telephone questionnaire consisting of three questions and a do-it-yourself Valsalva manoeuvre was used by five independent researchers. When using this tool, some doubt was raised about the effectiveness of all individual elements of this questionnaire. Up to our knowledge, the PINQ-PHONE had not yet been used in clinical trials after its validation study.[36] Therefore, it would be interesting to conduct further analysis on the feasibility of and researchers experience with this questionnaire.

The debate about the optimal follow-up period after inguinal hernia surgery is ongoing. The five-year analysis of the TULP trial pointed out that the majority of recurrences were detected within two years of follow-up. Conducting this extensive follow-up was time-consuming and barely resulted in detection of patients with new complaints. Furthermore, it was demonstrated that the majority of patients that developed complaints that started after the two-year period after surgery, contacted the surgical department upon their own initiative. The results of this study point in the direction of few additional value of fixed long-term follow-up after inguinal hernia repair. It would be interesting to see if this trend can be confirmed in a large sample of patients that would receive long-term follow-up in addition to the regular follow-up routine after elective TEP inguinal hernia repair in a specialized hernia center. We aim to do so by conducting a prospective study of a large sample of consecutively operated patients in our clinic that will be followed-up one year after TEP hernia repair, in addition to the fixed six-weeks follow-up. When conducting follow-up after hernia repair in general, adequate and standardized registration is of great importance. By means of, preferably standardized, registration systems not only audit of own outcomes will be possible, but also (long-term) outcomes of different repair techniques performed in different hernia centers can be compared.

The analysis of all reoperated groins with recurrence-like symptoms suggested that not in all cases a clear indication for diagnostic imaging existed, since in some cases the hernia

was already clinically apparent. Furthermore, this study also pointed out that not all imaging findings correlated with clinical or reoperation findings and that in some cases where imaging was negative for inguinal hernia there was still decided to reoperate. The guidelines state physical examination in combination with ultrasound is most suitable for the evaluation of patients where a hernia recurrence is suspected, with optional CT or MRI when diagnostic doubt remains present.[1] However, the role of imaging for diagnosing groin hernia recurrence has not thoroughly been investigated yet, since all available proof at this moment is based on two low quality studies.[50,51] Further research regarding this issue is warranted.

The five-year analysis of recurrences demonstrated a disadvantageous effect of lightweight mesh compared to heavyweight mesh with lightweight meshes being independently associated with higher recurrence rates. From the long-term follow-up results regarding pain, use of lightweight mesh was also discouraged. Even though these study results imply that regardless of hernia type lightweight mesh would not be recommended, still a trend was observed in the five-year recurrence analysis, implying that use of lightweight mesh might particularly be inadvisable in direct defects. Performing a separate analysis of only indirect defects assessing recurrences and pain when comparing the two mesh types in this study population might be of additional value.

Mesh fixation is recommended in large direct defects, since these are more likely to recur.[1] Another procedure that has been proposed as effective to prevent hernia recurrence, mesh protrusion and seroma formation is the so-called reduction of the dead space, involving inversion and fixation of the extended fascia transversalis to Cooper's ligament.[52] However, the current guidelines for endoscopic hernia surgery only describe effective prevention of seroma formation when this method is used, based on a single prospective non-randomized study, while no proof for recurrence reduction is provided.[38,39] It would be very interesting to conduct further research regarding this topic, where the ideal setting would be a randomized controlled trial where patients with direct inguinal hernias will be randomized between regular TEP repair and TEP repair with additional reduction of this dead space. The main outcomes of interest would be hernia recurrence, mesh bulging, seroma formation and inguinal pain.

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10

Comments on and reply to "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)"

Comments
J Li, W Zhang

Reply
MM Roos, JPJ Burgmans

Ann Surg 2018 Jul 3

Dear editor:

We read with great interest the recent article by Roos et al, published in Annals of Surgery.[1] The author reported the 5-year follow-up recurrence rate of a randomized trial comparing lightweight mesh and heavyweight mesh in totally extraperitoneal (TEP) inguinal hernia repair, found that lightweight meshes were associated with higher recurrence rates, direct hernia was an independent risk factor, thus, they recommended not using lightweight mesh in TEP inguinal hernia repair. We congratulate the authors for their well-designed and long-term follow-up study; however, in our opinion, several points need further discussion, especially on their recommendation not using lightweight mesh in TEP procedure, we believe this recommendation was too strong.

My first comment is regarding the recurrence pattern following TEP, in agreement with the present study, it has been reported from several previous large series studies that medial/direct inguinal hernia had a higher recurrence rate than indirect hernia after endoscopic TEP repair, and which could not be offset by mesh fixation.[1-3] Similarly, it could also be seen in the present Roos et al study that the difference of recurrence rate after indirect hernia repair was not that significant between lightweight mesh (n=6) and heavyweight mesh (n=4), and the significant difference was clearly in direct hernia (12 vs 1). Thus, we would like to point out that, the author's recommendation of ''not to use lightweight Ultrapro mesh in TEP inguinal hernia repair'' was a too strong statement to follow.

