Sequelae of Endoscopic Inguinal Hernia Repair

Incidence, evaluation and management

J.P.J. Burgmans

Sequelae of Endoscopic Inguinal Hernia Repair
Incidence, evaluation and management

Thesis University of Utrecht. With summary in Dutch

ISBN: 978-94-6233-108-2

Author: J.P.J. Burgmans
Lay-out: Optima Grafische Communicatie, Rotterdam
Print: Gildeprint, Enschede
Cover: Leo Hamers

The studies described in this thesis were financially supported by Johson & Johnson Ethicon B.V. and Giard de Mielet van Coehoorn Stichting.
Printing of this thesis was financially supported by Dutch Hernia Society, Chipsoft BV, Olympus Nederland BV and Takeda Nederland BV.

Sequelae of Endoscopic Inguinal Hernia Repair

Incidence, evaluation and management

Sequelae van de endoscopische liesbreuk correctie:
Incidentie, evaluatie en behandeling
(met een samenvatting in het Nederlands)

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit Utrecht,
op gezag van de rector magnificus prof.dr. G.J. van der Zwaan,
ingevolge het besluit van het college voor promoties in het openbaar te verdedigen
op donderdag 19 november 2015 des middags te 12.45 uur

door

Josephina Petronella Johanna Burgmans
geboren op 2 juni 1970 te Bergeijk

Promotoren:
Prof. dr. I.H.M. Borel Rinkes
Prof. dr. J.F. Lange

Copromotoren:
Dr. T. van Dalen
Dr. R.K.J. Simmermacher

CONTENTS

1

Introduction and outline of thesis

INTRODUCTION

Inguinal hernia is one of the most common disorders seen by a general surgeon and its repair is the most frequent operation performed annually (20 million procedures worldwide and 31000 procedures in The Netherlands in 2009)[1,2]. Treatment of this condition and its possible sequelae have a major impact on health care budgets. In addition, as most patients are between 40 and 65 years old, many of those patients are men in their active working life, for whom unfortunate sequelae might indicate economic problems.

The principles of inguinal hernia repair have changed throughout history. The basic principles of modern inguinal hernia surgery stem from the 19th century when Bassini introduced the enforcement of the weak posterior wall[3]. The main problems of his reconstruction principle, consisting of suturing the fascial structures bordering the hernia defect, were frequent recurrences and chronic postoperative inguinal pain (CPIP). With the introduction of synthetic mesh in 1958[4], conceptually a change from suturing the defect to covering it was introduced with a subsequent drop of the recurrence rate from 30% to 2-4%. Ever since the golden standard to repair a primary inguinal hernia is represented by a tension-free open anterior approach according to Lichtenstein[5,6].

With the introduction of mesh in inguinal hernia repair, recurrences no longer appeared to be the main sequelae but CPIP, foreign body sensation, impairment of sexual function and other symptoms affecting the quality of daily life during recovery have become the focus of interest[7]. The reported incidence of CPIP following inguinal hernia repair varies between 2 to 43%, with approximately one third of these patients experiencing functional impairment in work or leisure activities[8,9,10]. The wide variation in incidence of CPIP is caused by a lack of clear definition and validated questionnaires. Recently, efforts were done to solve these problems in order to assess the real incidence of CPIP and its impact on the quality of life[11,12]. However, the use of questionnaires and definitions still lack consistency, hampering comparison of different studies including meta-analyses and systematic reviews[13].

Over the last few decades, knowledge of the pathophysiology of CPIP has accumulated and -apart from a recurrent hernia- two important causative factors were defined: neuropathic pain (direct nerve injury or perineural scarring) and nociceptive pain (tissue inflammation and foreign material-induced reaction)[14,15]. To prevent nerve injury, surgeons have improved their acquaintance of the groin anatomy and the risk of CPIP after open anterior hernia repair decreased with 2-5% due to the intraoperative identification and (if possible) preservation of all three inguinal nerves[12].

The development of endoscopic inguinal hernia repair in the late 20th century resulted in another significant reduction of acute postoperative pain and CPIP, leading to faster reinstatement of work and daily activities, whereas recurrence rates were similar to those after open anterior mesh repair techniques[7,16,17]. Additionally an endoscopic repair has the great advantage to visualize all the hernia orifices in the groin region (myopectineal orifice of Fruchaud) with a single view making it possible to repair any ipsilateral synchronous hernia during the same session. There are two endoscopic techniques for inguinal hernia repair: 1) the transabdominal approach (TAPP) and 2) the total extraperitoneal (TEP) approach. Both techniques are effective treatment options with similar results regarding CPIP and recurrence rates while TAPP is associated with a longer hospital stay and significant longer operation time than TEP hernia repair and the higher risk of a port-site hernia[18].

The lower incidence of CPIP after endoscopic repair is probably due to the preperitonal position of the mesh instead of the intermuscular position in the anterior approach adjacent to nerves. In the preperitoneal space, direct contact of the inguinal nerves is rather limited. Fixation of the mesh- which may cause CPIP due to hematoma formation or nerve entrapment- is unnecessary as abdominal pressure, according to Pascal's hydrostatic principles, should firmly position the prosthesis. The important steps in the evolution of the preperitoneal approaches to the groin have been described in a historical review[19]. TEPP and TAPP are now the most frequently performed preperitoneal techniques worldwide.

Possible drawbacks of endoscopic techniques are higher costs, the necessity to use general anaesthesia and their documented long learning curve[6,20]. Increased costs are particular due to the need of special equipment and general anaesthesia. However, when including social costs, in many studies total costs were similar or even lower after endoscopic repair[6]. General anaesthesia might be harmful in elderly patients and is sometimes contra-indicated in pulmonary compromised patients. Some experimental research indicates a correlation between postoperative cognitive changes and anaesthetic drugs, but evidence is conflicting and surgical trauma or underlying pathology may be of greater importance[21]. To avoid general anaesthesia but keep the advantages of the preperitoneal position of the mesh, new techniques have been developed. These open anterior approaches with preperitoneal mesh placement, such as TIPP (Trans Inguinal PrePeritoneal technique) and TREPP (TransREectus sheat PrePeritoneal mesh repair)) are currently being explored, however the number of studies so far is too small to draw conclusions[22-24]. The length of the learning curve depends on its definition. As suggested by the European guidelines the first 30 to 50 TEP procedures are most critical regarding major complications and recurrences and it is recommended to perform the first 50 procedures under the supervision of an experienced surgeon[6]. After this introduction, the starting TEP surgeon could avoid frustration, perform

the TEP procedure in a safe and feasible way and overcome the on-going learning curve up to 400 procedures smoothly by initially selecting relatively young (<60 years of age) and slender male patients with a unilateral hernia and no previous abdominal surgery[25].

Today, preperitoneal endoscopic approaches are favoured by many as the superior techniques for repairing inguinal hernias. Nevertheless, the risk of developing CPIP is still 2-5% after TEP repair and the impact of this on daily activities as well as the proper management of this annoying and at times invalidating side-effect is unknown. In general, there are no consensus guidelines regarding the assessment and management of CPIP after any type of hernia repair. Despite unsolved problems, a correct diagnosis of the cause of CPIP is important in order to select the best treatment modality [26-28]. The first problem is the difficulty in differentiation between neuropathic and nociceptive pain due to the great number of presentations of pain, the complex coupling between different nerve fibres and pain centralization. Classically, in case of neuropathic pain, various types of sensory dysfunction in the surgical area (hypo or hyperesthesia, allodynia and paraesthesia) can be found. In case of nociceptive pain the symptoms are more diffuse and vague and typically sensory changes are not present. In case of CPIP, history, physical examination and ultrasound are generally performed. This could identify patients with a recurrent hernia or neuropathic pain. However, it might be insufficient to detect soft tissue changes caused by the operation or other disorders around the groin that mimic groin pain. MRI is known to be useful to diagnose soft tissue pathology[29-31]. The yield of MRI in the assessment of CPIP after TEP has been insufficiently evaluated thus far.

The second problem is how to choose the best treatment option in case of neuropathic pain. Neuropathic pain can be treated conservatively, by injections or nerve stimulation or surgically. However, efficacy of conservative treatments including anti-inflammatory and neuropathic medications has not been proven, patients suffer recurrence of pain and side effects are frequently reported[28]. Non-surgical treatment includes local nerve blocks, but literature is limited to small series or case reports[32,33]. Surgical neurectomy is a more invasive technique with favourable results. However the reported effect varies and long-term outcome data are scarce[27,28,34]. In addition, this approach is irreversible and may cause other side effects like numbness. Nerve stimulation, including PNS, SCS (Spinal Cord Stimulation) and DRG (Dorsal Root Stimulation), can be an effective and reversible treatment option, relying on the stimulation- induced paresthesia overlapping the pain area[35-39]. PNS and DRG achieve more targeted pain relief compared to SCS, avoiding stimulation in non-pain areas side effect[37-40].

The third problem is the treatment of nociceptive pain. It is assumed that nociceptive pain (reaction induced by foreign material) is the most important causative factor for CPIP after preperitoneal mesh placement. It has been postulated that the inflammatory reaction to foreign material correlates with the amount of material and the pore size of the material inserted. Therefore, so-called lightweight meshes have been developed in recent years. Lightweight meshes proved significantly better in open anterior inguinal hernia repair in terms of CPIP and foreign body awareness and today are advocated when performing an anterior mesh repair[41]. However, in endoscopic repair this benefit has not been confirmed and there is still no consensus which type of mesh is optimal for endoscopic hernia repair. In addition, possible adverse effects of a lightweight mesh on fertility have been published and there is concern about the incidence of recurrences[42-44].

In summary, the endoscopic preperitoneal technique is an appealing inguinal hernia repair technique, theoretically superior to other approaches. However in practice some problems remain unsolved. Real incidences of CPIP and other possible sequelae after endoscopic hernia repair are unknown and the best method to assess them is not clear.

GENERAL AIM OF THIS THESIS

The aim of this thesis was to analyse the incidence of some important sequelae of endoscopic hernia repair and to explore strategies for the evaluation and the management of these problems.

Specific aims

1. To develop an algorithm for assessment and treatment of postherniorrhaphy pain.
2. To evaluate the yield of MRI in evaluating CPIP after TEP hernia repair
3. To describe the incidence, type and course of pain during the first year after TEP repair
4. To describe the impact and incidence of pain related to sexual activity before and after TEP repair
5. To assess the effects of different types of meshes (lightweight and heavyweight) on CPIP, foreign body feeling and quality of life.
6. To describe results of TEP repair in women

Outline

CPIP after inguinal hernia repair is a well-recognized sequel after any type of hernia repair with an incidence of long-lasting disabling pain of 12%. The incidence of CPIP is less after endoscopic repair compared to open anterior repair, but still 2-5% of patients report CPIP

interfering with daily life. In our hernia center, TEP repair is the preferred treatment for inguinal surgery. However, the number of referred patients visiting our center with CPIP after open and/or endoscopic inguinal repair rises. It is a clinical challenge to systemically assess the type of pain and treat it accordingly. In order to develop a protocolled CPIP treatment, our departments of surgery and anaesthesiology have designed an algorithm to diagnose the type of pain and then select the appropriate therapy. In **Chapter 2** the results of this protocolled treatment are described.

The prevailing pathophysiology of CPIP after TEP repair is thought to be inflammatory-mediated rather than neuropathic due to the preperitoneal position of the mesh. History and physical examination are frequently insufficient to detect possible causes of CPIP after preperitoneal repair and ultrasound of the groin seldom shows disorders. MRI has superior abilities to evaluate changes within the soft tissues and is well established in diagnosing a primary inguinal hernia in clinically unclear cases or diagnose soft tissue pathology. In **Chapter 3** the role of MRI in detecting causes of CPIP following endoscopic hernia repair is evaluated.

Reported incidence rates of CPIP pain vary widely due to differences in definition, measurement and timing of assessment. Despite an overwhelming amount of publications on CPIP, real incidence rates and the course in time of CPIP remain unclear. **Chapter 4** focuses on the course of pain over one year after TEP inguinal repair.

An important sequel of inguinal hernia and its repair is the alleged impairment of sexual function. Data on this topic are scarce. In **Chapter 5** the incidence and effect of pain related to sexual activity before and after TEP inguinal repair were evaluated

Meshes prevent recurrences in inguinal hernia repair. However, mesh might have disadvantages inducing an inflammatory reaction with subsequent fibrosis. If this reaction is too long and too intense , exaggerated fibrosis might develop, possibly resulting in CPIP and discomfort. Lightweight meshes with less material and larger pores significantly result in reduced CPIP after open anterior repair, in endoscopic repair discussion about this benefit is ongoing. In **Chapters 6** and **7** the early postoperative and 2-years results of a large prospective randomized clinical trial comparing both meshes are reported.

Chapter 8 describes the results of endoscopic inguinal hernia repair in women. Femoral hernia in women is common, and the frequency of a femoral recurrence after open repair is high. Recommendations for the best treatment modality of a groin hernia in female pa-

tients is mandatory. The results ensuing from these studies are summarized and discussed in Chapter 9. Future perspectives are provided at the end of this chapter.

REFERENCES

1. Kingsnorth A, LeBlanc K. Hernias: inguinal and incisional. *The Lancet* 2003; 362:1561-1571.
2. Statline, Centraal Bureau voor statistiek.
3. Thomas AD, Rogers A. Eduardo Bassini and the wound that inspires. *World J Surg* 2004; 28:1060-1062
4. Read RC. The contributions of Usher and others to the elimination of tension from groin herniorrhaphy. *Hernia* 2005; 9:208-211
5. Lichtenstein IL. Local Anesthesia for Hernioplasty. Immediate ambulation and return to work: a preliminary report. *Calif Med* 1964; 100:106-109
6. Simons MP, Aufenacker T, Bay-Nielsen M et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2009; 13:343-403.
7. Kehlet H. Chronic pain after groin hernia repair. Br J Surg 2008; 95:135-136
8. Eklund A, Montgomery A, Bergkvist L, et al. for the Swedish Multicentre Trial of Inguinal Hernia Repair by Laparoscopy (SMIL) study group. Chronic pain 5 years after randomized comparison of laparoscopic and Lichtenstein inguinal hernia repair. *Br J Surg* 2010; 97:600-608
9. Bay-Nielsen M, Perkins FM, Kehlet H. Pain and functional impairment 1 year after inguinal herniorrhaphy: a nationwide questionnaire study. *Ann Surg* 2001; 233:1-7
10. Hindmarch AC, Cheong E, Lewis MPN, et al. Attendance at a pain clinic with severe chronic pain after open and laparoscopic inguinal hernia repairs. *Br J Surg* 2003; 90: 1152-1154
11. Poobalan AS, Bruce J, King PM, et al.. Chronic pain and quality of life following open inguinal hernia repair. *Br J Surg* 2001; 88: 1122-1126
12. Alfiery S et al. Influence of preservation versus division of ilioinguinal, iliohypogastric and genital nerves during open mesh herniorrhaphy: prospective multicentric study of chronic pain. *Ann Surg* 2006; 243:553-558
13. Bhangu A, Singh P, Pinkney T, et al. A detailed analysis of outcome reporting from randomised controlled trials and meta-analyses of inguinal hernia repair. *Hernia* 2015; 19:65-75.
14. Aasvang EK, Brandsborg B, Christenen B, et al. Neurophysiological characterisation of postherniotomy pain. *Pain* 2008; 137:173-181
15. International Association for the Study of Pain, Subcommittee on Taxonomy. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. *Pain.* 1986;3:1–226
16. Kuhry E, van Veen RN, Langeveld HR, et al. Open or endoscopic total extraperitoneal inguinal hernia repair? A systematic review. *Surg Endosc* 2007; 21:161-166
17. O'Reilly EA, Burke JP, O'Connell PR. A meta-analysis of surgical morbidity and recurrence after laparoscopic and open repair of primary unilateral inguinal hernia. *Ann Surg* 2012; 255:846-853
18. Bittmer R, Montgomery MA, Arregui E, et al. Update of guidelines on laparoscopic (TAPP) and endoscopic (TEP) treatment of inguinal hernia (International Endohernia Society). *Surg Endosc* 2015;29:289-321
19. Read RC. Crucial steps in the evolution of the preperitoneal approaches to the groin: an historical review. *Hernia* 2011; 15:1-5
20. Lau H, Patil NG, Yuen WK, et al. Learning curve for unilateral endoscopic totally extraperitoneal inguinal hernioplasty. *Surg Endosc* 2002; 16: 1724-1728.
21. Strom C, Rasmussen LS, Sjeber FE. Should general anaesthesia be avoided in the elderly? *Anaesthesia* 2014; 69:35-44.
22. Koning GC, Koole D, de Jongh MAC et al. The transinguinal preperitoneal hernia correction vs Lichtenstein's technique; is TIPP top? *Hernia* 2011; 15:19-22

23. Koning GC, Keus F, Koeslag L et al. Randomised clinical trial of chronic pain after the inguinal preperitoneal technique compared with Lichtenstein's method for inguinal hernia repair. *Br J Surg* 2012; 99:1465-1373
24. Koning GC, Andeweg CS, Keus F et al. The transrectus sheath preperitoneal mesh repair for inguinal hernia: technique, rationale and results of the first 50 cases. *Hernia* 2012;16:295-299
25. Schouten N, Elshof JWM, Simmermacher RKJ, et al. Selecting patients during the "learning curve" of endoscopic Totally Extraperitoneal (TEP) hernia repair. *Hernia* 2013;17:737-743
26. Loos MJA, Roumen RMH, Scheltinga RMR. Classifying Postherniorrhaphy Pain Syndromes Following Elective Inguinal Hernia Repair. *World J Surg* 2007; 31:1760–1765
27. Amid PK. Causes, prevention, and surgical treatment of postherniorrhaphy neuropathic inguinodynia: Triple neurectomy with proximal end implantation. *Hernia* 2004; 8:343–349
28. Hakeem A, Shanmugam V. Current trends in the diagnosis and management of postherniorrhaphy chronic groin pain. *World J Gastrointest Surg* 2011; 27: 73-81
29. Leander P, Ekberg O, Sjoberg S, et al. MR imaging following herniography in patients with unclear groin pain. *Eur Radiol* 2000; 10:1691-1696.
30. Amid PK. Radiologic images of meshoma: a new phenomenon causing chronic pain after prosthetic repair of abdominal wall hernias. *Arch Surg* 2004; 139:1297-1298.31. Barile A, Erriquez D, Cacchio A, et al. Groin pain in athletes: role of magnetic resonance. *Radiol Med* 2000; 100: 216-222
32. Palumbo P, Minicucci A, Nasti AG, et al. Treatment for persistent chronic neuralgia after inguinal hernioplasty. *Hernia* 2007 ;11:527-31
33. Carr DB. Local Anesthetic Blockade for Neuralgias: "Why Is the Sky Blue, Daddy?". *Anesth Analg* 2011;112:1283-85
34. Bischoff JM, Koscielniak-Nielsen ZJ, Kehlet H, et al. Ultrasound-guided ilioinguinal/iliohypogastric nerve blocks for persistent inguinal postherniorrhaphy pain: a randomized, double-blind, placebo-controlled, crossover trial. *Anesth Analg* 2012; 114:1323-9
35. Carayannopoulos A, Beasley R, Sites B. Facilitation of percutaneous trial lead placement with ultrasound guidance for peripheral nerve stimulation trial of ilioinguinal neuralgia: a technical note. *Neuromodulation* 2009; 12:296-301
36. Stinson LW, Roderer GT, Cross NE, et al. Peripheral Subcutaneous electrostimulation for Control of Intractable Post-operative Inguinal Pain: A Case Report Series. *Neuromodulation* 2001; 4:99-104
37. Schu S, Gulve A, Eldabe S, et al. Spinal cord stimulation of the dorsal root ganglion for groin pain – a retrospective review. *Pain Pract* 2014; April 1 [Epub ahead of print]
38. Yakovlev AE, Al Tamimi M, Barolat G. Spinal cord stimulation as alternative treatment for chronic postherniorrhaphy pain. *Neuromodulation* 2010; 13:288–290
39. Elias M. Spinal cord stimulation for post-herniorrhaphy pain. *Neuromodulation* 2000; 3:155–157
40. Lepski G, Vahedi P, Tatagiba MS, et al. Combined spinal cord and peripheral nerve field stimulation for persistent post-herniorrhaphy pain. *Neuromodulation* 2013;16:84–88
41. Miserez M, Peeters E, Aufenacker T, et al. Update with level 1 studies of the European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2014; 18:151-163
42. Curry A, Andrew H, Tonsi A, et al. Lightweight versus heavyweight mesh in laparoscopic inguinal hernia repair: a meta-analysis. *Surg Endosc* 2012; 26:2126-2133
43. Chowbey PK, Garg N, Sharma A, et al. Prospective randomized clinical trial comparing lightweight mesh and heavyweight polylropylene mesh in endoscopic totally extraperitoneal groin hernia repair. *Surg Endosc* 2010; 24:3073-3079

44. Peeters E, Spiessens C, Oyen R, et al. Laparoscopic inguinal hernia repair in men with lightweight meshes may significantly impair sperm motility: a randomized controlled trial. *Ann Surg* 2010; 252:240-246

2

An algorithm for assessment and treatment of postherniorraphy pain

CEH Voorbrood
JPJ Burgmans
T Van Dalen
J Breel
GJ Clevers
F Wille
RKJ Simmermacher

Hernia 2015;19:571-7

ABSTRACT

Background: Inguinal pain after groin hernia repair is a challenging issue. About 50% of postherniorrhaphy pain allegedly is neuropathic, treatment of which is cumbersome given the limited efficacy of current therapeutic modalities. Possibly a clear protocol assessing the type of pain and treating it accordingly could improve its treatment

Methods: A prospective study was done to evaluate an algorithm in patients with chronic postherniorrhaphy groin pain, aiming to select those with neuropathic pain and to treat appropriately. Treatment consisted of ultrasound-guided nerve blocks as an initial treatment for neuropathic pain. If long-term pain reduction proved inadequate, peripheral nerve stimulation was offered.

Result: After our diagnostic work-up consisting of anamnesis, physical examination and imaging, 68 patients out of 105 were diagnosed as having non-neuropathic pain. These patients were referred to the most appropriate consultant, treated accordingly or sometimes pain appeared to be self-limiting. Thirty-seven (35%) patients were diagnosed as having neuropathic pain with a median NRS of 7 (range 4-9) and were referred for further treatment to our pain-clinic. The majority (21 of 28 patients) suffered ileo-inguinal nerve involvement. After ultrasound-guided nerve blocks, a permanent reduction in pain was achieved in 18 patients (62%) with a median post-treatment NRS of 1 (range 0-3). In 6 patients to which an additional peripheral nerve stimulator (PNS) was offered, pain reduction to a level of mild complaints with a median NRS of 2 (range 1-8). In total, 24 of the 28 patients (83%) diagnosed with neuropathic postherniorrhaphy pain achieved significant pain reduction after algorithm-based treatment.

Conclusions: In the present study we implemented a diagnostic work-up for patients with postherniorrhaphy inguinal pain to select those with neuropathic pain. Eighty-tree percent of the patients with neuropathic groin pain obtained significant improvement of their pain scores after our protocolled treatment. The effect was achieved by nerve infiltrations and in some cases by an implanted PNS when the former was unsuccessful.

INTRODUCTION

Postherniorrhaphy pain is a well-recognized sequel after any type of inguinal hernia repair. The incidence of disabling postoperative inguinal pain is suggested to be around 12%.[1-4] Identification of the type of pain is important in order to select the most appropriate treatment.[1, 4, 5] About 50% of postherniorrhaphy pain is allegedly neuropathic, characterized by an activity-induced pain with sensory dysfunction in the surgical area and most probably due to direct nerve injury.[6-8] Treatment of this neuropathic pain is a clinical challenge given the limited efficacy of current therapeutic modalities.[9,10] Although knowledge about the treatment of postherniorrhaphy neuropathic pain is growing, there is lack of consensus regarding the most effective treatment.[11-13]

Nerve infiltration with anaesthetics is a minimally-invasive technique for treating peripheral neuropathy after inguinal surgery.[14,15] Varying success rates have been reported, but the relative ease of application is a main advantage.[16,17] In patients with neuropathic conditions in other body areas, electrical peripheral nerve stimulation (PNS) has been described as a successful treatment and thus may be an alternative in patients with neuropathic groin pain. [18-21]

Protocolled postoperative inguinal pain treatment is difficult due to the great number of presentations of pain. Again, discrete distinction between neuropathic and non-neuropathic or nociceptive pain can be difficult because many factors including the overlap of different nerve fibres, pain centralization and patient-related factors play a role in the presentation of postoperative groin pain. Therefore, a clear work-up is required to assess the type of pain and to subsequently treat it accordingly.

Our Departments of Surgery and Anaesthesia first designed an algorithm to divide patients with postherniorrhaphy pain in two groups: neuropathic and non-neuropathic pain. Patients with neuropathic pain are offered a treatment algorithm starting with sonography guided local infiltrations followed, if necessary, by PNS. The aim of the present study is to show that selected patients with neuropathic chronic postherniorrhaphy groin pain, given a protocolled treatment, have a reasonable chance to be relieved.

METHODS

We implemented an algorithm to select patients with chronic neuropathic post groin hernia repair. To differentiate between possible causes of inguinal pain, the work-up consisted

of taking history, physical examination and additional imaging. Chronic pain was defined as pain persisting at least three months after surgery with a severity score of at least 4 on a Numerous Rating Scale (NRS, range 0-10).[12,22] Pain scores were classified as no pain (NRS 0), mild (NRS 1-3), moderate (4-7) or severe (8-10). Mild pain was considered as clinically non-relevant pain (NRS 0-3).[23]

Anamnesis focuses particularly on the history of previous surgery as well as on the duration, localisation, character and provoking factors of pain. Apart from viewing and palpation of the inguinal area and examination of sensory changes of the skin, additional investigations were performed; palpation of the pubic tubercle for pubalgia, test of Carnett (discerning visceral pain from parietal pain in ACNES), test of Lasegue (spinal disc herniation), pain on the hip-adductor insertion (adductor tendinitis) or painful movement of the hip (bursitis iliopectinea, arthrosis). Both ultrasonography and MRI were performed in all patients. Neuropathic pain is defined as an activity- or trigger point-induced sharp pain with a burning, painful cold and/or electric character, associated with a tingling, sharp, numbness and/or itching sensation without spontaneous decrease and is caused by a lesion of the sensory nervous system.[6, 7, 24] Nociceptive pain results from activity in neural pathways secondary to actual tissue damage or potentially tissue-damaging stimuli,[25] as well as other identifiable diseases that can cause groin pain.[6]

When anamnesis, physical examination and imaging showed another cause of pain than neuropathic of nociceptive, appropriate treatment was offered by the most relevant consultant. The first step in treatment of chronic neuropathic inguinal pain is ultrasound-guided nerve blocks. We start with transverse placement of the ultrasound probe adjacent to the affected nerve which allows accurate visualisation of the neurovascular plane.[26, 27] Subsequently, hydro dissection of the inguinal wall with 2 ml of saline is provided. When the affected nerve is identified, a mixture of 80 mg/ml depomedrol and 2,5 mg/ml chirocaïne is infiltrated additionally, an average of 4-10 ml dilution is infused depending on the local anaesthetic spread.

Evaluation of the effect of the nerve block is assessed after 6 weeks using the NRS-score and compared to the pain intensity measured during intake. A reduction of 30 to 50% on pain intensity is considered as clinically significant.[23] If the nerve block gained sufficient effect, expectative policy is agreed upon. In case of temporary or insufficient effect after 6 weeks, the nerve block as described earlier is repeated for a maximum of 2 times as an institutional policy. If no long-term pain reduction is achieved after 3 nerve blocks, the patient is offered a peripheral neurostimulation implant. In patients consenting to undergo this procedure, inguinal nerve exploration is performed under general anaesthesia. An

Octad™, Medtronic lead is inserted close to the affected nerve, tunnelled to the ipsilateral side of the abdominal wall and attached to an internal pulse generator (Prime Advanced™, Medtronic). Impedances of the lead and linkage with the battery are tested during the operation. Allowing to reduce direct postoperative pain, the electrical stimulation of the peripheral inguinal nerve is only started one week postoperative to relieve neuropathic pain. After 3 months, outcome is measured on an NRS.

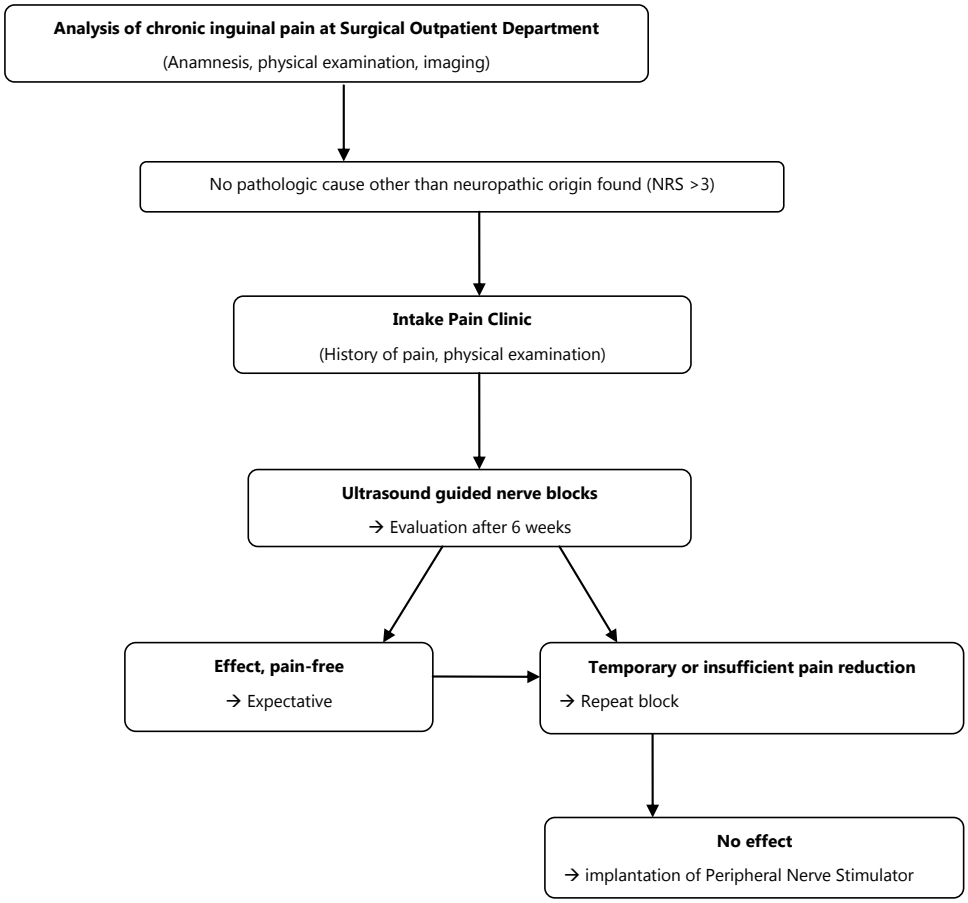

Figure 1. Treatment algorithm

The diagram of our clinical algorithm is presented in Fig. 1.

RESULTS

Between October 2009 and August 2012, 105 consecutively referred and own patients with chronic postherniorrhaphy groin pain were seen at the outpatient department. After our diagnostic workup 68 patients were diagnosed with non-neuropathic pain. Diagnoses of the patients are listed in Table 1. All patients with non-neuropathic pain were referred to the relevant specialist; disorders were treated accordingly or the pain sometimes appeared to be self-limiting.

Table 1. The diagnoses of patients whom were considered having non-neuropathic pain

Spontaneous decrease of pain	21
Recurrence of hernia	11
Musculotendinous	
Adductor tendinitis	9
Pubalgia	6
Rectus femoris muscle insertion	1
Referred lumbosacral pain	3
Sacroiliac joint dysfunction	3
Arthrosis	2
Urologic	2
ACNES	2
Femoral nerve irritation (not resulting from hernia surgery)	1
Refractory pain of L1 after previous neurectomy	1
Pelvic varicoses	1
Unclear/other	5
Total	**68**

Thirty-seven patients (35%) were diagnosed as having neuropathic pain and were offered a referral to the pain clinic. Eight patients refused this, leaving 29 patients who were treated according to our protocol for neuropathic pain (Fig. 2). The median age of these 29 patients was 49 years (range 22-78), with a predominance of men (96,6%). The median duration of complaints usually without any treatment was 18 months (range 4 months- 6 years) with a median NRS of 7 (range 4-9) before treatment. The median number of previous ipsilateral inguinal operations was 2 (range 1-5) and consisted of one or more hernia operations, listed in Table 2. Twenty-one patients (72,4%) presented with pain consistent with ileo-inguinal nerve involvement. In six patients (20,7%) the genito-femoral nerve was affected, in one patient (3,4%) the ileo-hypogastrical nerve and in one (3,4%) patient both ileo-inguinal and genito-femoral nerves.

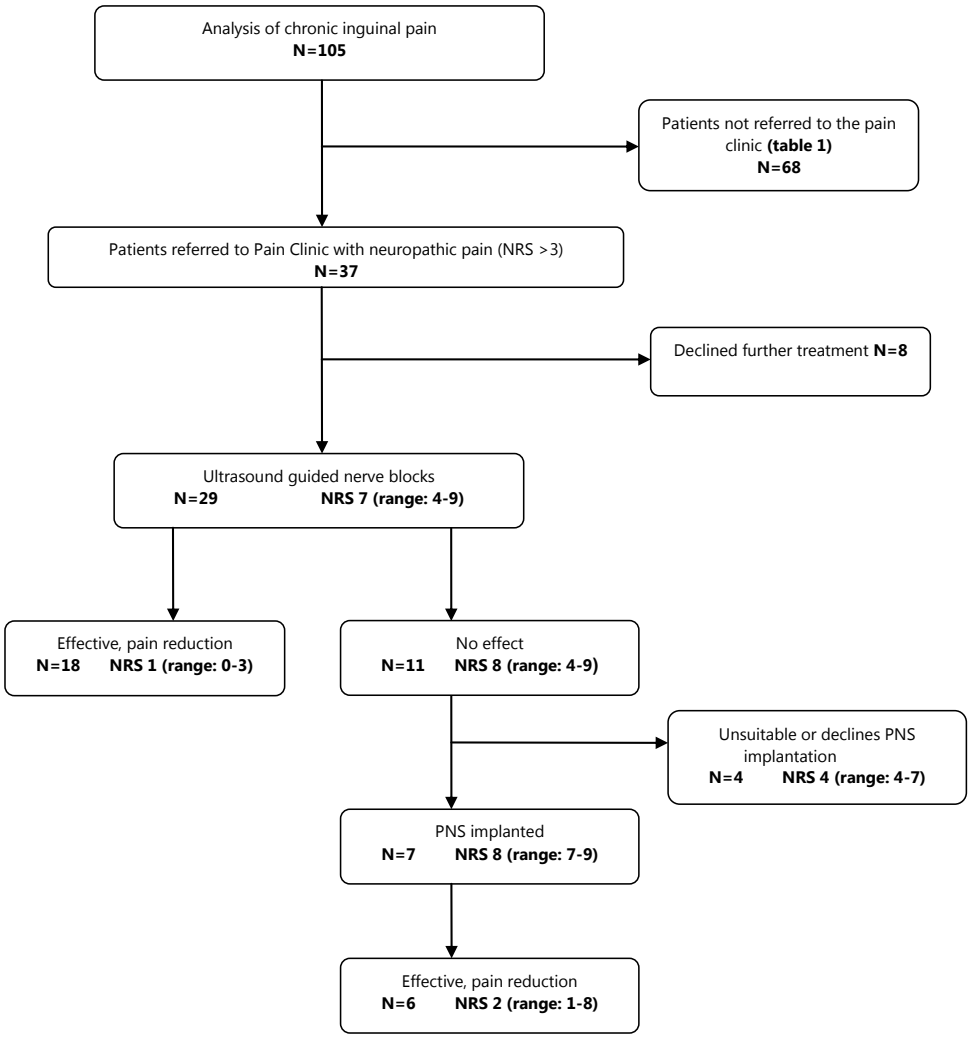

Figure 2. Results after using the flowchart

Following nerve block treatment, 18 patients (62,1%) obtained satisfactory pain relief. In this group, a median of 2 (range 1-8) infiltrations were performed. A significant reduction of the NRS score was observed with a median NRS of 1 (range 0-3) post-treatment. Two of the eighteen patients experienced significant temporary pain relief for respectively four and seven months, still occasionally requiring an additional nerve block. In 11 patients (37,9%) nerve infiltration had only a limited effect (hours to days) or did not reduce pain sufficiently. These patients were offered peripheral nerve stimulation treatment of the affected nerve. Four patients declined PNS implantation due to mild subjective complaints

Table 2. Performed previous inguinal operations and types of implanted meshes of patients presented at the pain clinic (n=29)

Number of patients	Type(s) of surgery	Number of operations per patient*	Type(s) of mesh
4	Lichtenstein	1	1 Prolene 1 Parietene Progripp 2 Unknown
4	Lichtenstein and TEP	2	1 Marlex and Prolene 3 Prolene and Prolene
3	Lichtenstein and exploration (1 x neurolysis 2 x neurectomy)	2	3 prolene
1	Lichtenstein and Stoppa	2	1 Prolene and Marlex
1	Lichtenstein and Stoppa and exploration (RIVAS)	3	1 Ultrapro and Prolene and Prolene
1	Lichtenstein and plug & patch and exploration (plug removal and neurectomy)	3	1 Prolene and plug
1	Plug & patch and exploration (plug & patch removal and Lichtenstein)	2	1 Plug & patch and Progripp
1	R & R plasty (plug) and exploration (plug removal and neurectomy)	2	1 Plug
1	Ugahary and Lichtenstein	2	1 Prolene and Prolene
6	TEP	1	5 Prolene 1 Ultrapro
1	TEP (with hernial sac resection)	1	1 Prolene
1	TEP and TAPP	2	1 Prolene and Prolene
2	Shouldice and TEP	2	2 Prolene
2	Multiple (5) inguinal operations	5	2 unknown

*The Number of operations indicates the number of operations performed per patient. Overall 56 operations were performed in 29 patients

(NRS 4) and seven patients received a PNS. After three months follow-up, a significant reduction of pain from 8 to a level of 2 on the NRS scale was seen ($p<0.001$). In one patient the PNS was not successful; a surgical neurectomy was performed previously. This patient was offered dorsal root ganglion stimulation. Overall, 24 of the 29 patients (82,8%) who were treated for postoperative neuropathic groin pain obtained significant improvement of their pain scores, while four (14%) refused to finish the whole protocol.

DISCUSSION

In this study we show a 82% reduction-rate in chronic postherniorrhaphy neuropathic pain in a group of patients that had a standardized work-up of their pain and subsequent a

protocolled treatment sequence. The effect was achieved by initial nerve infiltrations and if necessary implanting a peripheral nerve stimulator.

Other authors also underline the importance of correct diagnosis to subsequently select proper treatment. [6, 7, 9] A common cause of chronic postherniorrhaphy pain next to nociceptive pain or pain due to other pathology is neuropathic in origin and present in 35% of the patients in this study. Comparable results are reported by others; Amid observed a neuropathic origin of the pain in 44% of the patients, whilst Loos found neuropathic pain as a cause for chronic postoperative pain following inguinal hernia repair in 46,5% of the patients.[6,7] In the latter study, funiculodynia was also common and present in 28% of the patients with postherniorrhaphy pain, whilst it was rare in the present study (7%).

Twenty-nine patients with neuropathic pain, selected out of a group of 102 were treated for their inguinal pain using ultrasound-guided nerve blocks, resulting in effective pain relieve in 61% of these patients, in the first leg. Little information exists on conservative treatment of postherniorrhaphy neuropathic groin pain. Medical management of neuropathic pain is difficult; efficacy has not been proven, patients suffer recurrence of pain and side effects are frequently reported. To add to this, the information reported merely reflects neuropathic pain treatment in other body areas.[9] Palumbo et al., describes a cohort of 32 patients who were treated by medication and subsequent repeated nerve infiltrations (with local anaesthetics and cortisone) for persistent chronic neuralgia after inguinal hernioplasty; they report lasting pain relief in 30 patients.[28] Also, Carr described the phenomenon of pain relief after the infiltration technique for neuralgia in general, emphasizing the minimally invasive character of this therapy.[14] On the other hand he emphasizes the lack of performed investigations and the need for studies in this field. Surgical neurectomy is a more invasive technique with favourable results, however, the reported effect varies and long-term outcome data are scarce.[7,9,16] In addition, this approach is irreversible and may cause other side effects like numbness.