My second comment is about the mechanism of recurrence in direct hernia after TEP procedure, especially after the use of lightweight mesh, and this point was not emphasized in the original study. Practically, the recurrence pattern after lightweight mesh direct hernia repair after TEP could be the dislocation or even protrusion of the mesh through the direct hernia defect rather than reason of ''the weakness or less fibrosis formation'' of the lightweight mesh. This could be explained by the characteristic of direct inguinal hernia as well as the nature of TEP procedure. TEP is a fine procedure for inguinal hernia repair with the mesh placed in the preperitoneal space; however, in this region, the mesh is supported only by the peritoneum from below. Furthermore, in direct inguinal hernia, the layers above the mesh are much attenuated transversalis fascia (which was still loose), fat tissue and skin. Thus, there is no strong sandwich fixation effect in this region; therefore, the meshtissue interface overlap is usually insufficient in large direct hernia. Taken together, a lightweight soft mesh is much easy to dislocate or protrude into the direct hernia sac after TEP procedure, which could be the main cause of direct hernia recurrence after lightweight mesh TEP repair.

Third, should lightweight mesh be used in direct hernia? We believe the answer is yes.We would like to introduce our routine method when performing TEP for direct hernia with lightweight

mesh.[4,5] In large direct hernia (especially over 4 cm in defect diameter), we routinely closed the direct hernia defect by suturing the transversalis fascia with 3-0 barbed suture prior to the placement of mesh, meanwhile, the apex of the attenuated transversalis fascia was also retracted and tied together (*figure 1,2,3*). We believe this method is paramount for TEP in large direct hernia repair. As the overlap area of mesh-tissue interface is increased, and the direct hernia cavity is diminished, therefore, this method has two advantages, to prevent the mesh protrusion and recurrence, and also prevent the seroma formation.[4,5] At last, we want to emphasize the standard and important final step of TEP procedure, be sure to prevent the mesh curling, especially using soft mesh, mesh curling can be another risk factor for recurrence with lightweight mesh.

Even though we felt the need to discuss these few points, we congratulate Roos et al for their work, and furthermore, we believe that TEP with the using of lightweight mesh is a reliable procedure for both direct and indirect inguinal hernia repair, and with the closure of direct hernia defect, the recurrence rate of direct hernia after TEP is not higher than that of indirect hernia, meanwhile, the overall recurrence rate of lightweight mesh is not higher than that of heavyweight mesh when handled properly. As lightweight mesh was strong enough for incisional hernia repair, it is certainly strong enough and reliable in inguinal hernia repair.

Figure 1. Left direct inguinal hernia.

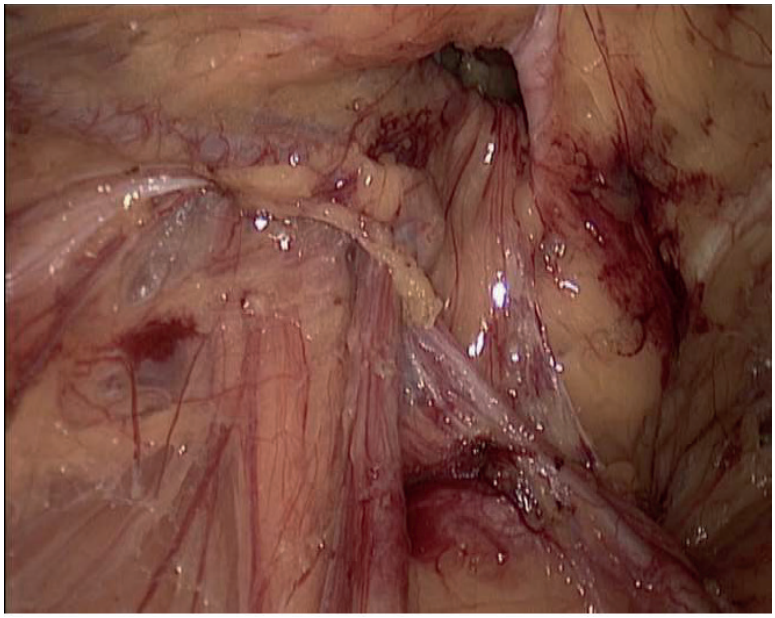


Figure 2. The direct hernia defect was closed with 3-0 Barbed suture (note the apex of the transversalis fascia was retracted and tied together).