Nerve stimulation, including PNS, SCS (Spinal Cord Stimulation) and DRG (Dorsal Root Stimulation), can be an effective and reversible treatment option, relying on the stimulation- induced paresthesia overlapping the pain area.[20, 21, 29-31] Some small patient series showed effective pain relief after SCS, however unwanted stimulation in non-pain areas frequently occur due to the complex anatomical trajectory of the peripheral nerves into the spinal cord.[32] PNS and DRG achieve more targeted pain relief without the abovementioned side-effect.[29] Six of the seven patients (86%) implanted with a PNS showed substantial pain relief to a level of 2 on the NRS scale ($p<0.001$). Patients with refractory peripheral neuropathy at other sites (lower or upper extremity), have been treated successfully with

a peripheral nerve stimulator as has been reported by Huntoon and Burgher.[19] Weiner supports the use of a peripheral nerve stimulator as an alternative to potentially destructive surgical procedures for chronic neurogenic pain control.[18] This treatment modality was reported to be effective for inguinal neuralgia in two other studies.[20,21] Carayannopoulos et al. placed a percutaneous lead for peripheral nerve stimulation in 2 patients with ileoinguinal neuralgia. During the seven-day trial-stimulation period, both patients reported 90% reduction in pain.[20] In another study of Stinson et al., three patients experienced 75–100% pain relief one year after placing the PNS for intractable postoperative inguinal pain.[21] As the PNS gives good results for the treatment of peripheral neuropathic pain, we suggested this modality is an effective treatment option for patients with chronic postherniorrhaphy neuropathic groin pain. In our algorithm it is reserved for patients who do not benefit from nerve infiltration. A potential side-effects of PNS is erosion and migration of the stimulation lead along with the potential need for high stimulation amplitudes, which occurred in one of our patients.[33] A recent publication by Schu et al. demonstrated promising results of a new neuromodulation system stimulating the dorsal root ganglion.[29] In this study 29 nine patients were treated successfully after DRS. Further exploration of PNS and DRS is necessary to assess best treatment option for inguinal pain after groin surgery.

The strength of the study is a clear algorithm for the treatment of postherniorrhaphy pain patients with a multidisciplinary work-up with successful results. The study has a number of limitations. It is a prospective cohort study, precluding comparison of the effect of an alternatively treated group of patients. In addition, no detailed follow-up information was available for patients who rejected therapy and the group was not homogenous regarding previous operative treatments. The results of peripheral nerve stimulation in this study are promising but it is only a small case series without long term results. Further testing of this algorithm in the setting of a randomized controlled trial including the option of DRS, is recommended to test its validity and to achieve meaningful use.

Given the unsatisfactory status of current treatment and the potentially debilitating character of neuropathy in postherniorrhaphy patients, efforts are needed to improve treatment of this condition. With the presented algorithm, appropriate diagnosis can be made in a majority of patients and the selected patients with neuropathic pain succeeded in significant pain relief after treatment. Treatment prescribed nerve blocks initially, followed by implantation of a PNS when nerve blocks had limited or no effect. The cumulative success rate of all treatments was 83 percent.

We believe patients benefit from a multidisciplinary surgery and pain team evaluation with subsequent treatment instead of a single treatment strategy to ensure optimal care in

an experienced centre. This study demonstrated that for adequate selected patients with chronic neuropathic pain of the inguinal nerves, non-invasive injection therapy is generally sufficient to relieve pain. In those patients without success, further management with a peripheral nerve stimulator is an effective alternative.

REFERENCES

1. Bay-Nielsen M, Perkins FM, Kehlet H. Pain and Functional Impairment 1 Year After Inguinal Herniorrhaphy: A Nationwide Questionnaire Study. *Ann Surg* 2001; 233:1–7
2. Poobalan AS, Bruce J, Cairns W et al. A Review of Chronic Pain After Inguinal Herniorrhaphy. *Clin J Pain* 2003; 19:48–54
3. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaesth* 2005; 95: 69–76
4. Ferzli GS, Edwards ED, Khoury GE. Chronic Pain after Inguinal Herniorrhaphy. *Am Coll Surg* 2007; 205: 333–341
5. Nienhuis S, Staal E, Strobbe L et al. Chronic pain after mesh repair of inguinal hernia: a systematic review. *Am J Surg* 2009; 194:394–400
6. Loos MJA, Roumen RMH, Scheltinga RMR. Classifying Postherniorrhaphy Pain Syndromes Following Elective Inguinal Hernia Repair. *World J Surg* 2007;31:1760–1765
7. Amid PK. Causes, prevention, and surgical treatment of postherniorrhaphy neuropathic inguinodynia: Triple neurectomy with proximal end implantation. *Hernia* 2004; 8:343–349
8. Treede RD, Jensen TS, Campbell JN et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology* 2008; 70:1630–1635
9. Hakeem A, Shanmugam V. Current trends in the diagnosis and management of postherniorrhaphy chronic groin pain. *World J Gastrointest Surg* 2011; 3: 73-81
10. O'Connor AB, Dworkin RH. Treatment of Neuropathic Pain: An Overview of Recent Guidelines. *Am J Med* 2009; 122:22–32
11. Kehlet H, Roumen RM, Reinpold W et al. Invited commentary: persistent pain after inguinal hernia repair: what do we know and what do we need to know? *Hernia* 2013; 17:293-7
12. Alfiery S et al. International guidelines for prevention and management of post-operative chronic pain following inguinal hernia surgery. *Hernia* 2011;15:239-49
13. Simons MP, Aufenacker T, Bay-Nielsen M et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2009;13:343–403
14. Carr DB. Local Anesthetic Blockade for Neuralgias: "Why Is the Sky Blue, Daddy?" *Anesth Analg* 2011;112:1283-85
15. Kissin I, Vlassakov KV, Narang S. Local anesthestic blockade of peripheral nerves for treatment of neuralgias: systematic analysis. *Anesth Analg* 2011;112:1487–93
16. Bischoff JM, Koscielniak-Nielsen ZJ, et al. Ultrasound-guided ilioinguinal/iliohypogastric nerve blocks for persistent inguinal postherniorrhaphy pain: a randomized, double-blind, placebo-controlled, crossover trial. *Anesth Analg* 2012; 114:1323-9
17. Vlassakov KV, Narang S, Kissin I. Local anesthetic blockade of peripheral nerves for treatment of neuralgias: systematic analysis. *Anesth Analg* 2011; 112:1487-93
18. Weiner RL. Peripheral nerve stimulation. *Neurosurg Clin N Am* 2003;14:401-8.
19. Huntoon MA, Burgher AH Ultrasound-guided permanent implantation of peripheral nerve stimulation (PNS) system for neuropathic pain of the extremities: original cases and outcomes. *Pain Med* 2009;10:1369-77.
20. Carayannopoulos A, Beasley R, Sites B. Facilitation of percutaneous trial lead placement with ultrasound guidance for peripheral nerve stimulation trial of ilioinguinal neuralgia: a technical note. *Neuromodulation* 2009;12:296-301

21. Stinson LW, Roderer GT, Cross NE et al. Peripheral Subcutaneous electrostimulation for Control of Intractable Post-operative Inguinal Pain: A Case Report Series. *Neuromodulation* 2001; 4:99-104.
22. Loos MJA, Houterman S, Scheltinga MRM, et al. Evaluating postherniorrhaphy groin pain: visual analogue or verbal rating scale? *Hernia* 2008; 12: 147-151
23. Haanpää M, Attal N, Backonja M et al. NeuPSIG guidelines on neuropathic pain assessment. *Pain* 2011; 152;14–27
24. Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain* 2005; 114: 29-36.
25. Nicholson B. Differential diagnosis: nociceptive and neuropathic pain. *Am J Manag Care* 2006; 12:256-262.
26. Johansson A, Bennett GJ. Effect of local methylprednisolone on pain in a nerve injury model. A pilot study. *Reg Anesth* 1997; 22:59–65
27. Gofeld M, Christakis M. Sonographically guided ilioinguinal nerve block. *J Ultrasound Med* 2006; 25:1571-1575
28. Palumbo P, Minicucci A, Nasti AG, et al. Treatment for persistent chronic neuralgia after inguinal hernioplasty. *Hernia* 2007; 11:527-31
29. Schu S, Gulve A, Eldabe S, et al. Spinal cord stimulation of the dorsal root ganglion for groin pain – a retrospective review. *Pain Pract* 2014; April 1 [Epub ahead of print]
30. Yakovlev AE, Al Tamimi M, Barolat G. Spinal cord stimulation as alternative treatment for chronic postherniorrhaphy pain. *Neuromodulation* 2010; 13:288–290
31. Elias M. Spinal cord stimulation for post-herniorrhaphy pain. *Neuromodulation* 2000; 3:155–157
32. Lepski G, Vahedi P, Tatagiba MS, et al. Combined spinal cord and peripheral nerve field stimulation for persistent post-herniorrhaphy pain. *Neuromodulation*2013; 16:84–88
33. Stuart RM, Winfree CJ. Neurostimulation techniques for painful peripheral nerve disorders. *Neurosurg Clin N Am* 2009; 20:111–120

3

Chronic pain after TEP inguinal hernia repair, does MRI reveal a cause?

JPJ Burgmans
CEH Voorbrood
T Van Dalen
RN Boxhoorn
GJ Clevers
FBM Sanders
DBJ Naafs
RKJ Simmermacher

Submitted

ABSTRACT

Purpose: Persistent pain is a known side effect after TEP inguinal repair disabling 2-5% of patients. A standardized diagnostic work-up so far is not available. MRI is a diagnostic tool in the work-up of inguinal hernias. In the present study the yield of MRI in evaluating chronic pain after TEP hernia repair is addressed.

Methods: In our database patients receiving an MRI scan for groin pain lasting more than 3 months after TEP inguinal hernia repair were identified. A checklist with potential pathologic findings was filled out for each groin by two blinded observers. Findings in painful, pain-free and unoperated groins were compared and statistical analysis done based upon their relative incidences. Cohen's kappa coefficients were calculated to determine interobserver agreement.

Results: Imaging studies of 53 patients revealed information regarding 106 groins. Fifty-five groins were painful after the initial operation, twelve were pain-free postoperatively and 39 groins were not operated. None of the predefined disorders was observed statistically more often in the patients with painful groins. Only fibrosis appeared more prevalent in patients with chronic pain ($P = 0.11$). Interobserver agreement was excellent for identifying the mesh ($\kappa = 0.88$) and observing bulging or a hernia ($\kappa = 0.74$) and was substantial for detecting fibrosis ($\kappa = 0.63$). In 40% of the patients, MRI showed a correct mesh position and observed nothing else than minor fibrosis. A wait and see policy resolved complaints in the majority of the patients. In 15% of the patients, MRI revealed treatable findings explanatory for persisting groin pain.

Conclusion: For patients with post TEP hernia groin pain MRI is useful to confirm a correct flat mesh-position and to identify possible not operation related causes of groin pain. It is of little help to identify a specific cause of groin repair-related pain.

INTRODUCTION

Currently morbidity associated with inguinal hernia repair consists of chronic postoperative inguinal and genital pain rather than recurrences. Chronic pain can be debilitating, leading to costly multidisciplinary medical consultations.[1] Endoscopic techniques reduce the occurrence of postoperative pain compared to other groin hernia repair techniques but still result in approximately 2-5 % of patients having pain every day.[2-5]

So far no diagnostic work-up has been defined to evaluate patients with chronic postoperative pain after groin-hernia surgery. Types of pain and their estimated duration after hernia surgery are well defined.[6] In general, pain is categorized into two groups: neuropathic pain, defined as pain caused by direct nerve injury characterized by various types of sensory dysfunction in the surgical area and non-neuropathic or nociceptive pain due to tissue injury or an inflammatory reaction[7]. Differentiation between these two may be difficult.[5,6,8] The origin of pain after endoscopic mesh repair is thought to be less related to direct nerve injury as the involved nerves are left untouched intraoperatively. Inflammatory-mediated nociceptive pain seems the prevailing pathophysiology for chronic pain following endoscopic hernia repair.

If pain occurs after inguinal hernia surgery, a history has to be taken, physical examination has to be performed and ultrasound of the groin will be done. This however might be insufficient to detect soft tissue changes caused by the operation or other different disorders around the groin that mimic groin pain. MRI, with its superior soft tissue evaluation possibilities could have a role to further evaluate the patient but has been insufficiently evaluated thus far. The role of MRI is well established in diagnosing a primary inguinal hernia in clinically unclear cases and MRI is known to be useful to diagnose soft tissue pathology.[9-14] Nonetheless, little is known about its use in detecting causes of postoperative pain in the groin, in particular following endoscopic hernia repair when the incidence of neuropathic pain is allegedly low.

In order to evaluate the role of MRI in detecting causes of chronic pain following endoscopic hernia repair, we used MRI in a prospective cohort of patients with chronic postoperative pain by comparing the images of the painful groins to pain-free operated or not afflicted contralateral groins. An interobserver variability analysis in the MRI assessment of postoperative groins (painful and pain-free) and unoperated groins was added to test the MRI validity.

METHODS

Design of the study

The study was conducted in a dedicated hernia clinic in the Netherlands; in this clinic endoscopic Totally Extraperitoneal (TEP) hernia repair is the preferred operative technique in adult patients with groin hernias. There is a vast experience as 1200 TEP procedures are performed yearly. The hernia clinic has become a reference centre for recurrent hernias and patients with chronic postoperative inguinal pain. The departments of surgery, radiology and anaesthesia are working close together in the work-up of patients with inguinal problems.

Patients

All patients undergoing MR imaging of the groin because of unclear groin pain after totally extraperitoneal endoscopic (TEP) hernia repair between January 2011 and July 2012 were identified from the radiology database. In the study period MR-imaging was done in patients with chronic postoperative pain according to a protocol. Patients were included if they had undergone a previous TEP-hernia repair and had groin pain persisting at least 3 months after the operation with a minimum reported intensity (VAS >3). Most patients (n=39) were initially operated in our hernia centre, while fourteen patients were operated elsewhere and referred to our institute for chronic postoperative inguinal pain. Information regarding the localisation of pain, the subsequent treatment (based on clinical findings and original MRI findings) and the presence of pain at the end of follow-up was collected from the medical records. Pain at the end of follow-up was defined as acceptable if the pain did not interfere daily life activities, as reported by the patient.

MRI

MRI examinations of the groins were performed with a 1.5T MR system (Siemens Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany). The protocol was identical for all scans and consisted of a coronal and transverse T-2 weighted turbo spin echo sequence with 6- and 4-mm slices respectively and 3 T-1 weighted fast low-angle shot 2D sequences with fat saturation, each with a slice thickness of 5mm. MRI was performed in rest and during straining (Valsalva maneuver).

Evaluation

A test environment was created within PACS (Picture Archiving and Communication System, Oldelft Benelux BV, Veenendaal, The Netherlands) and examinations of the 53 patients were uploaded in random order, stripped of patient ID, date of examination, clinical details and original report. Two experienced radiologists assessed all examinations independently. In order to obtain stratifiable data for analysis, a checklist was created containing the following

items: a hernia (i.e. inguinal, obturator or femoral), bulging (shallow ballooning of the content of the abdominal cavity without forming an actual sac), a spermatic cord lipoma, a meshoma (a folded and wrinkled mesh or a mesh completely wadded up into a ball[13], spermatic cord oedema, signs of fibrosis, iliopectineal bursitis, adductor tendinitis, coxarthrosis, testicular pathology and prostate pathology. When fibrosis was identified, the observers were asked to quantify the degree of fibrosis by rating it as absent, minor, moderate or extensive. The checklist was filled out for both groins in every patient. The radiologists were unaware for the fact whether patients had been operated unilaterally or bilaterally as well as for the operated side. They were considered to confirm the presence and absence of the aforementioned items and were in addition asked to identify a mesh and its position. To compare the observations in the painful and pain-free groins we rank-ordered the occurrence of pathology by scoring each groin from 0 to 2, zero indicating no pathology (both observers reported that no specific pathology was seen), 1 indicating potential pathology (reported by one observer) and 2 meaning definite pathology (reported by both). The extent of fibrosis was dichotomised into: “none to minor” and moderate to extensive” to allow for statistical analysis (Fig. 1-3).

Clinical outcome of the patients were described in relation to the MRI findings of the present study; these study MRI-assessments had not affected the treatment of the patients.

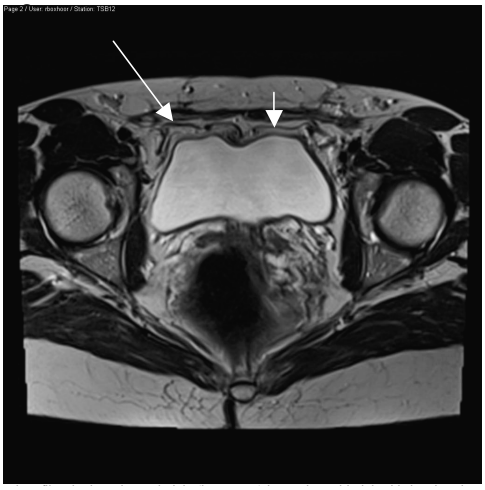

Figure 1.
Minor fibrosis along the mesh right (long arrow) in a patient with right sided groin pain after bilateral TEP repair. No fibrosis is seen on the pain-free left side.

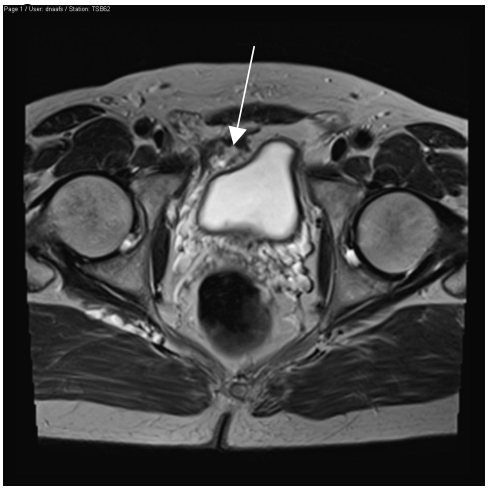

Figure 2.
Moderate fibrosis in a patient with right sided pain after right sided TEP repair

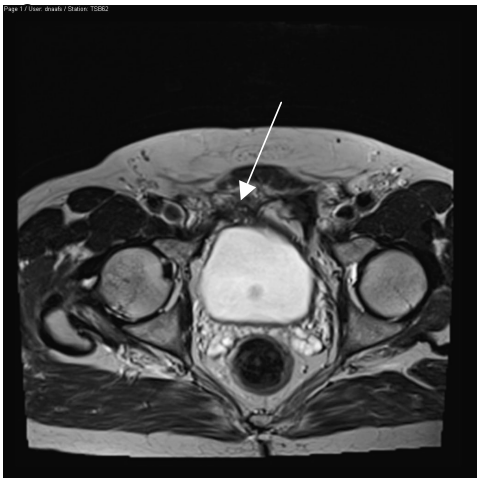

Figure 3.
Extensive fibrosis in a patient with right sided pain after right sided TEP repair

Statistical analysis

In order to assess interobserver agreement in this sample with two observers and nominal data, Cohen's kappa coefficients were calculated. Values < 0,2 indicate poor agreement, 0,21-0,40 fair, 0,41-0,60 moderate, 0,61-0.80 substantial and >0,80 close to perfect agreement [15]. A linearly weighted kappa with equal relative distances between the categories was calculated to determine the agreement on the extent of fibrosis. No points were awarded when no fibrosis was seen and 1, 2 or 3 points were rewarded when minor, moderate or extensive fibrosis was seen respectively. A Mann Whitney U test was performed on the rank-ordered data to compare pathology in painful and pain-free groins.

RESULTS

A total of 53 patients were identified and imaging studies of 106 groins were available for analysis. There were 67 operated and 39 unoperated groins since 14 patients underwent bilateral hernia repair. The median observation period between the primary operation and the MRI scan for a chronic postoperative pain was 17 months (range 3-58 months). In 26 patients (49%) a Prolene mesh was used, in fourteen patients (26%) an Ultrapro mesh, in two patients a Bard 3D mesh, in two patients a Physiomesh and in one patient a Parietex mesh. In eight patients the type of mesh was unknown. In 47 patients the mesh was not fixated, in one patient tackers were used and in 5 patients data regarding mesh fixation were missing. Fifty-five operated groins were painful, and twelve operated groins were pain-free. The pain was frequently experienced in more than one region. Most patients reported scrotal and/ or testicular pain (53%). We could not exactly differentiate between scrotal

skin pain and testicular pain though most patients complained of pain in their testicle. Inguinal pain was reported by 32% of the patients, pain at the lateral side of the pubic bone by 43%, funicular pain by 15% and adductor tendon pain by 4%. At the time that MRI scanning was done patients were untreated and only used paracetamol in case of pain.

Interobserver agreement

The presence and the correct alignment of the mesh was seen by both radiologists in 59 of the 67 operated groins (88 %). This observation was associated with an excellent interobserver agreement (κ = 0.88; see Table 1a). The presence of a hernia and the existence of bulging were least agreed upon, with κ values of 0.52 and 0.28 respectively, but interobserver agreement was substantial when further discrimination between a hernia or bulging was not required (κ = 0.74). For the subgroup of operated painful groins (table 1b) agreement considering the existence of bulging or a recurrent hernia remained substantial (κ = 0.67). Agreement on the presence of fibrosis in all analysed groins was moderate to substantial (κ =0.63), but in the subgroup of operated groins only fair to moderate

Table 1a. Interobserver agreement regarding MRI-findings in all groins (n = 106).

	Observer B		Interobserver agreement
Observer A	**No**	**Yes**	**κ-coefficient (95% CI)**
Preperitoneal mesh seen			0.88 (0.79-0.98)
No	41	0	
Yes	6	59	
Hernia			0.52 (0.30-0.73)
No	80	12	
Yes	3	11	
Bulging			0.28 (0.00-0.61)
No	95	1	
Yes	8	2	
Hernia or bulging			0.74 (0.58-0.89)
No	76	6	
Yes	4	20	
Lipoma			0.69 (0.41-0.98)
No	97	2	
Yes	2	5	
Fibrosis			0.63 (0.46-0.80)
No	71	6	
Yes	9	20	
Fibrosis extent*			0.61 (0.39-0.83)
No: No or minor	85	7	
Yes: Moderate or extensive	3	10	

*Fibrosis extent: dichotomised results using the groups “none or minor” and “moderate or extensive” as negative and positive values respectively.

Table 1b. Interobserver agreement regarding MRI-findings in painful operated groins (n = 55).

	Observer B		Interobserver agreement
Observer A	**No**	**Yes**	**κ-coefficient (95% CI)**
Hernia or bulging			
No	46	3	0.67 (0.38-0.97)
Yes	1	5	
Fibrosis			
No	24	6	0.44 (0.21-0.68)
Yes	9	16	
Fibrosis extent:*			
No: No or minor	37	5	0.62 (0.38-0.86)
Yes: Moderate or extensive	3	10	

*Fibrosis extent: dichotomised results using the groups “none or minor” and “moderate or extensive” as negative and positive values respectively.

(k = 0.44). Moderate to extensive fibrosis was identified with substantial agreement in all groins as well as in painful operated groins (κ =0.61 and 0.62 respectively). A lipoma of the funiculus spermaticus was observed rarely but substantially agreed upon (κ = 0.69).

Observed pathology

One or both radiologists observed abnormalities on MRI in 73% of the painful groins, in 58% of the asymptomatic operated groins and in 62% of the unoperated groins. The most commonly observed abnormalities in painful operated groins were fibrosis (56%), extensive fibrosis (33%), inguinal hernia (13%) and bulging (9%). Other potential explanations were sporadically observed: a lipoma (n=3), a femoral hernia (n=1), a meshoma (n=2), an ileopectineal bursitis (n=2), arthrosis (n=3), funicular oedema (n=2), adductor tendinitis (n=2), testicular pathology (n=3) and prostate pathology (n=4). A meshoma (n=2) and iliopectineal bursitis (n=2) were only seen in the painful operated group. None of the patients showed pubic bone marrow oedema on MRI.

Fibrosis was more often observed in painful operated groins than in unoperated groins (p<0.00). Hernias were seen more often in unoperated groins (p<0.00, see table2a). None of the predefined disorders was observed significantly more often in painful operated versus pain-free operated groins. A trend towards significance was seen for the observation of fibrosis in painful groins (P=0.11, see table 2b). Moderate to Extensive fibrosis was seen significantly more often when a Prolene® mesh had been used (in 13 of 26 patients) than after implantation of an Ultrapro® mesh (1 of 14 patients; p=0.02).

Table 2a. Observed pathology in painful operated (n = 55) vs unoperated (n = 39) groins.

	Pathology on MRI*						
	No		Potential		Definite		p-value
Item	n	%	n	%	n	%	
Fibrosis							
Painful	24	44	15	27	16	29	<0.00
Unoperated	39	100	0	0	0	0	
Fibrosis extent**							
Painful	37	67	8	15	10	18	<0.00
Unoperated	39	100	0	0	0	0	
Hernia							
Painful	48	87	6	11	1	2	<0.00
Unoperated	21	54	8	21	10	26	
Bulging							
Painful	50	91	4	7	1	2	0.62
Unoperated	35	90	4	10	0	0	
Hernia or bulging							
Painful	46	84	4	7	5	9	<0.00
Unoperated	21	54	4	10	14	36	
Lipoma							
Painful	52	95	1	2	2	4	0.35
Unoperated	34	87	3	8	2	5	

* MRI findings are rank-ordered into 3 levels of pathology: No pathology if not reported by either observer, potential if reported by one observer and definite if reported by both observers.

** Fibrosis extent: dichotomised results using the groups “none or minor” and “moderate or extend” as negative and positive values respectively.

Clinical outcomes of the painful groins

The management and outcome of patients with postoperative groin pain are listed in Table 3. In the majority of patients (40%) a wait and see policy was adopted, and in them outcome was favourable at the end of follow-up. Nineteen patients (36%) were referred to a pain specialist and most of them underwent invasive pain treatment by injections (n=11) or implantation of a neuromodulating device (n=3). Outcome in these patients was also good. MRI had shown extensive fibrosis in eight patients and iliopectineal bursitis in one possibly contributing to the pain. Eight patients (15%) were treated for conditions that were detected by MRI: three patients had a recurrent hernia or lipoma and underwent a re-operation, two patients were referred to the physiotherapist for an adductor tendinitis, 2 patients were referred to the urologist for prostate pathology and one patient was referred to the orthopaedic surgeon because of hip arthrosis. Overall, 41 (77%) of the 53 patients with chronic pain were pain-free after a mean follow-up of 4 months (SD 4,5).

Table 2b. Observed pathology in painful operated (n = 55) vs pain-free operated (n = 12) groins.

	Pathology on MRI*						
	No		Potential		Definite		p-value
Item	n	%	n	%	n	%	
Fibrosis							
Painful	24	44	15	27	16	29	0.11
Pain-free	8	67	0	0	4	33	
Fibrosis extent**							
Painful	37	67	8	15	10	18	0.28
Pain-free	10	83	2	17	0	0	
Hernia							
Painful	48	87	6	11	1	2	0.86
Pain-free	11	92	1	8	0	0	
Bulging							
Painful	50	91	4	7	1	2	0.48
Pain-free	10	83	1	8	1	8	
Hernia or bulging							
Painful	46	84	4	7	5	9	0,59
Pain-free	9	75	2	17	1	8	
Lipoma							
Painful	52	95	1	2	2	4	0.70
Pain-free	11	92	0	0	1	8	

* MRI findings are rank-ordered into 3 levels of pathology: No pathology if not reported by either observer, potential if reported by one observer and definite if reported by both observers.
*Fibrosis extent: dichotomised results using the groups “none or minor” and “moderate or extent ”as negative and positive values respectively.

DISCUSSION

In this study MRI in patients with post TEP hernia pain identified a correctly placed mesh, but it did not identify a specific cause for groin-repair related pain. Differences in fibrosis in the operated areas can be observed with MRI and there was a trend toward significance for the observation of extensive fibrosis in painful groins.

Meshes were correctly identified by the observers in the vast majority of the examined groins with very good agreement. The effectiveness of MRI in the assessment of mesh placement after endoscopic hernia surgery is described in one study before. Van den Berg et al. assessed the value of MRI in 10 patients with 13 groin hernias treated by TAPP[11]. In all patients the mesh and its position were clearly identified, however interobserver agreement was not tested. In the study of Aasvang, evaluating MRI findings after open anterior repair, agreement regarding mesh identification was modest (K=0.55).[16]

Table 3. Treatment and outcome of patients with painful operated groins (n=53)

Policy	Patients	Treatment	LTFU	No/acceptable pain at the end of FU	MRI pathology (as observed by both observers)
Wait and see	21 (40)	21 no treatment	1	20 /20	19 no or minor fibrosis 1 oedema spermatic cord 1 bulging and hernia or bulging
Pain clinic referral	19 (36)	4 no treatment 11 injections 3 neuromodulation	5	14/14	8 no or minor fibrosis 7 extensive fibrosis 1 meshoma and extensive fibrosis 1 bursitis ileopectinea 1 lipoma 1 hernia or bulging
Physiotherapy	6	1 no treatment 2 physiotherapy 1 pain clinic	2	3 / 4	3 no or minor fibrosis 1 extensive fibrosis and adductor tendinitis 1 hernia or bulging and adductor tendinitis 1 meshoma and extensive fibrosis and hernia or bulging
Reoperation	3	3 hernia reoperation		3/3	1 hernia 1 hernia or bulging and prostate cancer 1 funicular lipoma
Neurology referral	1	1 pain clinic	1	n.a.	1 no or minor fibrosis
Urology referral	2*	1 prostate resection 1 hernia reoperation	1	1 /1	2 prostate cancer
Orthopaedics referral	1	1 medical treatment	1	n.a.	1 no or minor fibrosis
Gynaecology referral	1	1 no treatment	1	n.a.	1 no or minor fibrosis

Median follow-up was 4 months; MRI signs of moderate to severe fibrosis were grouped as extensive fibrosis.
No/ acceptable pain was defined as pain not interfering with daily life (as reported by the patient).
LTFU, lost to follow-up
n.a., no information available
* one patient was operated because of a recurrent hernia and referred to the urologist because of prostate cancer

Previous studies have reported MRI to have a high detection rate for primary hernias and MRI is advised in cases of unclear groin pain after non-conclusive clinical examination and ultrasound.[9-12] In the present study, a primary hernia or bulging was frequently reported by both observers in 36% of the unoperated groins, with good (κ = 79) interobserver agreement. This contra lateral hernia is a common phenomenon, and described by others with incidences ranging from 13-51%.[17-19] Conversely, since patients with post-operative groin

pain are usually concerned of having a recurrent hernia, MRI assessment during Valsalva manoeuvre can confirm the correct position of the mesh. Excluding recurrent hernia helps to reassure patients allowing for a wait and see policy in 40% of patients.

The incidence of recurrent hernia after TEP surgery in centres focussing on hernia repair is low (0,22-0,37).[20] It is apparent from the interobserver agreement analysis in our study that it is difficult to distinguish between an actual recurrent hernia and only bulging as there was only fair to moderate agreement (κ = 0.20 and 0,42 respectively). In the study of Aasvang et al, recurrent hernia was rare and κ-coefficients were not calculated.[16] No other studies reported about the use of MRI to detect recurrent hernias. We found one case report describing the role of MRI in distinguishing hematoma from recurrence as useful in case of clinical diagnostic dilemma.[21] The clinical relevance of MRI to reveal recurrences is debatable. In addition recurrences are usually painless and due to a lipoma or bulging, hence not requiring re-operation.[22-24] In our study a recurrent hernia was observed by both observers in only one patient and by one observer in 7 patients. Only 3 patients were operated, in one patient a recurrent hernia was confirmed, the other two turned out to be a lipoma. The other patients with a possible recurrence became pain-free spontaneously.

Post-herniorrhaphy pain may be the result of different pathogenic mechanisms like nerve damage, inflammatory response with concomitant fibrosis due to the presence of a the mesh, mechanical irritation through the mesh and/or its fixation-device or not-operation related pathology in the groin area.[22-25] The origin of pain after TEP surgery is thought to be less related to direct nerve injury and more inflammatory-mediated and related to mechanical or fibrotic responses of scar tissue formation.[5,22] To date, no relation has been shown between the degree of inflammatory response or fibrosis and post-operative pain after TEP. This study shows fibrosis to occur in the groins that are painful, with groins that have been radiological identified as having extensive fibrosis being exclusively prevalent in the painful arm. However, we also found fibrosis in the pain-free groins and the significance of fibrosis and the degree of it on post-operation groins remains to be determined in future studies. In patients with moderate to extensive fibrosis pain diminished over time with or without treatment. Spontaneous pain reduction after TEP repair has been described before and can be explained by the self-limiting condition of the inflammatory reaction, lasting up to 6 months after surgery.[6]

In addition, we analysed the relation between mesh type and the degree of fibrosis. Patients treated with a Prolene® mesh showed significantly more moderate to extensive fibrosis on MRI compared to an Ultrapro® mesh, but numbers were small. Also data were collected retrospectively, groups were not equal and data were not corrected for operation time and

perioperative and postoperative complications (e.g. hematoma). It is generally agreed that meshes containing more material result in a more extensive inflammatory response resulting in more fibrosis. Therefore light weight meshes are recommended for open inguinal repair.[26] However, pain after TEP seems to have a different origin and it is still unclear if extensive fibrosis after TEP correction results in an increase of chronic postoperative pain or not. Further research of this topic is necessary.

In times of saving medical costs one has to be critical to implement expensive radiological examinations like MRI. Patients that are concerned about the situation of their groin, visit the surgeon or pain clinic frequently leading to unnecessary medical costs which can be avoided after an MRI without abnormal findings. In this study 40% of all patients were reassured by MRI about a correct position of their mesh and the fact that no abnormalities other than minor fibrosis were found. They accepted a wait and see policy and the majority of patients became pain-free.

In conclusion, for patients with post TEP groin pain MRI is useful to confirm a flat mesh-position with excellent inter observer agreement. MRI is also useful to identify bulging *or* recurrent hernia but not to distinguish between them. MRI cannot be recommended to identify a specific cause for groin repair-related pain, but it does identify rare other causes of pain and to some extent does demonstrate the presence of (extensive) fibrosis.

REFERENCES

1. Poobalan AS, Bruce J, King PM, et al. Chronic pain and quality of life following open inguinal hernia repair. *Br J Surg* 2001; 88: 1122-1126
2. Poobalan AS, Bruce J, Smith WC, et al. A Review of Chronic Pain After Inguinal Herniorrhaphy. *Clin J Pain* 2003; 19:48–54
3. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaest* 2005; 95: 69–76
4. Nienhuijs S, Staal E, Strobbe L, et al. Chronic pain after mesh repair of inguinal hernia: a systematic review. *Am J Surg* 2007; 194: 394–400
5. Linderoth G, Kehlet H, Aasvang EK, et al. Neurophysiological characterization of persistent pain after laparoscopic inguinal hernia repair. *Hernia* 2011; 15: 521-529
6. Alfieri S, Amid PK, Campanelli G, et al. International guidelines for prevention and management of postoperative chronic pain following inguinal hernia surgery. *Hernia* 2011; 15:239-49
7. Aasvang EK, Brandsborg B, Christenen B, et al. Neurophysiological characterisation of postherniotomy pain. *Pain* 2008; 137:173-181
8. Aasvang EK, Gmaehle E, Hansen JB, et al. Predictive risk factors for persistent post-herniotomy pain. *Anesthesiology* 2010; 112: 957-969
9. Simons MP, Aufenacker T, Bay-Nielsen M, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2009; 13: 343–403
10. Van den Berg JC, de Valois J, Rosenbusch G. Detection of groin hernia with physical examination, ultrasound and MRI compared with laparoscopic findings. *Invest Radiol* 1999; 34-739-743
11. Van den Berg JC, Go PM, de Valois J, et al. Preoperative and postoperative assessment of laparoscopic inguinal hernia repair by dynamic MRI. *Invest Radiol* 2000; 35: 695-698
12. Leander P, Ekberg O, Sjoberg S, et al. MR imaging following herniography in patients with unclear groin pain. *Eur Radiol* 2000; 10:1691-1696
13. Amid PK. Radiologic images of meshoma: a new phenomenon causing chronic pain after prosthetic repair of abdominal wall hernias. *Arch Surg* 2004; 139:1297-1298
14. Barile A, Erriquez D, Cacchio A, et al. Groin pain in athletes: role of magnetic resonance. *Radiol Med* 2000; 100: 216-222
15. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; 33:159-174
16. Aasvang EK, Jensen K, Fiirgaard B, et al. MRI and pathology in persistent postherniotomy pain. *Am Coll Surg* 2009; 208:1023-1028
17. Koehler RH. Diagnosing the occult contralateral inguinal hernia. *Surg Endosc* 2002; 16: 512-20
18. Crawford DL, Hiatt JR, Philips EH. Laparoscopy identifies unexpected groin hernias. *Am Surg* 1998; 64: 976-8
19. Bochkarev V, Ringley C, Vitamvas M, et al. Bilateral laparoscopic inguinal hernia repair in patients with occult contralateral inguinal defects. *Surg Endosc* 2007; 21: 734-6
20. Dulucq JL, Wintringer P, Mahajna A. Laparoscopic totally extraperitoneal inguinal hernia repair: lessons learned from 3,100 hernia repairs over 15 years. *Surg Endosc* 2009; 23: 482-6
21. Salati U, Mansour E, Torreggiani W. True-FISP MRI in diagnosis of postoperative hernia recurrence: a brief report. *Hernia* 2014; 18:597-600
22. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet* 2006; 367: 1618-25
23. Lau H. Recurrence following endoscopic extraperitoneal inguinal hernioplasty. *Hernia* 2007; 11: 415-418

24. Lilly MC, Arregui ME. Lipomas of the Cord and Round Ligament. *Ann Surg* 2002; 235:586-590
25. Lau H, Patil NG, Yuen WK, et al. Prevalence and severity of chronic groin pain after endoscopic totally extraperitoneal inguinal hernioplasty. *Surg Endosc* 2003; 17:1620-162326. Miserez M, Peeters E, Aufenacker T, et al. Update with level 1 studies of the European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2014; 18:151-163

4

Pain after Totally Extraperitoneal (TEP) hernia repair might fade out within a year

JPJ Burgmans
N Schouten
GJ Clevers
EJMM Verleisdonk
PHP Davids
CEH Voorbrood
RKJ Simmermacher
T Van Dalen

Hernia 2015;19:579-85

ABSTRACT

Background: The incidence of chronic pain after endoscopic hernia repair varies between 1-16 %. Studies regarding the course of pain in time after the operation are scarce.

Methods: 473 male patients ≥ 18 years of age, scheduled for totally extraperitoneal (TEP) hernia repair (Prolene® mesh) between March 2010 and August 2012 were requested to record pain symptoms preoperative, and 1 day, 1 week, 6 weeks, 3 months and 1 year postoperatively and visit the outpatient department 3 months and 1 year postoperatively for a standardized interview and physical examination.

Results: Preoperatively, 25% (n= 114) of the patients had moderate to severe pain (NRS 4-10). Six weeks postoperatively, 3% (n= 12) of the patients still experienced moderate to severe pain. Three months after TEP, only 3 patients (0.6%) had moderate-to-severe pain, while 83 patients (18%) experienced mild pain. One year after TEP, 39 patients experienced mild pain (8%) and 3 patients moderate pain (0.7%), no patients experienced severe pain after one year. Patients with moderate-to-severe pain preoperatively had a higher risk of pain persisting until 3 months and one year postoperatively (p= 0.03). In most patients who had pain 3 months postoperatively and were pain-free 1 year after TEP, pain 'faded out' at 4 to 6 months postoperatively. Two patients had a not-painful recurrent hernia, diagnosed 2 months and 5 months after TEP repair.

Conclusion: Moderate-to-severe pain after TEP hernia repair is self-limiting, with less than 1% of the patients reporting moderate pain 1 year postoperatively.

INTRODUCTION

Ever since the introduction of mesh repair in groin hernia surgery, postoperative pain has outnumbered recurrence as the most important complication after groin hernia repair.[1] Pain following inguinal hernia repair can be debilitating and often leads to costly multidisciplinary medical consultations.[2] The reported incidence of pain after all types of inguinal hernia repair varies between 2 to 53%, with approximately a third of these patients encountering functional impairment in work or leisure activities.[3,4] About one percent of all patients are referred to a specialized pain clinic.[5] Endoscopic inguinal hernia repair is a well-accepted alternative to open surgery and has advantages as a faster postoperative recovery and an alleged lower incidence of postoperative pain than after open repair.[6]

The wide variety in incidence rates of pain described after inguinal hernia repair is due to differences in the definition, measurement and timing of assessment.[2] According to the International Association for the Study of Pain (IASP), chronic pain is defined as pain or discomfort lasting for more than 3 months after the injury.[7] Other authors define chronic pain after inguinal hernia repair as "persisting for at least 6 months or even a year postoperatively".[8] To extend the definition of chronic postoperative groin pain to at least 6 months seems to be more realistic, since this allows alleged mesh-related inflammatory response reaction, as a causative factor of pain, to cease.[9] According to the European Association of Endoscopic Surgery (EAES), reliable instruments for the evaluation of post-herniorrhaphy pain are the Numeric Rating Scale (NRS) and the Inguinal Pain Questionnaire (IPQ).[10]

Despite an overwhelming amount of publications on post-herniorrhaphy pain, little is known about the course in time of postoperative pain. This information might be important to inform patients about and for the design of protocols for diagnostic and treatment strategies in future. The aim of the present study is to prospectively describe the incidence and course of pain over time following TEP hernia repair.