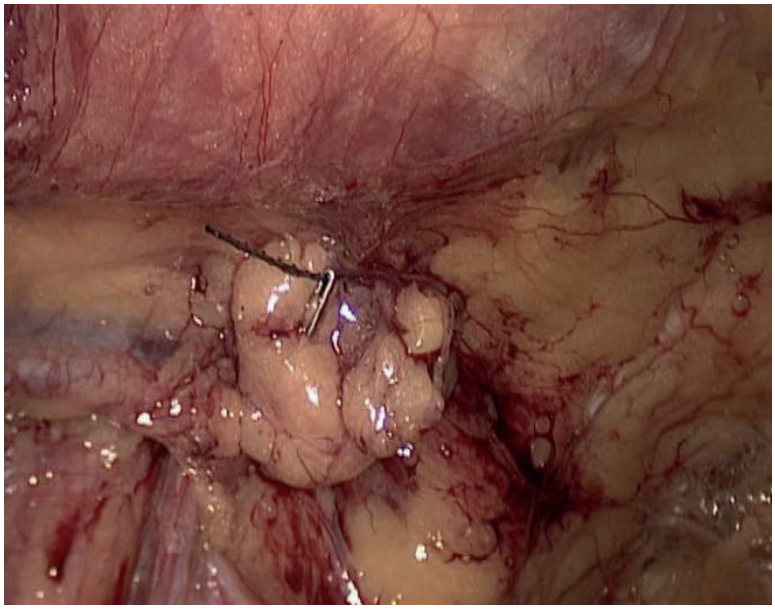
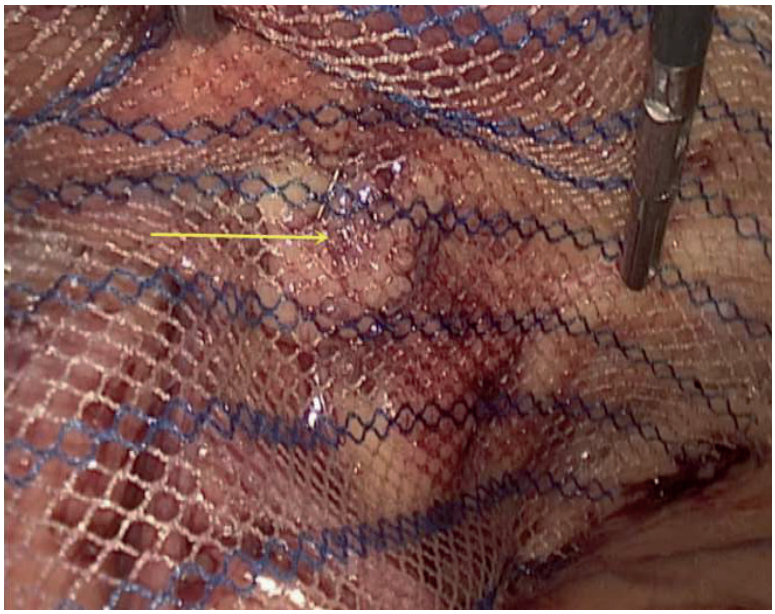


Figure 3. A Lightweight Ultrapro mesh was placed.



Arrow: the defect closed site could be seen through the mesh.

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Dear editor:

We would like to thank Dr. Li and Dr. Zhang for their congratulations on our work and their time and effort to write a commentary to our article.[1]

Li and Zhang state several points need further discussion and overall, they feel our recommendation not to use lightweight mesh in totally extraperitoneal (TEP) inguinal hernia repair is too strong.

The first issue they address is the recurrence pattern following TEP. As we and other studies have demonstrated patients with primary direct hernias are at the greatest risk of developing a hernia recurrence.[1-3] They point out that in the 13 recurrences that developed after direct hernia repair indeed far more lightweight meshes were used (12 lightweight, 1 heavyweight). However, the proportion of lightweight and heavyweight mesh in recurrences that developed after indirect hernia repair did not differ that much (6 lightweight, 4 heavyweight). We agree with the writers that based on these numbers the recommendation not to use lightweight mesh in TEP hernia repair seems to be mainly applicable to direct defects instead of all hernia defects. However, we also conducted a multivariate analysis, that demonstrated that after correcting for primary hernia type use of lightweight mesh was still independently associated with development of hernia recurrence (Odds ratio (OR) 3.86, 95%-confidence interval (CI) 1.41-10.61, p=0.009). Taking these results into account, we would still prefer heavyweight mesh over lightweight mesh, since lightweight mesh was independently associated with recurrence development, yielded clear unfavourable results in direct defects, and showed no advantage over heavyweight mesh in indirect hernia repair.

The second comment involves the mechanism of recurrence following TEP hernia repair for direct hernias, especially after the use of lightweight mesh. The writers propose dislocation or protrusion of lightweight mesh through the hernia defect is more likely than the intrinsic weakness and decreased fibrotic response as stated in our article. We agree on this point with regard to large direct defects, since it is more likely that a less strong lightweight mesh will protruse if the primary defect is big. We mainly expect this to occur in the early postoperative period, when the fibrotic response and subsequent fixation of mesh just started. With regard to this last argument we think protrusion through large defects early postoperatively may happen when heavyweight mesh is used as well. In line with this, current guidelines advise mesh fixation during TEP hernia repair in patients with large direct hernias.[4] However, if the primary defect is not large, we still think it is more likely that the intrinsic weakness and less adequate fixation of lightweight mesh are responsible for recurrence development.