METHODS

The study was conducted in a dedicated hernia clinic in the Netherlands; in this clinic endoscopic Totally Extraperitoneal (TEP) hernia repair is the preferred operative technique in adult patients with groin hernias. All patients are operated upon by four surgeons with reasonable experience (> 1000 procedures/surgeon), procedures are performed under general anaesthesia. The operative details of the TEP technique is well described elsewhere.[11] Fixation of the mesh is not performed, since this reduces operative time, saves

costs and avoids possible entrapment neuralgia.[12] Skin closure is achieved using subcutaneous Monocryl. Patients are routinely discharged on the day of surgery. Patients are advised to avoid strenuous physical activity during the first postoperative week.

All hernia repairs are registered in a database, where demographic data, hernia type, method of repair, and information regarding outcome are collected prospectively. Male patients, at least 18 years old with a primary, unilateral inguinal hernia were eligible for inclusion in this study and scheduled for a TEP with a heavy weight mesh (Prolene®) between March 2010 and July 2012. Preoperatively, informed consent was obtained. The study was approved by the local medical ethical committee (VCMO, Nieuwegein, The Netherlands).

Patients were requested to record pain symptoms preoperatively, at day 1, day 7, after 6 weeks, 3 months and 1 year postoperatively. Inguinal pain was scored by the patients using a numeric rating scale (NRS 0= no pain, 10= worst pain imaginable). These pain scores were categorized as no (0), mild (1-3), moderate (4-7) or severe (8-10) pain; Moderate and severe pain were combined and as such considered to represent substantial pain (NRS 4-10).[14] The NRS pain scores were general and not specified between pain during rest and pain during activity. Pain and feelings of discomfort related to daily activities and sports were scored by the patients using the Inguinal Pain Questionnaire (IPQ).[13] Pain related to sexual function was assessed by the PSF (Pain related to Sexual Function) questionnaire, a Dutch translation of the questionnaire described by Aasvang et al.[15] To analyse the localisation of the pain we used the PSF Questionnaire. Patients could report the following localisations and one or more answers were permitted: scrotum, penis, medial thigh, pubic bone, groin (site of hernia) and surgical incision (umbilical, pubic, lateral). Pain in the testis was explicit questioned by the IPQ.

All patients visited the outpatient department at 3 months and 1 year after surgery for a standardized interview and physical examination by one of the hernia surgeons or a trained resident. Current pain intensity, character and location of pain and recurrences were evaluated. In patients with substantial groin pain 3 months after surgery, an Ultrasound or MRI scan was done in addition.

Statistical analysis

Statistical analyses were performed using SPSS® version 17.0 (SPSS, Chicago, Illinois, USA). Continuous data were analysed using descriptive statistics. To compare the differences in the 3 groups Chi-square analysis was used for categorical variables. For continuous variables three intergroup comparisons were made using a Student's *t*-test (normally distributed

continuous) or Mann-Whitney analysis (not normally distributed continuous). Significance was set at a level of $p \leq 0.05$.

RESULTS

A total of 452 (96%) consecutive patients treated between March 2010 and July 2010 completed the three months follow-up and 429 (91%) patients the one year follow-up (Fig. 1). Among the 23 patients lost to follow-up after 3 months, 19 patients had no pain at 3 months, 2 patients mild pain and 1 patient substantial pain.

Patients were divided into 3 groups based on the preoperative pain score: group 1 no pain (NRS 0), group 2 mild pain (NRS 1-3) and group 3 substantial pain (NRS 4-10). Baseline characteristics are summarized in table 1. Groups were similar according to all baseline characteristics, only lateral hernias were seen more frequent in group 3 (*p=0.03*). Almost 71% of all patients reported pain preoperatively, 207 of them (46%) experienced mild pain (group 2) and 114 patients (25%) moderate to severe pain (group 3). The remaining 131

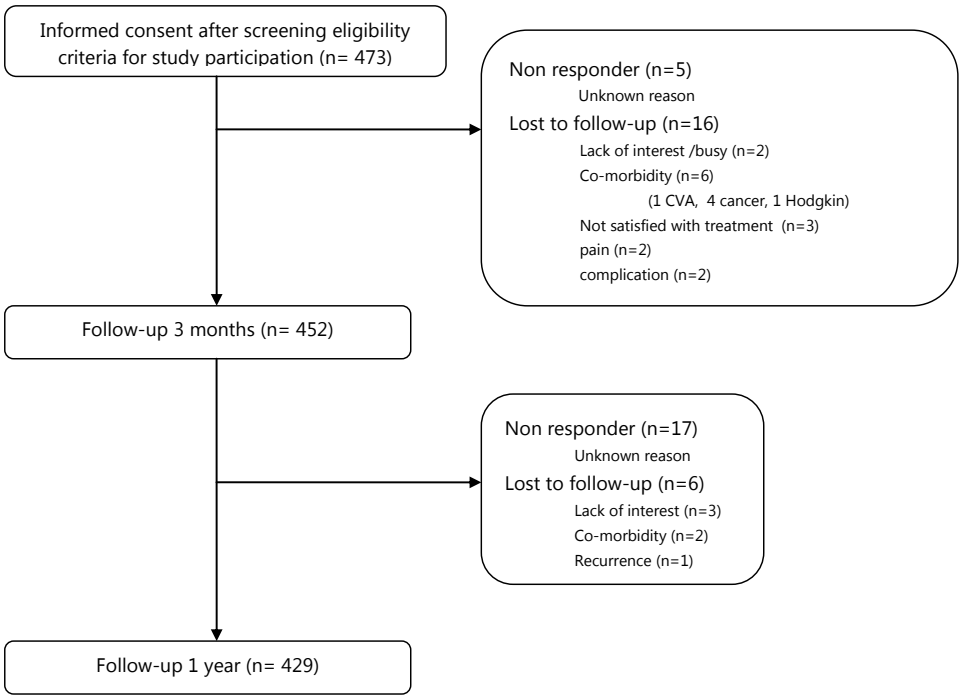

Figure 1. Flowchart of included patients between Marc hand September 2010

Table 1. Clinical characteristics of patients

	all patients n=452 (100%)	**group 1* n=131 (29%)**	**group 2* n=207 (46%)**	**group 3* n=114 (25%)**	**p****
Median age, years (range)	55 (18-94)	55 (18-83)	55 (19-94)	55 (18-82)	n.s.***
Mean BMI (SD)	25 (2.5)	25 (2.4)	25 (2.5)	25 (2.7)	n.s.***
Hernia Type (%)					**0.03**
Direct	24	30	26	16	
Indirect	75	69	74	83	
Femoral	1	1	0	1	
Side (%)					0.4
left	41	46	38	42	
right	59	54	62	58	
Surgeon (%)					0.6
1	29	28	31	26	
2	27	27	24	30	
3	14	14	12	16	
4	28	28	30	26	
5 resident	3	3	3	2	
Intra-operative complications					**0.08**
Bleeding	n=10	n=2	n=8	n=0	
Conversion	n=1	n=0	n=1	n=0	
Mean operation time (SD)	20 (6.3)	20 (6.1)	20 (6.5)	20 (6.0)	n.s.***
Other pain complaints (%)					0.6
headache	4	3	4	5	
back pain	8	3	9	12	
other pain	11	9	11	12	

*group 1: no pain preoperatively (NRS=0), group 2: mild pain preoperatively (NRS=1-3), group 3 substantial pain preoperatively (NRS=4-10)

** $p<0.05$ is significant

*** Medians were compared using three intergroup comparisons; none of these were statistically significant

patients (29%) who had no pain before hernia repair (group 1) were operated since they were young (<60 years of age) and had an uncomfortable sensation of a swelling in the groin or mechanical complaints resulting in impairment of daily activities, sports and sex or for cosmetic reason.

Preoperative, the groin pain affected daily life activities, ranging from less concentration on daily activities to necessary bed rest, in 104 patients (23%). Sport activities were impaired in 37% of patients and sexual activities in 36% of all patients. Five patients were unable to work (1%) and 30 patients (7%) had to take 1-4 weeks off because of groin pain. The impact of pain on leisure activities and work was higher in patients with substantial pain ($p< 0.005$).

The course of pain in time after the operation for all patients is seen in Fig. 2a. One week postoperatively, 62 patients (14%) had moderate to severe pain and 262 patients (59%) complained of mild pain. Six weeks postoperatively, 12 patients (3%) had moderate to severe pain, mild pain was experienced by 103 patients (23%). The median time to return to work was 7 (SD ± 7) days for all patients. Three months after TEP repair, 4 (0.9%) patients still had substantial pain, while 83 patients (18%) experienced mild pain. Most patients (94%) experience pain starting at the day of operation and the pain decreased in the first

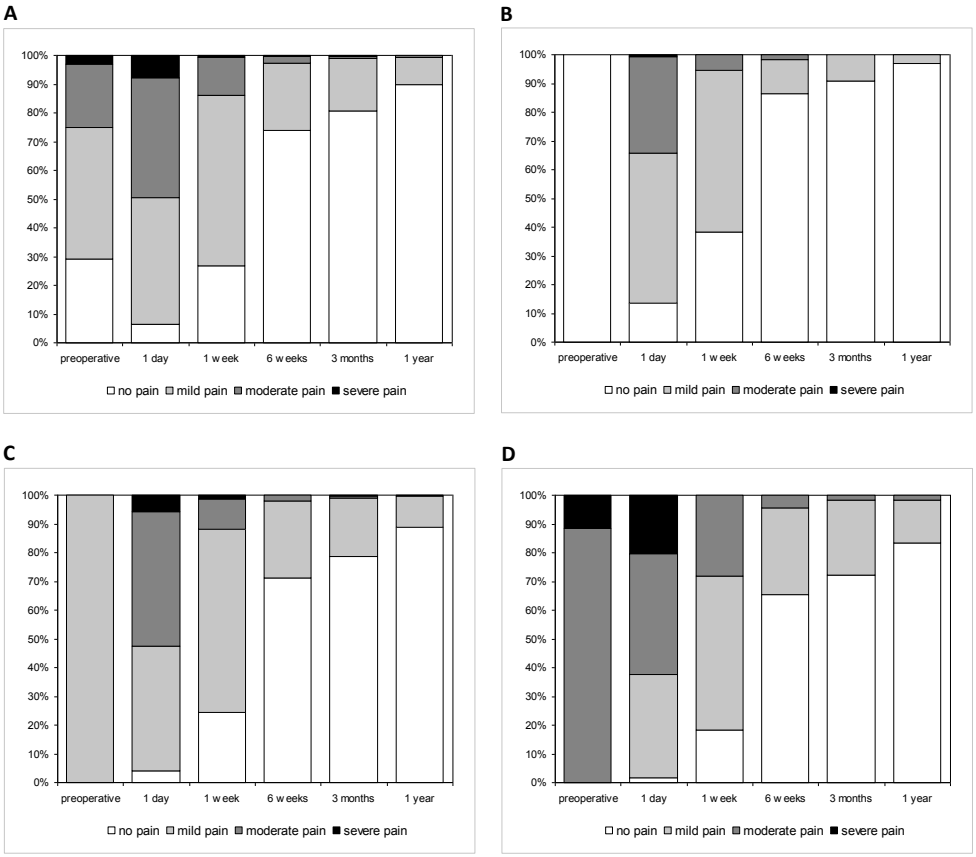

Figure 2A. % patients with pain before and after TEP: all patients (n=452)
Figure 2B. patients without pain before TEP: group 1 (n=131)
% patients with pain after TEP
Figure 2C. patients with mild pain before TEP: group 2 (n=207)
% patients with pain after TEP
Figure 2D. patients with substantial pain before TEP: group 3 (n=114)
% patients with pain after TE

weeks after TEP repair. Only in a few cases the pain started after the first week (11 patients) or between 6 weeks and 3 months postoperative (4 patients). This did not occur more often in one of the groups. One year after TEP the majority of patients (n= 382, 89%) had no pain. Most patients with pain 3 months after TEP repair mentioned that pain 'faded out' approximately 4 to 6 months postoperatively. Of the 47 patients who still experienced 'any' pain after one year, only 3 patients (0.7%) had moderate (NRS 4-6) pain, located in their scrotum (testis).

Pain courses of patients in group 1 with no pain preoperative differ from patients in group 3, starting with substantial pain: the amount of patients experiencing pain after the operation is higher at all time points (*p= 0.03*) and pain fades out less fast in group 3 (Fig. 2b,d). Eighteen patients (15%) of group 1 experienced any pain after 6 weeks: 15 patients reported mild pain (12%) and 3 patients substantial pain, however in group 3 as many as 38 patients (35%) experienced any pain after 6 weeks, 30% with mild pain and 5% with substantial pain. After one year only four (3%) patients of group 1 experienced any pain, all mild pain without impact on daily life activities or work. Among the patients of group 3 still 18 patients (16%) experienced pain after one year, 16 patients with mild pain and two with substantial pain impairing daily leisure activities in 13 patients. The pain course of group 2 is comparable to the complete cohort (Fig 2c).

The impact of pain on daily activities, sport, sex and work diminishes over time. After six weeks, daily life activities were impaired in 12 patients (3%), after one year, only three patients experienced influence of pain during daily life (Table 2). Ten percent of all patients (43 patients) were not able to do their sports 6 weeks after surgery, only 7 patients after

Table 2. Impact of pain on daily activities, driving car or perform sports by IPQ form.

Worst pain past week	Preoperatively	6 weeks	3 months	1 year
No pain	116 (24.5)	316 (68.7)	370 (81.8)	389 (90.7)
Can easily be ignored	146 (30.9)	101 (22.0)	56 (12.4)	28 (6.5)
Cannot be ignored, no interference with daily activities	101 (21.4)	31 (6.7)	19 (4.2)	9 (2.1)
Interference with concentration on chores and daily activities	55 (11.6)	7 (1.5)	5 (1.1)	2 (0.5)
Interference with most activities	33 (7.0)	4 (0.9)	0 (0.0)	1 (0.2)
Need bed rest because of pain	8 (1.7)	1 (0.2)	2 (0.4)	0 (0.0)
Need prompt medical advice because of pain	14 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
Interference driving a car	59 (12.5)	24 (5.2)	12 (2.7)	7 (1.6)
Interference sports	177 (37.4)	45 (9.8)	27 (6.0)	7 (1.6)

Values are number of patients with percentages in parenthesis

Grey rows indicate if pain interferes with daily activities, driving car or perform sports

one year (1%). Pain had influence on sexual activity in 18 patients (4%) after 6 weeks and in 6 patients (1.3%) after 1 year.

Patients often localized pain in different regions. While preoperative pain was most frequently experienced inguinal (72%), the scrotal region was most commonly used to localize postoperative pain (71-78% depending on the time-point; Table 3). Of all patients experiencing pain in the scrotal region, 82-86% (depending on the time point) reported testicular pain in the IPQ. Dysejaculation occurred in 10 patients preoperative, disappearing in 8 patients after 6 weeks and in 1 patient after 3 months. In 7 patients dysejaculation occurred after the operation and was still present in 3 patients after 1 year. Two patients had a painless recurrent hernia, in one patient diagnosed 2 months, in the other patient 5 months after TEP repair.

Table 3. Localisation of preoperative and postoperative pain (PSF questionnaire).

	Preoperatively	**6 weeks**	**3 months**	**1 year**
patients with pain (n)	170	112	76	28
Localization of pain[1] (n, %)				
Inguinal	123 (72)	43 (38)	24 (32)	10 (36)
Scrotum[2]	59 (35)	87 (78)	55 (72)	20 (71)
Medial thigh	9 (5)	6 (5)	4 (5)	1 (4)
Pubic region	29 (17)	14 (13)	8 (11)	4 (14)
Surgical incision				
Umbilical	-	15 (14)	5 (7)	-
Pubic	-	2 (1)	1 (1)	-
Lateral	-	9 (8)	-	-

[1]Patients often located pain in more than 1 region

[2] Depending on the time point 82-86% reported this pain to be testicular in the Inguinal Pain Questionnaire

Values are number of patients with percentages in parenthesis

DISCUSSION

This prospective cohort study shows that the overall incidence of substantial pain one year after endoscopic TEP hernia repair is 0.7%. This is low compared to other studies and it appears that in most cases postoperative pain is self-limiting, fading out during the first year postoperatively. Pain is higher and lasts longer in patients having moderate to severe pain preoperative.

The incidence of any pain one year after TEP repair was 10%, which is low and consistent with the findings of 2 other studies.[16,17] Clinically relevant pain (NRS 4-10) was only mentioned in 3 patients (0.7%). Comparable results were demonstrated by Lau and Chowbey

with rates of moderate to severe pain of 2.2% and 0.5% respectively.[17,18] The low rate of clinically relevant pain could potentially be due to the positive effect of experience and high volume and to the fact that fixation of the mesh was not performed. The most recent systemic review reported an overall incidence of chronic pain after endoscopic repair of 6% (range 1-16) but follow-up, methods of pain assessment and definition of chronic pain varied and no final conclusion about the exact incidence of chronic pain was made.[19]

Data of this study also showed that pain fades out during the first postoperative year after TEP repair. In the first six weeks postoperatively, a substantial proportion of patients (i.e. 26%) experienced some degree of pain, but this decreased to respectively 19% and 10%, three months and one year postoperatively. One year after TEP, only 1% of the patients had moderate pain interfering with daily activities in less than 1%, with sports in 2% and with sexual functioning in 1.3%. Detailed and well-designed data assessing the time course of pain after endoscopic inguinal hernia repair are limited. Only one study described pain course during the first year after TEP in detail reporting any pain after 3 months and 1 year as 7.1 and 4.8% and severe pain as 2.6% and 0.5 % respectively.[18] Bittner et al. found comparable declining pain incidences when patients were seen postoperative, at 1 week, 4 weeks, 6 months and one year after TAPP surgery.[20] Previous studies describing pain after conventional mesh or non-mesh techniques suggest a similar 'burn out' effect' of pain.[21-23] This phenomenon can be explained regarding pathophysiology of post hernia repair pain. As described by Amid et al. post hernia repair pain can be classified in neuropathic and non-neuropathic or nociceptive causes, and is not infrequently a combination of both.[24] Inflammatory-mediated nociceptive pain, assumed as the causative factor after endoscopic repair, is basically a self-limiting condition because the inflammatory reaction diminishes over time. It is assumed to last up to 6 months postoperatively.[25] The difference of the time course of pain one year after TEP in patients without pain preoperatively compared to patients with substantial pain in this study was significant and not described in former studies. These data are important to inform patients about their prognosis and reset patient's expectations regarding recovery.

In this study, postoperative pain was often localized at the scrotal or genital region, while inguinal pain was seen more frequently pre-operatively. Genital or scrotal skin pain might be caused by injury to the genital branch of the genitofemoral nerve.[26] However, most patients in our study with pain in the scrotal region, complained of testicular pain. Amid et al. hypothesized that this orchalgia might be related to injury to nerve fibres originating from the hypogastric plexus, rather than being related to direct injury of the (genital branch) of the genitofemoral nerve.[27] The testis is innervated by the spermatic plexus, a complex set of nerves originating from the hypogastric plexus.[28] However, branches of the ileoinguinal

and genitofemoral nerves also supply sensation of the tunica vaginalis. Dissection of the preperitoneal space, expanding the space of Bogros and Retzius and isolating the spermatic cord might cause injury of these small nerve branches. The mechanism responsible for post-TEP orchialgia is complex, but merely temporary as testicular pain ceases over time in 96% of patients in our study. In a study analysing ipsilateral orchialgia after laparoscopic donor nephrectomy, testicular pain spontaneously resoluted after 6.3 months.[29]

Only two patients developed a recurrent hernia; one occurred within two months after TEP, suggestive for technical failure, the other occurred 5 months postoperatively. Both patients did not experience postoperative pain. This suggests that, although a recurrence is often the only diagnosis that surgeons consider when a patient presents with pain following inguinal hernia repair, the origin of (chronic) postoperative pain should be often found elsewhere.[4]

In conclusion, the incidence of substantial pain one year after endoscopic TEP hernia repair is low, although a relatively high percentage of patients experience any pain symptoms in the first six weeks to three months after TEP repair. Patients with preoperative substantial pain have a higher risk to have complaints after 3 months and 1 year but still in most patients pain fades away after 4-6 months. Following this self-limiting time course of pain and the low risk of hernia recurrence in patients with pain, (surgical) re-intervention or diagnostic re-examination should not be considered too early in the follow-up of these patients.

REFERENCES

1. Kehlet H. Chronic pain after groin hernia repair. *Br J Surg* 2008; 95: 135-136
2. Poobalan AS, Bruce J, King PM, et al. Chronic pain and quality of life following open inguinal hernia repair. *Br J Surg* 2001; 88: 1122-1126
3. Eklund A, Montgomery A, Bergkvist L, et al. for the Swedish Multicentre Trial of Inguinal Hernia Repair by Laparoscopy (SMIL) study group. Chronic pain 5 years after randomized comparison of laparoscopic and Lichtenstein inguinal hernia repair. *Br J Surg* 2010; 97: 600-608
4. Bay-Nielsen M, Perkins FM, Kehlet H. Pain and functional impairment 1 year after inguinal herniorrhaphy: a nationwide questionnaire study. *Ann Surg* 2001; 233: 1-7
5. Hindmarch AC, Cheong E, Lewis MPN, et al. Attendance at a pain clinic with severe chronic pain after open and laparoscopic inguinal hernia repairs. *Br J Surg* 2003; 90: 1152-1154
6. Simons MP, Aufenacker T, Bay-Nielsen M, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2009; 13: 343-403
7. Classification of chronic pain Description of chronic pain syndromes and definitions of pain terms. Prepared by the International Associaton for the study of pain Subcommittee on Taxonomy. *Pain Suppl* 1986; 3:1-226
8. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaesth* 2005; 95: 69-76
9. Kehlet H, Roumen RM, Reinpold W, et al. Invited commentary: persistent pain after inguinal hernia repair: what do we know and what do we need to know? *Hernia* 2013; 17: 293-297
10. Poelman M, van den Heuvel B, Deelder J et al. EAES Consensus Development Conference on endoscopic repair of groin hernias. *Surg Endosc* 2013; 27:3505-19
11. Langeveld HR, Riet M. van 't, Weidema WF, et al. Total Extraperitoneal Inguinal Hernia Repair compared with Lichtenstein (the LEVEL-Trial): A randomized Controlled Trial. *Ann Surg* 2010; 251: 819-824
12. Koch CA, Greenlee SM, Larson DR et al. Randomized prospective study of totally extraperitoneal inguinal hernia repair: fixation versus no fixation of mesh. *JSLS* 2006; 10: 457-460
13. Fränneby U, Gunnarsson U, Andersson M, et al. Validation of an Inguinal Pain Questionnaire for assessment of chronic pain after groin hernia repair. *Br J Surg* 2008; 95:488-493
14. Loos MJA, Houterman S, Scheltinga MRM, et al. Evaluating postherniorrhaphy groin pain: visual analogue or verbal rating scale? *Hernia* 2008; 12: 147-151
15. Aasvang E, Mohl B, Bay-Nielsen M, et al. Pain related sexual dysfunction after inguinal herniorrhaphy. *Pain* 2006; 122: 258-263
16. Ali SM, Zendejas B, Yadav S, et al. Predictors of chronic groin discomfort after laparoscopic totally extraperitoneal inguinal hernia repair. *J Am Coll Surg* 2013; 217:72-78
17. Lau H,Patil G, Yuen WK, et al. Prevalence and severity of chronic pain after endoscopic totally extraperitoneal inguinal hernioplasty. *Surg Endosc* 2003; 17:1620-1623
18. Chowbey PK, Garg N, Sharma A, et al. Prospective randomized clinical trial comparing lightweight mesh and heavyweight polylropylene mesh in endoscopic totally extraperitoneal groin hernia repair. *Surg Endosc* 2010; 24:3073-3079
19. Hanswijck de Jonge van P, Lloyd A, Horsfall L. The measurement of chronic pain and health-related quality of life following inguinal hernia repair: a review of the literature. Hernia 2008:12:561-569.
20. Bittner R, Leibl BJ, Kraft B, Schwarz J. One-year results of a prospective, randomized clinical trial comparing four meshes in laparoscopic inguinal hernia repair (TAPP). *Hernia* 2011; 15:503-510

21. Van der Pool AEM, Harlaar JJ, den Hoed PT, et al. Long-term follow-up evaluation of chronic pain after endoscopic total extraperitoneal repair of primary and recurrent inguinal hernia. *Surg Endosc* 2010, 24: 1707-1711
22. Aasvang E, Bay-Nielsen M, Kehlet H. Pain and functional impairment 6 years after inguinal herniorrhaphy. *Hernia* 2006; 10: 316-32
23. Singh AN, Bansal VK, Misra MC, et al. Testicular functions, chronic pain, and quality of life after laparoscopic and open mesh repair of inguinal hernia: a prospective randomized controlled trial. *Surg Endosc* 2012; 26: 1304-1317
24. Amid PK. Causes, prevention, and surgical treatment of postherniorrhaphy neuropathic inguinodynia: Triple neurectomy with proximal end implantation. Hernia 2004; 8: 343-349
25. Alfieri S, Amid PK, Campanelli G, et al. International guidelines for prevention and management of postoperative chronic pain following inguinal hernia surgery. *Hernia* 2011; 15: 239-249
26. Ducic I, Dellon AL. Testicular pain after inguinal hernia repair: An approach to resection of the genital branch of genitofemoral nerve. *J Am Coll Surg* 2004; 198:181-184
27. Amid PK, Hiatt JR. New understanding of the causes and surgical treatment of postherniorrhaphy inguinodynia and orchalgia. *J Am Coll Surg* 2007; 205: 381-385
28. Colby F. Embryology, anatomy and psysiology of the testis and epididimis. In: Essential Urology, ed 2. Williams & Wilkins, Baltimore 1953, pp 101-103
29. Kim FJ, Pinto P, Ming Su L, et al. Ipsilateral orchialgia after laparoscopic donor nephrectomy. *J Endourol* 2003; 17:405-409

5

Impairment of sexual activity before and after Totally Extraperitoneal Endoscopic (TEP) hernia repair

N Schouten
T Van Dalen
N Smakman
GJ Clevers
PHP Davids
EJMM Verleisdonk
H Tekatli
JPJ Burgmans

Surg Endosc 2012; 26:230-4

ABSTRACT

Background: In patients with inguinal hernias, sexual activity may be impaired due to hernia- related pain. Surgical repair may improve these complaints but can also lead to similar symptoms as a long term complication of the operation. Endoscopic hernia repair is associated with less postoperative pain and earlier return to normal activities, but its effect on pain related sexual function is unknown. In this study, the incidence and effect of pain related to sexual activity are evaluated before and after Totally Extraperitoneal Endoscopic (TEP) hernia repair.

Methods: A hospital-based questionnaire study of pain related sexual dysfunction was conducted in November 2009 in 500 male patients ≥ 18 years, who underwent a TEP repair for a primary hernia between March 2006 and December 2008. The response rate was 77.2%.

Results: Pain of any severity during sexual activity was reported by 124 patients (32.1%) preoperatively and 35 patients (9.1%) postoperatively. Only 2.3% of the 262 patients with no history of preoperative pain experienced moderate to severe (VAS 4-10) pain postoperatively. Pain impaired sexual function in 63 patients (16.3%) preoperatively and in 18 patients (4.7%) postoperatively. The majority of patients who reported pain during sexual activity preoperatively (n=102, 82.3%) had no pain postoperatively. The frequency of moderate to severe painful sexual activity decreased from 21.2% (preoperatively) to 3.4% after TEP repair ($P< 0.001$), and the frequency of moderate to severely impaired sexual function decreased from 6.0% to 1.0% ($P<0.001$). The preoperative presence of pain during sexual activity and chronic non-hernia related pain syndromes were predictive for the occurrence of postoperative pain.

Conclusion: Painful sexual activity, present in one third of patients with inguinal hernias, improved in the majority of patients following TEP hernia repair. Postoperatively, moderate to severe painful sexual activity occurred in 2.3% of the patients with no history of preoperative complaints.

INTRODUCTION

The risk of hernia recurrence has been the primary endpoint in inguinal hernia studies for many years, but more recently attention is being paid to several quality of life (QoL) aspects. In particular, time to full recovery and chronic postoperative pain have been addressed.[1,2] [1,2]. Recent reports indicate that improvement of QoL-related issues is the main reason for patients to undergo elective inguinal hernia repair.[3]

While chronic pain has been the subject of several studies, little is known about sexual function in patients with inguinal hernias. Symptoms associated with an inguinal hernia can affect sexual function and surgical repair may improve quality of (sexual) life.[4,5] On the other hand, genital pain and dysejaculation following inguinal hernia repair have been described too.[2,6-8]

The studies regarding quality of sexual function after inguinal hernia repair are scarce and were conducted on patients who underwent open hernia repair.[2,6,9] A relationship between the presence of pain and an adverse effect on sexual function is conceivable. Endoscopic repair techniques are associated with less postoperative pain and earlier return to normal activities.[10,11] This may suggest a potential beneficial effect of endoscopic hernia repair on sexual function as well.

In the present study the incidence of pain during sexual activity and the effect on sexual function before and after endoscopic Totally Extraperitoneal (TEP) hernia repair was assessed.

METHODS

Since 2005, the Totally Extraperitoneal Endoscopic (TEP) hernia repair is the preferred operative technique for hernia repair in our hospital and all elective operations are done by four surgeons. The operative technique has been described previously.[10,11] The mesh graft is not fixated, with no exception for bilateral hernias.[12,13] Furthermore, patients are discharged on the day of surgery without restrictions regarding any physical activity. All hernia repairs are registered prospectively. Demographic data, hernia type, method of repair, and information regarding short term outcome (six-weeks postoperatively) are collected in a database.

In November 2009, a questionnaire survey was sent to selected of patients registered in the institutional database. Inclusion criteria were: male gender, age ≥ 18 years, a primary unilateral inguinal hernia, and a Totally Extraperitoneal Endoscopic (TEP) hernia repair performed between March 1, 2006 and December 31, 2008. Patients with incarcerated inguinal hernias, patients with diseases of the testicles (orchitis or tumors) and patients with recurrent hernias during the observation period were excluded.

Between March 1, 2006 and December 29, 2008, 1.505 male patients 18 years of age or older underwent TEP hernia repair for a unilateral primary inguinal hernia. With a median observation period of 27 (range 18-50) months, questionnaires were mailed to 500 randomly selected male patients who fulfilled the inclusion criteria (Fig. 1). Non responders were sent a new questionnaire after 8 weeks. The questionnaire was similar to the one previously described by Aasvang et al. and was based on the International Index of Erectile Function (IIEF) to assess presence, frequency, intensity and location of pain during sexual activity and the effect of pain on sexual function.[6,14] A 10-point VAS scale, ranging from 0 (no pain) to 10 (worst pain), was used for pain assessment. VAS scores were categorized into no pain (VAS 0), mild pain (VAS 1-3), moderate pain (VAS 4-7) and severe pain (VAS 8-10).[15] The

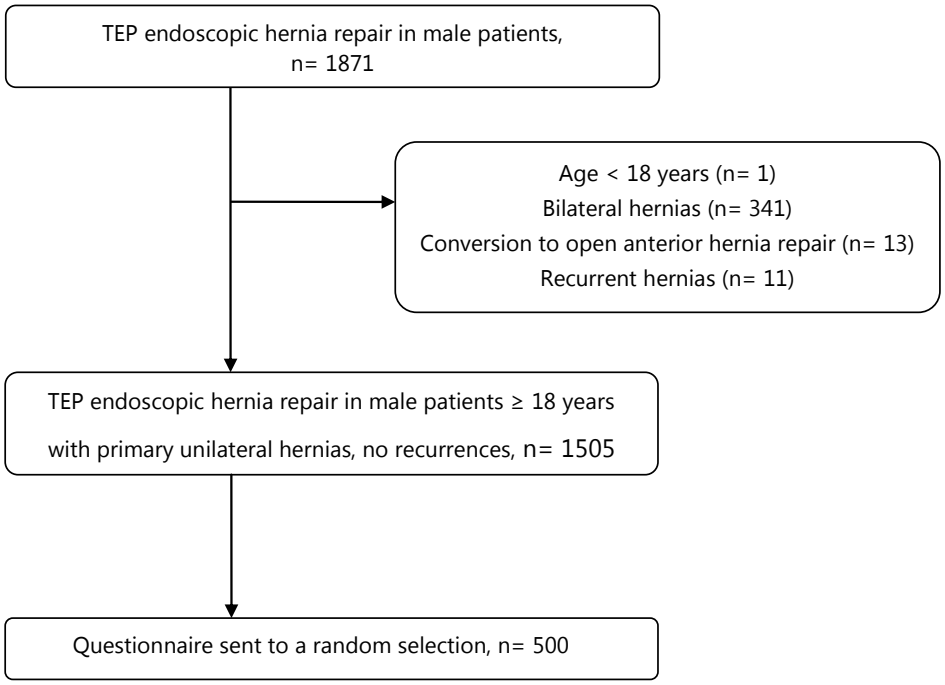

Figure 1. Flowchart

location of pain during sexual activity and the presence of chronic non-hernia-related pain (i.e. back pain, frequent headaches or other non-specified chronic pain complaints) were also documented. Impairment of sexual function was classified as “no”, “minor”, moderate” or “severe”.

The main endpoints of this study were the preoperative and postoperative presence of any pain during sexual activity and pain-related impairment of sexual activity. Moderate and severe pain were combined to represent substantial pain when exploring the relation between pain and other factors; similarly moderate and severe impact on sexual functioning were grouped as “substantial” impairment. In addition, the relation between the presence of pre- and postoperative substantial pain and sexual impairment and the association with other factors was evaluated.

Data-analysis

Statistical analyses were performed using SPSS version 17.0 (SPSS, Chicago, Illinois, USA). Two-sided p values were calculated from Fischer’s exact test and Pearson χ^2 test where appropriate. McNemar analysis was used to assess the correlation between the presence of preoperative pain, chronic non-hernia related pain or postoperative complications as predictors of postoperative pain (for the total study population, n= 386). The significance level was defined as $p < 0.05$.

RESULTS

Questionnaires were returned by 386 patients, a median 27 (range 18-50) months after TEP hernia repair (response rate 77.2%). Mean age at operation was 54 years (SD ± 12.9). Baseline characteristics of the patients are listed in Table 1. Complications during the operation occurred in 14 patients (3.6%) and all complications receded with conservative measures.

Preoperatively, 124 patients (32.1%) reported pain during sexual activity, categorized as moderate to severe in 82 patients (21.2% of all patients). As shown in Table 2, the groin (n=108) and the testis (n=25) were the most common locations of preoperative pain during sexual activity. Sixty-three patients reported pain related impaired sexual function (16.3%), classified as moderate to severe in 23 patients (6.0%). Seven patients (1.8%) reported ejaculatory pain, five patients (1.3%) mentioned erection disorders in relation to the groin hernia. The majority (94.4%) of the 124 patients with pain during sexual activity preoperatively mentioned hernia-associated pain during other activities and/or rest also.

Table 1. Baseline characteristics

	N	(%)
Total number of patients	386	(100)
Age (Mean ± SD)	54 ±12.9	
Hernia Type		
Indirect	254	(65.8)
Direct	114	(29.5)
Combined (direct + indirect)	11	(2.9)
Femoral	4	(1.0)
Combined (femoral and medial)	3	(0.8)
Chronic non-hernia-related pain	123	(31.9)
Back pain	58	(15.0)
Headache	17	(4.4)
Pain elsewhere	48	(12.4)
Perioperative complications		
Bladder injury	1	(0.3)
Hematoma/seroma	9	(2.3)
Wound infection	4	(1.0)

Non-hernia-related chronic pain was reported by 123 patients (31.9%): back pain (n=58), frequent headaches (n=17), pain elsewhere (hip, knee, shoulder, abdomen; n= 48).

After TEP repair, the incidence of painful sexual activity of any severity was significantly reduced (Table 2: n=35; 9.1% vs. 32.1% preoperatively, p= 0.001). Moderate to severe pain during sexual activity decreased from 21.2% (82 patients) to 3.4% (13 patients, p< 0.001). Twenty-two of the 35 patients with painful sexual activity postoperatively, also experienced pain preoperatively, while 13 patients had no history of preoperative pain (5.0% of 262 patients without pain preoperatively). Postoperatively, apart from the decrease in the proportion of patients having pain during sexual activity, pain was experienced less frequently, less severe and was more commonly located in the testis (Table 3).

In addition, only 2.3% of patients who had no preoperative complaints experienced moderate to severe pain during sexual activity postoperatively. Postoperatively, 18 patients (4.7%) reported impairment of their sexual function (vs. 63 patients (16.3%) preoperatively p< 0.001) and the postoperative incidence of moderate to severe sexual impairment was also significantly lower than preoperatively (1.0% vs. 6.0%, p< 0.001, Table 2). Three patients reported pain-related ejaculatory disorders (0.8%) and another three erection disorders (0.8%). Twenty-four of the 35 patients (68.6%) with postoperative painful sexual activity also experienced pain during other activities and/or rest.

Table 2. Incidence of painful sexual activity, localisation of pain and impairment of sexual function (n= 386)

	Preoperative (%)	Postoperative (%)	p-value
Pain during sexual activity	124 (32.1)	35 (9.1)	0.001
Substantial pain[a]	82 (21.2)	13 (3.4)	<0.001
Impairment during sexual activity	63 (16.3)	18 (4.7)	<0.001
Substantial impairment[b]	23 (6.0)	4 (1.0)	<0.001
Location of pain[c]			
Area of (previous) hernia	108 (28.0)	24 (6.2)	
Testis	25 (6.5)	16 (4.2)	
Ejaculatory	7 (1.8)	3 (0.8)	
Suprapubic	30 (7.8)	5 (1.3)	

[a] Substantial pain: VAS 4-10, see "Methods" section

[b] Substantial impairment of sexual function: moderate to severe impairment of sexual function, see "Methods" section

[c] Since some patients indicated more than one region (e.g. inguinal and testis), the sum of *n* is higher than the number of patients with pain during sexual activity preoperatively (n=124) or postoperatively (n=35). Percentage calculations are based on the total number of pain locations divided by the total number of patients included in this study (n=386).

Although the majority of patients who had pain during sexual activity preoperatively had no pain postoperatively (n=102, 82.3%), the preoperative presence of moderate to severe painful sexual activity was associated with a risk of having substantial pain during sexual activity postoperatively (12.9% vs. 2.3%; p< 0.001). Patients who had a history of chronic non-hernia-related pain also had a higher probability of having substantial painful sexual activity postoperatively (8.1% vs. 1.1%; *P*< 0.001). On the other hand, there was no significant correlation between postoperative complications and postoperative painful sexual activity.

DISCUSSION

In the present questionnaire study pain during sexual activity and impaired sexual function were observed in a substantial proportion of patients before TEP hernia repair and the operation had a significant beneficial influence. Both pain and sexual impairment were less common postoperatively, and in those who did experience postoperative pain during sexual activity, it was less severe. The preoperative presence of painful sexual activity or other chronic pain was predictive of postoperative complaints.

Few studies have dealt with sexual function after inguinal hernia repair, merely focusing on general sexual function (such as erectile disorders) and not so much on pain during sexual

Table 3. Severity of painful sexual activity, localisation of pain and impairment of sexual function before and after TEP hernia repair

	Preoperative		Postoperative		
	N=124	(%)	N=35	(%)	P-value*
Pain severity					0.007
VAS 1-3	42	(33.9)	22	(62.9)	
VAS 4-6	56	(45.1)	10	(28.5)	
VAS 7-10	26	(21.0)	3	(8.6)	
Frequency of pain					0.016
Seldom	60	(48.4)	26	(74.3)	
Often	48	(38.7)	5	(14.3)	
Always	16	(12.9)	4	(11.4)	
Location of pain[a]					
Groin	108	(87.0)	24	(68.6)	0.019
Testis	25	(20.2)	16	(45.7)	0.004
Ejaculatory	7	(5.6)	3	(8.6)	0.406
Suprapubic	30	(24.2)	5	(14.3)	0.254
Impairment of sexual function					0.726
None	61	(49.2)	17	(48.6)	
Minor	40	(32.3)	14	(40.0)	
Moderate	18	(14.5)	3	(8.6)	
Severe	5	(4.0)	1	(2.9)	

* Statistics calculations are based on the total number of patients with pain during sexual activity (n=124 preoperatively and n=35 postoperatively)

[a] Since some patients marked more than one region (e.g. inguinal and testis), the sum of *n* is higher than the number of patients with pain during sexual activity. Percentage calculations are based on the total number of pain locations divided by the total number of patients with pain (n=124 preoperatively an n= 35 postoperatively)

activity and pain-related impairment of sexual function.[2,5-7,9] To our knowledge, this is the first study that evaluates the incidence of painful sexual activity and impairment of sexual function before and after Totally Extraperitoneal Endoscopic (TEP) hernia repair.

The observed incidence of painful sexual activity and impaired sexual function in patients with inguinal hernias was substantial. One third of patients had painful sexual activity, scored as moderate to severe by one fifth of the patients. Furthermore this pain had a substantial adverse effect on sexual functioning in 6% of the patients. The observed incidences are higher than recently reported by Aasvang et al., who found that 12% of the patients had painful sex preoperatively, with an substantial associated impairment of sexual function in 2.3% of the patients.[16] In another study, Zieren et al. observed sexual disorders (erectile dysfunction and/or orgasm problems) in 23% of patients with inguinal hernias.[2] Thus, sexual activity, as a quality-of-life parameter, appears to be greatly affected by the presence of an inguinal hernia.