The writers introduce their routine method of closing the direct hernia defect, involving suturing the transversalis fascia, inverting the apex of this attenuated fascia and suturing it to the base to eradicate the direct cavity. This method is stated to prevent mesh protrusion, hernia recurrence and seroma formation. We think this is a very interesting technique that can indeed be advantageous. However, in the published literature up till now only prevention of seroma formation has been described, and this technique has not yet been proven to effectively prevent recurrences.[5-7] In our opinion, it would be very interesting to conduct further research on this technique regarding recurrence outcomes.

Lastly, the writers emphasize the important point of mesh curling prevention when using softer lightweight mesh. In our opinion, this can be achieved by performing adequate dissection to create sufficient preperitoneal space, to be able to position the mesh adequately without wrinkle formation. After placement, desufflation has to be performed under direct view to make sure the mesh maintains the right position. We would like to add to this recommendation that in our experience, lightweight mesh containing less prosthetic material is often harder to handle and position intraoperatively.

Li and Zhang conclude TEP hernia repair with use of lightweight mesh is a reliable procedure that they would recommend. Although the possibility exists that with the described routine method of closing direct hernia defects the number of recurrences after lightweight mesh direct hernia repair in our study might have been lower, up to this point this is only speculation. As stated before, further research on this technique regarding recurrences outcomes would be very interesting.

In conclusion, we still feel there is no clear advantage of lightweight mesh usage over heavyweight mesh usage in TEP hernia repair based on the results of our 5-year follow-up study. In addition to the independent higher recurrence risk, arguments supporting our recommendation not to use lightweight mesh are the occurrence of more chronic pain[8], higher costs and more difficult mesh handling when lightweight mesh is used.

References

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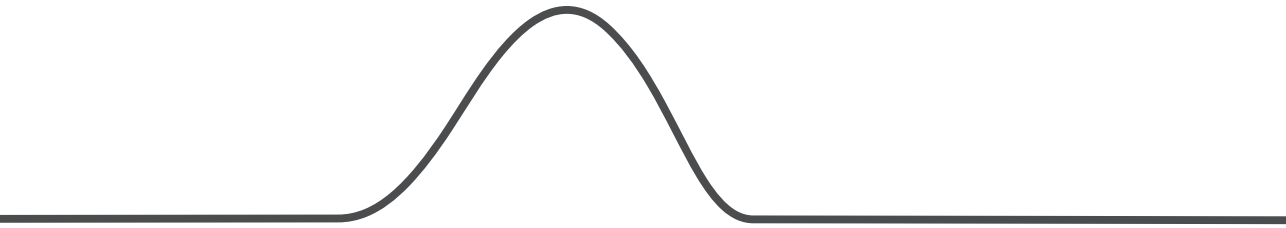
11

Nederlandse samenvatting

(Summary in Dutch)



Nederlandse samenvatting

Een liesbreuk is een veel voorkomende aandoening waarvoor een operatie vaak noodzakelijk is. De keuze voor het type operatie is afhankelijk van de aard van de liesbreuk, van patiënt-gerelateerde factoren en van de ervaring en de voorkeur van de chirurg. Daarom bestaat er geen standaard operatietechniek die geschikt is in voor elk type liesbreuk en voor iedere patiënt. Ondanks het belang van individualisering is een zekere mate van standaardisering wenselijk en worden er in de meest recent gepubliceerde internationale richtlijnen aanbevelingen gedaan over welke operatietechnieken het beste toegepast kunnen worden. Technieken met gebruik van een synthetische mat verdienen de voorkeur boven plastieken zonder mat, omdat de mat de kans op het ontwikkelen van een recidief aanzienlijk vermindert. De plaatsing van een mat kan zowel via een open anterieure benadering (de Lichtenstein plastiek) als via een endoscopische posterieure of preperitoneale benadering (de totale extraperitoneale techniek (TEP) en de transabdominale preperitoneale techniek (TAPP)) worden verricht. Laparo-endoscopische methoden geven in ervaren handen minder kans op pijn en een sneller herstel vergeleken met de Lichtenstein plastiek. Dit heeft geleid tot een toename in populariteit van deze technieken die zowel in Nederland als wereldwijd steeds meer worden toegepast als eerste keuze behandeling voor primaire liesbreuken.

In de laatste decennia heeft wetenschappelijk onderzoek geleid tot een substantiële kwaliteitsverbetering van de behandeling van liesbreuken. Teneinde de uitkomsten van de liesbreukchirurgie nog verder te optimaliseren, is het van belang de procedure vanuit verschillende perspectieven te benaderen: vanuit de patiënt zelf, maar ook vanuit het oogpunt van de chirurg, het ziekenhuis en de maatschappij.