Even more important was the significant improvement following surgery, reflecting a beneficial effect of the operative procedure. The incidence of pain and impaired sexual function was significantly less postoperatively. In addition, in patients who did report painful sexual activity postoperatively, the severity and frequency of the pain was significantly less than preoperatively.

The observed improvement in postoperative sexual functioning in this study appears promising in comparison to the scarce literature. The decrease of moderate to severe painful sexual activity following TEP hernia repair (21.2 vs. 3.4%) and decrease in substantial impairment of sexual function (6.0 vs. 1.0%) compare favourably to the results reported by Aasvang et al. In their study, moderate to severe pain-related impaired sexual function was present in 2.3% of patients preoperatively and in 1.2% of patients 6 months after open anterior mesh or endoscopic TAPP hernia repair. However, the incidence of pain-related impairment was not evaluated separately for endoscopic TAPP repair compared to open anterior mesh repair.[16] Improved sexual function (although not studied in relation to pain) has been observed by others too. Ertan and El-Awady reported a significant recovery of sexual function 3 months after open anterior mesh repair, with 85% of patients improving their IIEF scores, while Zieren observed a decline of "potency or orgasm disorders" after Plug and Patch repair from 23.2 to 16.1% postoperatively.[2,4,5]

It is well documented that TEP hernia repair, in experienced hands, is associated with less (chronic) postoperative pain and it is conceivable that this should also reflect on painful sexual activity and sexual function.[10,11] As such, it is illustrative that in the subset of patients who had no complaints of painful sexual activity and/or pain-associated sexual impairment preoperatively, the postoperative frequency of moderate to severe painful sexual activity was only 2.3%, quantitatively reflecting the limited adverse effect of hernia repair. Another adverse effect of operative treatment is hidden in the observed higher frequency of testicular and ejaculatory pain postoperatively than preoperatively, which is in accordance with another study by Aasvang et al.[6]

It is suggested that trauma to the vas deferens and nerves due to scarring is involved in the mechanism underlying genital (such as testicular or ejaculatory) pain and subsequent sexual dysfunction.[6,17,18] It is therefore suggested that in hernia repair, overzealous dissection of the (distal part of the) spermatic cord should be avoided.[19-21] In TEP hernia repair extensive dissection of the spermatic cord is not required, which is the likely explanation for the comparatively favourable as well as the absolute limited incidence of postoperative painful sexual activity and sexual impairment. Therefore, it may be the most appropriate technique for preventing postoperative genital pain and sexual dysfunction.[20,22]

Apart from the operation as a causative for painful sex postoperatively, other factors were also important. The preoperative presence of pain in the genital area as well as the preoperative presence of pain irrespective of the anatomical location were predictive of painful sex and impaired sexual function postoperatively. As such the effect of these factors appeared larger than the effect of the hernia repair.[23]

In conclusion, symptoms specifically associated with inguinal hernias, such as groin bulge or pain, can lead to limitations of a patient's sexual function. This study demonstrates the recovery of sexual function in the majority of patients, following endoscopic TEP hernia repair in male patients with primary unilateral hernias.

REFERENCES

1. Callesen T, Bech K, Nielsen R, et al. Pain after groin hernia repair. *Br J Surg* 1998; 85:1412-1414
2. Zieren J, Menenakos C, Paul M, et al. Sexual function before and after mesh repair of inguinal hernia. *Int J Urol* 2005; 12:35-38
3. Pokorny H, Klinger A, Scheyer M, et al. Postoperative pain and quality of life after laparoscopic and open inguinal hernia repair: results of a prospective randomized trial. *Hernia* 2006; 10:331-337
4. Ertan T, Keskek M, Kilic M, et al. Recovery of sexual function after scrotal hernia repair. *Am J Surg* 2007; 194:299-303
5. El-Awady SE, Elkholy AAM. Beneficial effect of inguinal hernioplasty on testicular perfusion and sexual function. *Hernia* 209; 13:251-258
6. Aasvang EK, Møhl B, Bay-Nielsen M, et al. Pain related sexual dysfunction after inguinal herniorrhaphy. *Pain* 2006; 122:258-263
7. Aasvang EK, Møhl B, Kehlet H. Ejaculatory pain: A specific postherniotomy pain syndrome? *Anesthesiology* 2007; 107:298-304
8. Bendavid R. Dysejaculation. *Probl Gen Surg* 1995; 12:237-238
9. Zieren J, Beyersdorff D, Beier KM, et al. Sexual function and testicular perfusion after inguinal hernia repair with mesh. *Am J Surg* 2001; 181:204-206
10. Lau H, Patil NG, Yuen WK. Day-case endoscopic totally extraperitoneal inguinal hernioplasty versus open Lichtenstein hernioplasty for unilateral primary inguinal hernia in males: a randomized trial. *Surg Endosc* 2006; 20:76-81
11. Langeveld HR, Van 't Riet M, Weidema WF, et al. Total Extraperitoneal Inguinal Hernia Repair compared with Lichtenstein (the LEVEL-Trial): A randomized Controlled Trial. *Ann Surg* 2010; 251:819-824
12. Spitz JD, Arregui ME. Sutureless laparoscopic extraperitoneal inguinal herniorrhaphy using reusable instruments: two hundred three repairs without recurrence. *Surg Laparosc Endosc Percutan Tech* 2000; 10:24-29
13. Koch CA, Greenlee SM, Larson DR, et al. Randomized prospective study of totally extraperitoneal inguinal hernia repair: fixation versus no fixation of mesh. *JSLS* 2006; 10:457-460
14. Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997; 49:822-830
15. Loos MJ, Roumen RM, Scheltinga MR. Classifying post-herniorrhaphy pain syndromes following elective inguinal hernia repair. *World J Surg* 2007; 31:1760-1765
16. Aasvang EK, Gmaehle E, Hansen JB, et al. Predictive risk factors for persistent postherniotomy pain. *Anesthesiology* 2010; 112:957-969
17. Christiansen CG, Sandlow JL. Testicular pain following vasectomy: A review of post vasectomy pain syndrome. *J Androl* 2003; 24:293-298
18. Uzzo RG, Lemack GE, Morrissey KP, et al. The effects of mesh bioprosthesis on the spermatic cord structures: a preliminary report in a canine model. *J Urol* 1999; 161:1344-1349
19. Wantz GE. Testicular atrophy as a sequela of inguinal hernioplasty. *Int Surg* 1986; 71: 159-163
20. Reid I, Devlin HB. Testicular atrophy as a consequence of inguinal hernia repair. *Br J Surg* 1994; 81:91-93
21. Koontz AR. Atrophy of the testicle as a surgical risk. *Surg Gynecol Obstet* 1965; 120: 511-513
22. Ersin S, Aydin U, Makay O, et al. *Surg Endosc* 2006; 20:685-689
23. Courtney CA, Duffy K, Serpell MG, et al. Outcome of patients with severe chronic pain following repair of groin hernia. *Br J Surg* 2002; 89:1310-1314

6

Three-months results of the effect of Ultrapro or Prolene mesh on post-operative pain and well-being following endoscopic totally extraperitoneal hernia repair (TULP-trial)

JPJ Burgmans
CEH Voorbrood
N Schouten
N Smakman
S Elias
GJ Clevers
PHP Davids
EJMM Verleisdonk
ME Hamaker
RKJ Simmermacher
T Van Dalen

Surg Endosc 2015 Jan 1 [Epub ahead of print]

ABSTRACT

Background: Recurrence rates after inguinal hernia repair have been reduced to a few per cent, since mesh repair has become standard of care. Lightweight meshes reduce postoperative pain and stiffness in open anterior repair but for endoscopic repair the discussion about this benefit is ongoing. This study was done to analyse the effects of light weight mesh versus heavy weight mesh following endoscopic totally extraperitoneal (TEP) hernia repair.

Methods: In a single-centre double-blindly randomized clinical trial 950 patients with unilateral primary inguinal hernia were randomized to undergo endoscopic TEP using either an Ultrapro® or a Prolene® mesh. Data were collected by validated questionnaires at day 1, day 7, after 6 weeks and after 3 months, and clinical assessment was performed after 3 months. The presence of groin pain after 3 months, defined as an NRS score >3 was evaluated as the primary outcome measure. Secondary outcomes were foreign body feeling and the impact of pain and foreign body feeling on daily activities.

Results: At 3-months follow-up, the incidence of pain (NRS 4-10) was 2 versus 0.9% in the lightweight and heavyweight mesh group respectively (p= 0.17). Pain interfered with daily activities in 1.7% of the lightweight and 1.5% of heavyweight group. In the lightweight group 20% of patients reported a foreign body feeling versus 18% in the heavy weight group (p=0.62). No differences between the groups were observed regarding time to return to work, interference with sports- and sexual activities, testicular pain and ejaculatory pain. Severe preoperative pain (OR 2.01, 95% CI 1.21-3.35, p=0.01) was the only independent predictor of any postoperative pain after 3 months.

Conclusion: Three months after TEP inguinal repair, there were no significant differences between lightweight and heavyweight mesh use regarding the incidence of pain, foreign body feeling or any other endpoint.

INTRODUCTION

Since the introduction of mesh repair for patients with inguinal hernias, low recurrence rates of 2-4 % are observed and the use of mesh irrespective its application, has become standard practice.[1] While mesh placement prevents recurrences, the mesh itself might be a source of mechanical impairment of the patient's moving abilities or generate a phenomenon called foreign body feeling. The subsequent inflammatory reaction after placement may cause chronic pain.[2] The incidence of postoperative pain after inguinal hernia repair is reported in up to 43% of the patients but the rate varies significantly due to heterogeneity in the definition of chronic pain, the methods to assess pain and the times of assessment.[3]

Persistent pain after groin operations affects daily activities in about 2-20% of patients.[4] There is ample evidence that endoscopic hernia repair is associated with less postoperative pain and earlier return to daily activities.[5-7] Assuming that the mesh characteristics are responsible for the long-term functional hindrance, lightweight meshes were introduced. These lightweight meshes have larger pores and contain less prosthetic material, and they assumedly produce less postoperative scarring of the abdominal wall.[8-10]

A number of studies have compared heavyweight with lightweight meshes in open anterior hernia repair and revealed a significant reduction in foreign body feeling and overall postoperative pain.[11-14] Lightweight meshes are, therefore, recommended as the material of choice in primary open inguinal hernioplasty.[15] In a recent meta-analysis of eight randomized controlled trials comparing lightweight versus heavyweight mesh in laparoscopic hernia repair, the benefit of lightweight meshes was not reproduced, although the quality of several studies was hampered by small sample size or missing data regarding the endpoint of interest, i.e. chronic pain after three months. [8,9,16-19] Two large RCT's showed a slight improvement in patient comfort and less foreign body feeling after lightweight mesh.[20,21] However, there is still no consensus which type of mesh should be used in laparoscopic hernia repair.

A randomized controlled trial was conducted in a high volume hernia centre to address the effect of different meshes on postoperative pain and mesh awareness following the first 3 months after endoscopic totally extraperitoneal (TEP) hernia repair using validated questionnaires for pain, mesh awareness and quality of life.

MATERIALS AND METHODS

A prospective double-blind randomized controlled trial (RCT) study was conducted in a high-volume hospital specialized in the TEP technique for inguinal hernia repair between March 2010 and October 2012. Male patients ≥ 18 years of age with a primary, reducible, unilateral inguinal hernia and no contraindications for endoscopic TEP repair were eligible for inclusion. Patients with collagen or connective tissue disorders as well as patients who were unlikely to complete the follow-up regimen since they had no fixed address or their comprehension of the language was insufficient were excluded. After screening for eligibility, informed consent was obtained. The study was approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, The Netherlands) and the local Ethic Board of the hospital. The study is registered in the Dutch Trial Register (NTR2131).[22]

In addition to standardized history and physical examination items, information regarding the preoperative presence of pain and data regarding quality of life was obtained. Pain was measured using the Numeric Rating Scale (NRS 0 = no pain, 10 = extremely painful, Dutch version). The Inguinal Pain Questionnaire (IPQ, Dutch version[23]) and the Carolinas Comfort Scale (CCS, Dutch version[24]) were used to assess the impact of pain on daily life activities. Pain related to sexual function and ejaculatory pain was measured using the Pain related to Sexual Function questionnaire (PSF, a Dutch translation of the questionnaire described by Aasvang et al.[25]

Patients were randomly assigned to the intraoperative use of either a lightweight mesh or a heavyweight mesh. Randomization was done in the operating room after administration of general anaesthesia by computerized block randomization of eight. For the lightweight mesh a 10 x 15 cm, polypropylene-poliglecaprone monofilament mesh was used with large pores (3-4 mm), weighing 55 g/ m^2 (after absorption of the poliglecaprone 28 g/ m^2) (Ultrapro, Ethicon, Johnson & Johnson company, Amersfoort, The Netherlands). The heavyweight mesh was a 10 x 15 cm polypropylene monofilament mesh with small pores (0.8-1.2 mm), weighing 80 g/m^2 (Prolene, Ethicon, Johnson & Johnson Company, Amersfoort, The Netherlands). Lightweight meshes have a disadvantage because handling and mesh positioning is impaired, especially in endoscopic repair. We choose Ultrapro® with a monocryl component lacking this disadvantage. The monocryl component poliglecaprone is completely absorbed by hydrolysis without increased cellularity, inflammatory and fibrotic reaction and even a decreased foreign body reaction compared to heavyweight polypropylene meshes is described.[26,27]

All patients were operated by one of four surgeons with vast experience (> 500 TEP procedures/surgeon) and all procedures were performed under general anaesthesia. The perioperative care and surgical technique were standardized and the same in all patients. The operative details of the TEP technique have been described previously.[28,29] In particular, the mesh graft was not fixated since staples may induce specific complaints that can be ascribed to nerve entrapment and hematoma. Hernia types were classified intraoperatively according to the Nyhus classification and the presence of a lipoma was recorded. Intraoperative complications and operative time were registered. The used mesh type was not mentioned in the operating chart.

Patients were discharged on the day of surgery, unless complications occurred. Post-operative complications were registered. At discharge, patients were advised to take analgesics during the first two days (1 g paracetamol every six h) and to avoid strenuous physical activity (lifting, sports) during the first post-operative week. There were no other restrictions.

Follow-up of patients took place in a standardized manner according to a fixed schedule. The patient, coordinating investigator and the surgeon involved in the follow-up of enrolled patients were blinded for the allocated mesh. NRS scores were measured daily during the first week in a patient diary and after six weeks and three months by questionnaires. IPQ, CCS and PSF questionnaires were filled in at six weeks and three months. All patients were examined physically after three months in the outpatient department by one of the four hernia surgeons (not being the surgeon having performed the operation). Post-operative complications and recurrences were registered. In case of unclear inguinal pain or complaints suggestive of a recurrent hernia, ultrasound of the groin or MRI scan was performed. For the registration of pain-symptoms a standardized clinical evaluation form was used (Inguinal Pain Form by Loos, translated in Dutch).[30]

The primary endpoint of the study was the presence of pain (NRS>3) three months after a TEP hernia repair, as measured by the NRS. The definition of the International Association for the Study of Pain (IASP) was used, chronic postoperative pain was defined as persistent pain at the site of the operation three months after the primary surgery that differed from the pain before the operation.[30] In accordance with the literature, pain intensity was categorized as follows: NRS 1-3 = mild pain; NRS 4-6 = moderate pain; and NRS 7-10 = severe pain. Moderate to severe pain (NRS 4-10) was considered clinically relevant and therefore used as the definition of pain in the present study.[30]

Power calculation and statistical analysis

The hypothesis used in the design of the study was that the incidence of pain three months after operation was lower after implantation of a lightweight mesh compared to a heavyweight mesh. According to the literature at the time of the initiation of our study and based on a pilot study in our hospital, a reduction of 7.5% in the incidence of pain was expected. With a two-sided alpha of 0.05 and a power of 0.80, a total of 429 patients were required in each allocation group. Secondary outcome measure were foreign body feeling, impact of pain and foreign body feeling on daily activities and sexual activities, ejaculatory pain and testicular pain and time to return to normal daily activities and work. Operation time, complications and recurrences were registered as well.

Data were prospectively collected on indigenously developed software and converted to SPSS software (SPSS, Chicago, IL, USA) for analysis. All data were analysed on an intention-to-treat basis. Descriptive statistics were used for baseline data. The incidence of pain was compared between lightweight and heavyweight by means of Chi-square analysis. To determine the effect of mesh type on chronic pain, a multivariable logistic regression analysis was performed. First, a univariate logistic regression analysis was performed for potential risk factors for pain at three months, including mesh type, age, body mass index (BMI), surgeon, type of hernia, the presence of severe preoperative pain, operation time and the presence of severe pain on day 1 of postoperative period.[32] Subsequently, factors with a p-value <0.20 in the univariate analysis. were entered in the multivariable analysis in addition to mesh type.

Secondary endpoints were analysed by using a Student's *t*-test (normally distributed continuous), Mann-Whitney analysis (not normally distributed continuous), or Chi-square analysis (categorical variables). Effect estimators were described with 95% confidence intervals. Significance is set at a level of $p \leq 0.05$.

RESULTS

From March 2010 to October 2012, 3.066 patients visited the hernia centre, 1.826 patients were eligible to include and 978 male patients with a unilateral primary reducible hernia planned for TEP repair, were enrolled in the study (Fig. 1). After inclusion 28 patients were not randomised because they did not meet the criteria, cancelled their operation or failed to be randomised. The study population comprised 950 patients, 478 patients randomised for lightweight mesh and 471 for heavyweight mesh. After randomisation one patient was excluded because the allocated mesh type was unknown. The three-month follow-up was

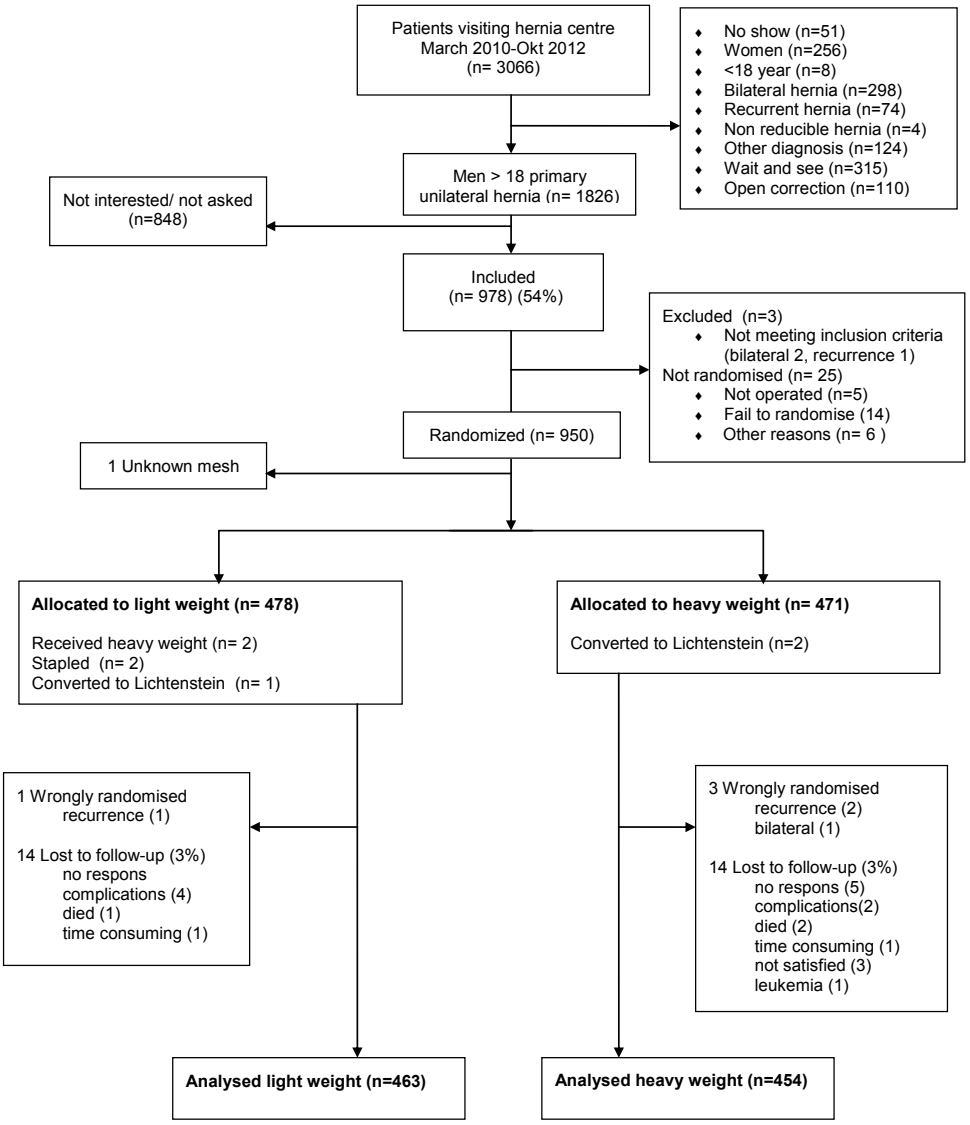

Figure 1. Flow chart

completed in 463 (97%) patients of the lightweight group and 454 (96%) patients of the heavyweight group. Both groups were statistically comparable regarding patient and hernia characteristics and peroperative details (Table 1).