De onderzoeksresultaten van dit proefschrift zijn verkregen in een groot expertisecentrum voor liesbreukchirurgie waarbij de TEP de eerste behandelkeuze is. Vele aspecten van de behandeling van een liesbreuk worden beschreven, variërend van diagnostiek en indicatiestelling tot postoperatieve uitkomsten en kosten.

In **Hoofdstuk 2** wordt het gebruik van de echografie van de lies door de huisarts bij verdenking op een liesbreuk geëvalueerd. In 95% van de gevallen is een liesbreuk een klinische diagnose die door middel van anamnese en lichamelijk onderzoek kan worden gesteld, derhalve is aanvullend onderzoek zelden nodig. Indien er toch twijfel bestaat over de diagnose, is echografie de aanvullende diagnostiek van eerste keus.
De resultaten van deze studie tonen aan dat er momenteel overdiagnostiek wordt verricht bij verdenking op een liesbreuk vanuit de eerste lijn. Ongeveer een kwart van de verwezen patiënten onderging een echografie van de lies voordat zij gezien werden door de liesbreukchirurg. In bijna vier vijfde van de patiënten die zich presenteerden met een reeds

verrichte echografie van de lies was de chirurg in staat om op basis van klinische kenmerken een liesbreuk te diagnosticeren. Wanneer de resultaten van de echografie en lichamelijk onderzoek van elkaar verschilden, waren de bevindingen bij lichamelijk onderzoek leidend voor de chirurg in de behandelkeuze.
Uiteraard is er een vaardigheidsverschil in het klinisch vaststellen van een liesbreuk te verwachten tussen de huisarts en de liesbreukchirurg, echter, adequate instructie van huisartsen in het lichamelijk onderzoek van de liesregio en de indicaties voor aanvullende diagnostiek zal zeer waarschijnlijk leiden tot een vermindering van het gebruik van de echografie en daarmee een verlaging van kosten. Indien de huisarts na het klinisch beoordelen van een patiënt een redelijke verdenking op een liesbreuk heeft, is het aan te bevelen direct te verwijzen naar de chirurg zonder voorafgaande beeldvorming ter bevestiging van de diagnose. In de huidige tijd waarin de kosten van de gezondheidszorg steeds meer stijgen, is bewustwording van het gebruik en de kosten van middelen in de zorg noodzakelijk.

De laatste jaren is er een toenemende trend van doelmatigheid in de zorg, waarbij de focus steeds meer verschuift naar zorg op maat en kosteneffectiviteit. Wanneer een bepaalde diagnose in aanmerking komt voor een chirurgische behandeling, moet er voldoende bewijs zijn van de effectiviteit van de betreffende procedure.
In **Hoofdstuk 3** wordt het studieprotocol van de EFFECT-trial beschreven. Dit betreft een gerandomiseerde klinische studie die de TEP liesbreukcorrectie vergelijkt met een afwachtend beleid bij patiënten met liespijn en een klinisch occulte liesbreuk. De klinisch occulte liesbreuk wordt gedefinieerd als een liesbreuk die klinisch niet detecteerbaar, maar wel zichtbaar is op aanvullende beeldvorming.
Er is veel discussie over de behandeling van de occulte liesbreuk. Studies die tot op heden gepubliceerd zijn, beschrijven met name de diagnostische waarde van beeldvorming bij deze occulte breuken. Er zijn geen interventionele studies van voldoende kwaliteit bekend en het is niet duidelijk wat de beste behandeling is van een liesbreuk die alleen op beeldvorming gesuggereerd wordt. Een studie die de uitkomsten van een operatieve benadering met een afwachtend beleid vergelijkt in deze patiëntenpopulatie is nodig om aan te tonen of een operatieve behandeling noodzakelijk is of een afwachtend beleid niet inferieur is. De uitkomsten van dit onderzoek resulteren mogelijk in minder opereren en het besparen van onnodige kosten.

Hoofdstuk 4 beschrijft de uitkomsten van de TEP in atleten met 'inguinal disruption'.[1] Chronische liespijn komt frequent voor bij atleten en is vaak van multifactoriële aard. 'Inguinal disruption' vormt vaak zowel een diagnostische als therapeutische uitdaging, en is gedefinieerd als chronische liespijn wanneer andere verklarende pathologie is uitgesloten.

1 Voor deze definitie bestaat geen gangbare Nederlandse term

Wanneer een conservatieve behandeling geen verbetering van symptomen geeft, kan chirurgie een oplossing bieden.
De resultaten van deze prospectieve studie laten zien dat atleten, geselecteerd door een systematische multidisciplinaire work-up bestaande uit een sportarts, radioloog en liesbreukchirurg, baat hebben bij het versterken van de achterwand van het lieskanaal middels de TEP. Preoperatieve pijnklachten en de mate van sportbeoefening werden vergeleken met postoperatieve resultaten. Drie maanden postoperatief werd een significante afname in pijnklachten gezien, en op de lange termijn werd bijna twee derde van de patiënten volledig pijnvrij. De maximale intensiteit van sportbeoefening nam significant toe van 40% naar 95% drie maanden na de TEP, op de lange termijn was de grote meerderheid van de patiënten in staat te sporten op maximale intensiteit.
Momenteel staat de optimale chirurgische techniek voor 'inguinal disruption' nog ter discussie. Er bestaan verschillende theorieën over het onderliggende mechanisme dat leidt tot chronische liesklachten. Op grond van deze theorieën is er ook een diversiteit aan hersteltechnieken beschreven. De meest geaccepteerde oorzaak van de pijn is een zwakte van de achterwand van het lieskanaal. Deze theorie ondersteunt de gunstige resultaten van de huidige studie. Men moet zich echter bewust blijven van het feit dat chronische liespijn bij atleten vaak door meerdere oorzaken wordt bepaald. Waarschijnlijk worden deze optimale resultaten alleen bereikt na een zorgvuldige selectie door een gespecialiseerd multidisciplinair team.

Na de introductie van de mat en de daaruit voortkomende aanzienlijke daling in het aantal recidieven werd chronische pijn de belangrijkste postoperatieve uitkomstmaat van liesbreukchirurgie. Een van de oorzakelijke factoren van het ontstaan van chronische pijn werd de mat zelf. Zo ontstond de hypothese dat de hoeveelheid synthetisch materiaal van de mat invloed zou kunnen hebben op de mate van fibrosevorming en het ontstaan van pijn. Lichtgewicht matten met grotere poriën en minder gewicht werden ontwikkeld met als doel chronische pijn na liesbreukchirurgie te verminderen.
Om meer inzicht te verkrijgen in het verminderen van pijn na het gebruik van een lichtgewicht mat vergeleken met een (reguliere) zwaargewicht mat in de endoscopische liesbreukchirurige, hebben wij in onze kliniek een grote gerandomiseerde studie verricht (TULP-trial). De TEP liesbreukcorrectie werd uitgevoerd in 950 patiënten, die gerandomiseerd werden tussen een lichtgewicht (Ultrapro®) en een zwaargewicht (Prolene®) mat. De totale incidentie van postoperatieve chronische pijn was zeer laag in beide groepen, maar na gebruik van de lichtgewicht mat werd er zowel na één als twee jaar een hogere incidentie van klinisch relevante pijn aangetoond.

Daarnaast toonden de resultaten na twee jaar follow-up een opvallend verschil tussen de lichtgewicht en zwaargewicht mat met betrekking tot het aantal recidief liesbreuken (2.7% versus 0.8%).
Om een goede uitspraak te doen over de kans op een recidief na liesbreukchirurgie, is een lange follow-up nodig. Tot op heden was er nauwelijks onderzoek verricht naar het optreden van recidieven meer dan twee jaar na de TEP liesbreukcorrectie.
In **Hoofdstuk 5** worden de lange termijn resultaten van deze studie met betrekking tot recidieven beschreven. Vijf jaar postoperatief werd de gevalideerde PINQ-PHONE telefonische vragenlijst afgenomen. Wanneer uit deze vragenlijst een verdenking op een mogelijk recidief liesbreuk naar voren kwam, werden patiënten klinisch beoordeeld. Patiënten met een lichtgewicht mat ontwikkelden een hoger aantal recidieven in vergelijking met de zwaargewicht mat (3.8% versus 1.1%), waarvan de meeste recidieven binnen twee jaar na de operatie waren ontstaan. De lichtgewicht mat lijkt met name nadelig in mediale (directe) breuken, aangezien 92% van alle patiënten die een recidief ontwikkelden na correctie van een mediale liesbreuk een lichtgewicht mat hadden gekregen tijdens de eerste operatie. Mogelijke verklaringen hiervoor kunnen zijn dat de lichtgewicht een intrinsieke zwakte heeft, en dat de mat minder fibrosevorming veroorzaakt en daardoor minder goed fixeert. Bij grotere hernia defecten zou dat kunnen leiden tot bulging of protrusie van de mat door de breukpoort, met name bij de mediale defecten (en in de vroege postoperatieve periode).
Gebaseerd op deze bevindingen zijn er geen duidelijke voordelen van de toepassing van de lichtgewicht mat in vergelijking tot de zwaargewicht mat voor de TEP, en bevelen wij aan lichtgewicht matten niet te gebruiken voor endoscopische liesbreukcorrecties.

Ondanks de implementatie van de mat, het ontwikkelen en verfijnen van laparo-endoscopische technieken en het verkrijgen van ruime expertise, treden er nog steeds recidief liesbreuken op.
Om meer inzicht te verkrijgen in de oorzaak van het ontwikkelen van een recidief in een hypothetisch optimale situatie, hebben wij een 11-jaars analyse verricht van alle patiënten die re-operaties ondergingen vanwege een verdenking op een recidief na een eerdere liesbreukcorrectie middels een TEP. De resultaten van deze studie staan beschreven in **Hoofdstuk 6**. Een groot voordeel van de analyse in een hoog-volume expertisecentrum is de eliminatie van de mogelijke invloed van onvoldoende chirurgische ervaring of van een onvoltooide leercurve voor de TEP.
In meer dan driekwart van de ge-reopereerde liezen werd een recidief gevonden. De meerderheid van deze recidieven betroffen mediale breuken na primair herstel van een mediale breuk. Wanneer het initiële defect als groot geclassificeerd was, was het recidief in 82% van de gevallen hetzelfde type als de primaire breuk. De ontwikkeling van hetzelfde type recidief ontstaat vaak sneller na de operatie en zou kunnen komen door inadequate

positionering van de mat, verplaatsing van de mat of protrusie van de mat in het geval van grote breuken. Een recidief dat kort na de operatie ontstaat , wordt vaak als een technische fout gezien.
In 18% van de liezen werd bij re-operatie alleen een lipoom gevonden zonder dat er sprake was van een recidief liesbreuk. Deze bevinding trad vaker op na primaire correctie van een indirecte (laterale) breuk. De mogelijkheid bestaat dat deze lipomen zich hebben ontwikkeld na de eerste ingreep, of dat dit in werkelijkheid 'vergeten' lipomen betreffen, die niet gezien zijn bij de initiële operatie.
Patiënten geopereerd aan bilaterale liesbreuken toonden een hoger risico op een recidief vergeleken met patiënten die een unilaterale liesbreukoperatie hadden ondergaan.
De bevindingen van deze studie komen (hoofdzakelijk) overeen met de meest recent opgestelde internationale richtlijn voor liesbreukchirurgie. Om recidieven na laparo-endoscopische liesbreukchirurgie te voorkomen, adviseren wij in het geval van grote mediale en bilaterale breuken de mat te fixeren. Daarnaast dient men een grondige inspectie van de gehele liesregio te verrichten en met name bij de indirecte, laterale breuken de inwendige liesopening te inspecteren en een eventueel lipoom te verwijderen. In het geval van een re-operatie in verband met symptomen passend bij een recidief na een TEP liesbreukcorrectie adviseren wij een anterieure benadering (conform de richtlijnen). Bij een solitair lipoom, kan volstaan worden met het verwijderen van het lipoom. Alleen in het geval van een duidelijk recidief liesbreuk, is herstel met gebruik van een mat aanbevolen.

Tijdens de TEP liesbreukcorrectie wordt de mat in nauw contact met de zaadstreng geplaatst, welke de zaadleider, de plexus pampiniformis, testiculaire vaten, lymfevaten en zenuwen bevat. De preperitoneale positie van de mat voorkomt direct contact met de sensibele lieszenuwen aan de anterieure zijde van de buikwand waardoor de kans op chronische pijn aanzienlijk lager is. Echter, het werd verondersteld dat mat-geïnduceerde fibrose danwel directe iatrogene schade tijdens de operatie de structuren van de zaadstreng zouden kunnen beschadigen, met ten gevolge hiervan mogelijk nadelige effecten op de fertiliteit.
Hoofdstuk 7 toont de resultaten van een prospectieve studie waarin de fertiliteitsparameters van fertiele mannelijke patiënten na een bilaterale TEP werden geëvalueerd. Preoperatieve waarden werden vergeleken met metingen zes maanden postoperatief. Er werden geen significante verschillen in testiculaire perfusie, testiculair volume of semen kwaliteit gevonden. Alhoewel een hogere waarde van het luteïniserend hormoon (LH) en een lagere inhibine B waarde werden gevonden bij de postoperatieve metingen, waren deze waarden beiden binnen het referentiekader en werden zij derhalve niet als klinisch relevant beschouwd.
Voor zover we weten is deze analyse de eerste prospectieve studie die mannelijke fertiliteit evalueert in patiënten die allen een bilaterale TEP hebben ondergaan. Door het kiezen van dit studieontwerp kon de mogelijke invloed van de gezonde, niet-geopereerde, zijde op de

studieresultaten voorkomen worden. Aangezien er geen klinisch relevante lange-termijn effecten van de bilaterale TEP liesbreukcorrectie op de mannelijke fertiliteit zijn aangetoond, zijn wij van mening dat deze procedure veilig kan worden uitgevoerd bij mannen in de vruchtbare leeftijd.

Sinds 2010 biedt onze kliniek de 'single-visit' TEP liesbreukcorrectie aan, waarbij de preoperatieve beoordeling en de operatie van een patiënt in één dag plaatsvinden. Eerder onderzoek naar deze methode demonstreerde hoge opkomstpercentages (99%), een hoog percentage patiënten dat daadwerkelijk dezelfde dag geopereerd werd (96%) en een hoge patiënttevredenheid. Vanuit deze resultaten leek het aannemelijk dat de 'single-visit' methode zou kunnen bijdragen aan de vermindering van zorgkosten, aangezien deze versnelling van behandeling het aantal ziekenhuisbezoeken minimaliseert en een spoediger patiëntherstel bewerkstelligt. Echter, een kostenvergelijking tussen de 'single-visit' TEP en de TEP volgens de reguliere methode was nog niet uitgevoerd.

Hoofdstuk 8 beschrijft een kostenanalyse die de 'single-visit' en de reguliere TEP liesbreukcorrectie vergelijkt vanuit het oogpunt van het ziekenhuis alsmede vanuit maatschappelijk perspectief. De resultaten laten zien dat in een populatie van gezonde, werkende patiënten de 'single-visit' procedure voordeliger blijkt dan de reguliere TEP procedure. De totale kostenafname wanneer de 'single-visit' methode werd gebruikt bedroeg 18%, waarvan de grote meerderheid bestond uit een reductie in maatschappelijke kosten. Binnen het ziekenhuis was de afname in kosten voornamelijk het resultaat van de telefonische preoperatieve screening die in plaats van de fysieke preoperatieve screening plaatsvond. De hogere maatschappelijke kosten in de reguliere groep konden worden verklaard door het grotere aantal ziekenhuisbezoeken, gepaard gaande met meer reiskosten en een hoger aantal gemiste werkdagen.

De aanzienlijke vermindering in maatschappelijke kosten door het bewerkstelligen van efficiëntere zorg binnen het ziekenhuis is een interessante bevinding. Aangezien de liesbreukcorrectie de meest frequent uitgevoerde chirurgische operatie is, ligt het in de lijn der verwachting dat het toepassen van de 'single-visit' methode zal leiden tot substantiële besparing in ziekenhuiskosten, en vermoedelijk nog meer kostenbesparing buiten het ziekenhuis.

Wij bevelen de 'single-visit' TEP liesbreukcorrectie aan voor patiënten met een liesbreuk in aanmerking komend voor dit traject. Het toepassen van de 'single-visit' methode zou tevens interessant kunnen zijn voor andere frequent uitgevoerde chirurgische ingrepen, aangezien hiermee een verdere reductie van zorgkosten in de lijn der verwachting ligt.

A

Appendices

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List of publications

Acknowledgements

Curriculum Vitae

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List of publications

Roos MM, van Hessen CV, Verleisdonk EJMM, Clevers GJ, Davids PH, Voorbrood CEH, Simmermacher RKJ, Burgmans JPJ. An 11-year analysis of reoperated groins after endoscopic totally extraperitoneal (TEP) inguinal hernia repair in a high volume hernia center. *Hernia 2018 Sep 22* [Epub ahead of print].

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Curriculum Vitae

Marleen Marianne Roos was born on May 14, 1987 in the Hague, the Netherlands. She is the daughter of Job Roos and Helga Vermaas. She grew up in The Hague and graduated from the Aloysius College in The Hague (Gymnasium, cum laude) in 2005. Following secondary school, she went to Australia for eight months, where she followed a three-month Camebridge course in English (Australian College of English, Sydney, Australia*)*, after which she combined work and travel along the coast of Australia.

In 2006, she started studying Medicine at the University of Utrecht, The Netherlands. During her studies, she had a wide interest and she did not focus on one particular specialty yet. As part of her studies she followed foreign clinical internships in Blantyre, Malawi (Gynaecology) and in Paramaribo, Suriname (Surgery). She graduated medical school in 2013.

After she graduated, she worked for one year at the Emergency Department (Ziekenhuis Gelderse Vallei, Ede), afterwards she pursued with clinical work at the Department of Surgery (Ziekenhuis Gelderse Vallei, Ede followed by the Diakonessenhuis, Utrecht). In february 2016, she started as a PhD candidate in the field of inguinal hernia surgery at the Diakonessenhuis Utrecht/Zeist under supervision of dr. J.P.J. Burgmans and dr. E.J.M.M. Verleisdonk, in cooperation with the University Medical Center Utrecht (Promoter Prof. Dr. I.H.M. Borel Rinkes). Her PhD programme was focused on several aspects of the endoscopic totally extraperitoneal (TEP) inguinal hernia correction. During this period, she coordinated multiple prospective studies and initiated a multicenter randomised controlled trial, for which a health effiency grant (ZonMw) was received.

In september 2018, she started as a general practitioner in training (Academic Medical Center, Amsterdam). In the future, she hopes to combine clinical work in general practice with research and education.