Table 1. Baseline characteristics

	Light weight	Heavy weight
n	463	471
Age (years), median (range)	55 (19-88)	55 (18-94)
Paid work (%)	70	67
BMI (kg/m^2), mean (SD)	25 (SD 2.7)	25 (SD 2.5)
Side (%)		
Left	45	41
right	55	59
Previous operations (%)		
Lower abdomen midline	7	8
Lower abdomen same side	7	10
Preoperative pain NRS (%)		
NRS 0	29	29
NRS 1-3	43	46
NRS 4-7	19	16
NRS 8-10	9	9
Preoperative testicular pain (%)	28	26
Preoperative ejaculatory pain (%)	2.6	2.2
Preoperative pain during sex (%)	38	38
Hernia type (%)		
lateral	73	75
medial	27	24
femoral	0.6	0.4
Surgeon (%)		
1	30	29
2	31	27
3	11	14
4	26	28
5 resident	2	2
Lipoma (%)	36	34

BMI: Body Mass Index

NRS: Numeric Rating Scale (NRS 0 = no pain, NRS 1-3 = mild pain, NRS 4-7 = moderate pain, NRS 8-10 = severe pain)

Median operation time for lightweight mesh was 20 minutes (range 10-50) compared to 19 minutes (range 7-60) for heavyweight mesh (p=0.12). Three procedures were converted to open repair, two in the heavy weight group, one patient in the lightweight group. In the lightweight group, two meshes were stapled and two patients received a heavyweight mesh instead of the randomised lightweight mesh because of a very large hernia defect. There were no statistically differences in per operative and postoperative complications in both groups: peroperative bleeding in five (1.1%) patients of the lightweight group and seven (1.5%) patients of the heavyweight group (p=0.83), postoperative bleeding in four (0.9%) and five (1.1%) patients (p=0.96), hematoma in 12.7% and 12.1% (p=0.92), infection

in 1.1% and 1.1% (p=0.98) and other complications in 1.3% and 0.9% (p=0.91) of patients in lightweight and heavyweight respectively.

Chronic relevant pain (NRS 4-10) at three months was present in four (0.9%) patients in the heavyweight group as compared with nine (2%) patients in the lightweight group (p=0.17). No significant differences were observed regarding the intensity of pain in the two groups (p=0.48). In the heavyweight group, 19.6% of the patients experienced any pain (18.7% mild pain, 0.7 % moderate pain and 0.2 % severe pain) as compared with 18.6% of the patients in the lightweight group (16.7% mild pain, 1.3% moderate pain and 0.7% severe pain, p=0.65; Table 2).

Table 2. Comparison of pain after 3 months in both groups

Chronic pain (at 3 months)	Lightweight n=463	Heavyweight n= 454	p-value
Relevant pain (NRS 4-10) %	2.0	0.9	0.17
Any pain (NRS >0) %	18.6	19.6	0.65
No pain (NRS 0) %	81.3	80.4	0.48
Mild pain (NRS 1-3) %	16.7	18.7	
Moderate pain (NRS 4-7) % (n)	1.3 (6)	0.7 (3)	
Severe pain (NRS 8-10) % (n)	0.7 (3)	0.2 (1)	

NRS: Numeric Rating Scale (NRS 0 = no pain, NRS 1-3 = mild pain, NRS 4-7 = moderate pain, NRS 8-10 = severe pain)

The feeling of a foreign body at 3 months follow-up was mentioned by 20.0% of patients with lightweight meshes and 17.6% in the heavyweight group (p=0.56). In four patients a recurrent hernia was diagnosed after 2-3 months: 2 (0.4%) patients in each group. The median time to return to work was equal in the groups: 7 days (range 1-45) (p=0.50).

No difference in pain intensity at any postoperative time point was observed between the patients treated with lightweight mesh and heavyweight mesh (Table 3). No significant differences were demonstrated on any aspect regarding quality of life using IPQ and PSF questionnaires (data not shown).

Table 3. Comparison of pain after 1 day, 1 week and 6 weeks

	1 day			1 week			6 weeks		
	Light	Heavy	p-value	Light	Heavy	p-value	Light	Heavy	p-value
No pain	5.2	6.3	0.23	27.2	26.8	0.81	70.2	73.9	0.50
Mild pain	49.0	44.2		58.4	59.2		26.1	23.5	
Moderate pain	35.9	41.5		13.1	13.3		3.1	2.4	
Severe pain	9.8	7.9		1.3	0.7		0.7	0.2	

Table 4 shows the univariate and multivariable analysis for possible risk factors for postoperative pain (mesh type, age, body mass index, hernia type, surgeon, severe preoperative pain, operation time, severe pain day 1 postoperative). Preoperative NRS pain scores of 8-10 and severe post-operative pain at day one (NRS 8-10) significantly prospect the risk of any pain after three months. After correction for potential cofounders no difference in any pain after three months was seen between the lightweight and heavyweight mesh groups. Severe preoperative pain (OR 2.01, 95% CI 1.21-3.35, p=0.01) was the only independent predictor of any postoperative pain after three months. Subgroup analysis of patients with or without relevant preoperative pain and influence of mesh on postoperative pain and mesh awareness was performed but no significant differences were found during the postoperative period and at 3 months.

Table 4. Univariate and multivariate analysis for <u>any</u> pain after 3 months

	Univariate analysis			Multivariate analysis		
	OR	**95% confidence interval**	**p-value**	**OR**	**95% confidence interval**	**p-value**
Mesh	0.93	0.67-1.29	0.65	0.91	0.65-1.28	0.60
Age (<25)	1.86	0.65-5.33	0.25			
BMI (>25)	1.20	0.86-1.67	0.28			
Surgeon	1.14	1.00-1.30	0.06	1.07	0.96-1.20	0.25
Hernia type	1.15	0.50-2.63	0.75			
Severe preoperative pain	2.03	1.22-3.39	**0.01**	2.01	1.21-3.35	**0.01**
Severe pain day 1	1.85	1.11-3.12	**0.02**	1.64	0.96-2.79	0.07
Operation time >35 min	0.67	0.23-1.96	0.47			

DISCUSSION

Despite numerous publications and one meta-analysis, there is still no consensus which type of mesh is optimal for endoscopic hernia repair regarding postoperative pain and foreign body feeling. There are only two RCT's comparing lightweight and heavyweight meshes in endoscopic repair with large sample sizes and at least a follow-up of three months.[20,21] Both studies showed slight benefits with lightweight meshes during the early postoperative period, regarding chronic pain and impairment of physical activities. However, in our large, randomized controlled trial comparing lightweight mesh with heavy weight mess for TEP inguinal repair, there was no difference regarding the incidence and intensity of pain, foreign body feeling or any other endpoint at 3 months after surgery. In addition no differences were found at other time moments throughout the early postoperative period up until 3 months.

The strength of this study is its volume: it is the largest double blind RCT studying different types of mesh used in TEP herniorrhaphy. The study is sufficiently powered and used validated questionnaires to assess pain, mesh awareness and quality of life pre- and postoperatively. However, a weakness of this study is the limited follow-up of 3 months. We chose this period while writing the study protocol according to the definition of chronic pain. [31] Recently, some suggested to adjust the definition of chronic postoperative groin pain to its presence at least six months postoperatively as this allows the mesh-related inflammatory response to subside as a causative factor of pain.[33] However, the study population will be followed for three years and data regarding pain and quality of life issues at one, two and three years after surgery are expected.

In the present study chronic relevant pain, according to the classification published by Loos et al.[30] present three months postoperatively, was reported by 2.0% of patients after lightweight mesh and 0.9% of patients after heavyweight mesh use. A comparable study of Chowbey et al showed similar results, reporting moderate to severe pain in 2.1% patients after lightweight mesh and 1.9% after heavyweight mesh.[21] The incidence of chronic pain in our study is low compared to previously data reporting an overall incidence of 6% (range 1-16%) after endoscopic repair.[34] This could potentially be due to the positive effect of experience and high volume and is confirmed by other groups with an abundant experience in performing endoscopic repair.[20,35]

Another relevant aspect of chronic pain is its impact on daily activity and work. Severe pain assumedly results in inability to work or to perform daily activities. Severe pain after three months (NRS 7-10) was mentioned by 0.7% and 0.2% of patients treated with lightweight and heavyweight meshes in the present study, compared to 0 and 0.5% respectively in the study of Chowbey, whereas Bittner did not report pain severity after three months.[20,21] The impact of pain on daily activities in our study was 1.7% and 1.5% and also comparable with the result of Chowbey et al.[21] The impact of pain on the days needed to return to work was seven days in both groups and low comparable with the literature, reporting 7.2-38.1 days.[9,21,36]

In our study we found a relatively high percentage of patients with any pain (NRS 1-10) after three months (18.6% lightweight and 19.6% heavyweight) which was higher when measured after six weeks (29.8% lightweight and 26.1% heavyweight). This was not statistically different between the two groups. The study of Bittner reported any pain in only 10% and 8.0% of patients after four weeks. However, pain was measured by VAS scores and it has previously been described that a higher failure rate is present using VAS compared to NRS.[37] When considering the endpoint any pain after three months Chowbey et al reported

lower frequencies and better results for lightweight mesh: 3.7% compared with 7.1% for heavyweight mesh. The difference was not statistically significant (p=0.164). In their study pain was not measured by VAS or NRS, but only assessed for severity (mild, moderate or severe) in the selection of patients who reported having pain. Thus these data probably under-estimate the true frequency. Other studies with small sample sizes used mean VAS scores to compare differences.[9,19,37] As the majority of patients report very low VAS-scores the mean VAS scores were very low. In the present study mean pain (measured by NRS) was also only 0.5 and 0.4 after 6 weeks and 0.4 and 0.3 after 3 months. Therefore mean VAS scores are not useful to assess pain and discomfort. As previously emphasized in 2002 by Kehlet, this underscores the importance of uniform assessment, the use of validated questionnaires and valid methods to measure pain to enable comparison of study results.[38]

Lastly, we observed no significant difference with respect to foreign body sensation, neither after 6 weeks nor after 3 months. At 3 months 20% of patients with lightweight meshes and 17.6% with heavyweight meshes reported awareness of a foreign body in the groin. Other studies only reported foreign body feeling after 1 year, and reported differences were not statistically different between lightweight and heavyweight meshes.

This study did not show any difference in pain and comfort between the two mesh types. Other studies reporting on mesh types in endoscopic repair showed absent or slight differences in comfort.[16] Then again, in open repair evidence is available that lightweight meshes provide better results. While all foreign bodies induce an inflammatory response, lightweight meshes with larger pores are associated with a reduced inflammatory response and less scar tissue.[39] This theoretical advantage of a reduced inflammatory response of lightweight meshes, as evident in open repair, does not translate into a clinical benefit after TEP hernia repair. The preperitoneal position of the mesh is the likely explanation and this position offers two potential benefits. First there is a reduced risk of direct nerve damage when working in the preperitoneal space in comparison to open anterior repair. Second the preperitoneal as a barrier consists of two layers (parietal and visceral) separated by a thin fascia.[40] The large sensory nerves are located behind this fascia in the parietal space. Direct contact between the mesh and the nerves is usually avoided. The extent of the inflammatory response and its resulting swelling and fibrosis has limited influence in this space because of the protecting fascia. Longer follow-up (1-2 years) is warranted to confirm this theory and to know if the effect of less fibrosis results in less comfort after three months and later and in a higher recurrence rate or not.

In conclusion no beneficial effect regarding postoperative pain, mesh awareness and impact on daily life was observed of a light weight over a heavy weight mesh three months after TEP hernia repair.

REFERENCES

1. Bay-Nielsen M, Kehlet H, Strand L, et al. Danish Hernia Database Collaboration. Quality assessment of 26,304 herniorrhaphies in Denmark: a prospective nationwide study. *Lancet* 2001; 358:1124-1128
2. Klinge U, Klosterhalfen B, Müller M, et al. Foreign body reaction to meshes used for the repair of abdominal wall hernias. *Eur J Surg* 1999; 165:665-73
3. Simons MP, Aufenacker T, Bay-Nielsen M, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2009; 13:343-403
4. Bay-Nielsen M, Perkins FM, Kehlet H. Pain and functional impairment 1 year after inguinal herniorrhaphy: a nationwide questionnaire study. *Ann Surg* 2001; 233:1-7.
5. Kehlet H. Chronic pain after groin hernia repair. *Br J Surg* 2008; 95:135-136
6. Kuhry E, van Veen RN, Langeveld HR, et al. Open or endoscopic total extraperitoneal inguinal hernia repair? A systematic review. *Surg Endosc* 2007; 21:161-166
7. O'Reilly EA, Burke JP, O'Connell PR. A meta-analysis of surgical morbidity and recurrence after laparoscopic and open repair of primary unilateral inguinal hernia. *Ann Surg* 2012; 255:846-853
8. Agarwal BB, Agarwal KA, Mahajan KC. Prospective double-blind randomized controlled study comparing heavy- and lightweight polypropylene mesh in totally extraperitoneal repair of inguinal hernia: early results. *Surg Endosc* 2009; 23:242-247
9. Bringman S, Wollert S, Osterberg J, et al. Early results of a randomized multicenter trial comparing Prolene and Vypro II mesh in bilateral endoscopic extraperitoneal hernioplast (TEP). *Surg Endosc* 2005; 19:536-540
10. Bringman S, Wollert S, Osterberg J, et al. Three-year results of a randomized clinical trial of lightweight or standard polypropylene mesh in lichtenstein repair of primary inguinal hernia. *Br J Surg* 2006; 93:1056-1059
11. Li J, Ji Z, Cheng T. Lightweight versus heavyweight in inguinal hernia repait: a meta-analysis. *Hernia* 2012; 16:529-539
12. Sajid MS, Leaver C, Biag MK, et al. Systematic review and meta-analysis of the use of lightweight *versus* heavyweight mesh in open inguinal hernia repair. *Br J Surg* 2012; 99:29-37
13. Smietanski M, Smiemanski IA, Modrzejewski A. Systematic review and meta-analysis on heavy and lightweight polypropylene mesh in Lichtenstein inguinal hernioplasty . *Hernia* 2012; 16:519-528
14. Uzzaman MM, Ratnasingham K, Ashraf N. Meta-analysis of randomized controlled trials comparing lightweight and heavyweight mesh for Lichtenstein inguinal hernia repair. *Hernia* 2012; 16:505-518
15. Miserez M, Peeters E, Aufenacker T, et al. Update with level 1 studies of the European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2014; 18:151-163
16. Currie A, Andrew H, Tonsi A, et al. Lightweight versus heavyweight mesh in laparoscopic inguinal hernia repair: a meta-analysis. *Surg Endosc* 2012; 26:2126-2133
17. Chui LB, Ng WT, Sze YS, et al. Prospective, randomized, controlled trial comparing lightweight versus heavyweight mesh in chronic pain incidence after TEP repair of bilateral inguinal hernia. *Surg Endosc* 2010; 24:2735-2738
18. Peeters E, Spiessens C, Oyen R, et al. Laparoscopic Inguinal hernia repair in men with lightweight meshes may significantly impair sperm motility: a randomised controlled trial. *Ann Surg* 2010; 252:240-246
19. Heikkinen T, Wollert S, Osterberg J, et al. Early results of a randomised trial comparing Prolene and Vyproll-mesh in endoscopic extraperitoneal inguinal hernia repair (TEP) of recurrent unilateral hernias. *Hernia* 2006; 10:34-40

20. Bittner R, Schmedt CG, Leibl BJ, et al. Early Postoperative and One Year Results of a Randomized Controlled Trial Comparing the Impact of Extralight Titanized Polypropylene Mesh and Traditional Heavyweight Polypropylene Mesh on Pain and Seroma Production in Laparoscopic Hernia Repair (TAPP). *W J Surg* 2011; 35:1791–1797
21. Chowbey PK, Garg N, Sharma A, et al. Prospective randomized clinical trial comparing lightweight mesh and heavyweight polylropylene mesh in endoscopic totally extraperitoneal groin hernia repair. *Surg Endosc* 2010 24:3073-3079
22. Schouten N, van Dalen T, Smakman N, et al.The effect of ultrapro or prolene mesh on postoperative pain and well-being following endoscopic Totally Extraperitoneal (TEP) hernia repair (TULP): study protocol for a randomized controlled trial. *Trials* 2012; 13:76
23. Fränneby U, Gunnarsson U, Andersson M, et al. Validation of an Inguinal Pain Questionnaire for assessment of chronic pain after groin hernia repair. *Br J Surg* 2008; 95:488-493
24. Heniford BT, Walters AL, Lincourt AE, et al. Comparison of generic versus specific quality-of-life scales for mesh hernia repairs. *J Am Coll Surg* 2008; 206:638-644
25. Aasvang EK, Mohl B, Bay-Nielsen M, et al. Pain related sexual dysfunction after inguinal herniorrhaphy. *Pain* 2006; 122:258-263
26. Schug-pas C, Tamme C, Sommerer F, et al. A lightweight, partially absorbable mesh (Ultrapro) for endoscopic hernia repair: experimental biocompatibility results obtained with a porcine model. *Surg Endosc* 2008; 22:1100–1106
27. Klosterhalfen B, Junge K, Klinge U. The lightweight and large porour mesh concept for hernia repair. *Expert Rev Med Devices* 2005; 2:103-117
28. Langeveld HR, van 't Riet M, Weidema WF, et al. Total extraperitoneal inguinal hernia repair compared with Lichtenstein (the LEVEL-Trial): a randomized controlled trial. *Ann Surg* 2010; 251:819-824.
29. Lau H, Patil NG, Yuen WK. Day-case endoscopic totally extraperitoneal inguinal hernioplasty versus open Lichtenstein hernioplasty for unilateral primary inguinal hernia in males: a randomised trial. *Surg Endosc* 2006; 20:76-81
30. Loos MJA, Roumen RMH, Scheltinga MRM. Classifying postherniorrhaphy pain syndromes following elective inguinal hernia repair. *World J Surg* 2007; 31:1760–1765
31. Classification of chronic pain. Description of chronic pain syndromes and definitions of pain terms. Prepared by the International Association for the study of pain Subcommittee on Taxonomy. *Pain Suppl* 1986; 3:1–226
32. Kalliomaki ML, Meyerson J, Gunnarsson U, et al. Long-term pain after inguinal hernia repair in a population-based cohort; risk factors and interference with daily activities. Eur J *Pain* 2008; 12:214-225
33. Kehlet H, Roumen RM, Reinpold W, et al. Invited commentary: persistent pain after inguinal hernia repair: what do we know and what do we need to know? *Hernia* 2013; 17:293-297
34. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *BJA* 2005; 95:69-76
35. Dulucq JL, Wintringer P, Mahajna A. Laparoscopic totally extraperitoneal inguinal hernia repair: lessons learned from 3,100 hernia repairs over 15 years. *Surg Endosc* 2009; 23:482-6
36. Langenbach MR, Schmidt J, Zirngibl H. Comparison of biomaterials: three meshes and TAPP for inguinal hernia. *Surg Endosc* 2006; 20:1511-1517
37. Loos MJA, Houterman S, Scheltinga MRM, et al. Evaluating postherniorrhaphy groin pain: visual analogue or verbal rating scale? *Hernia* 2008; 12:147-151
38. Kehlet H, Bay-Nielsen M, Kingsnorth A. Chronis postherniorrhaphy pain- a call for uniform assessment. *Hernia* 2002; 4:178-181

39. Hollinsky C, Sandberg S, Koch T, et al. Biomechanical properties of lightweight versus heavyweight meshes for laparoscopic inguinal hernia repair and their impact on recurrence rates. *Surg Endosc* 2008; 22:2679–2685
40. Amid PK, Hiatt JR. New understanding of the causes and surgical treatment of postherniorrhaphy inguinodynia and orchalgia. *J Am Coll Surg* 2007; 205:381-385

7

Long-term results of a Randomized Double-Blinded Prospective trial of a lightweight (Ultrapro) versus a heavyweight mesh (Prolene) in Endoscopic Totally Extraperitoneal Inguinal Hernia Repair (TULP-trial)

JPJ Burgmans
CEH Voorbrood
RKJ Simmermacher
N Schouten
N Smakman
GJ Clevers
PHP Davids
EJMM Verleisdonk
M Hamaker
JF Lange
T van Dalen

Submitted

ABSTRACT

Background: Lightweight meshes reduce postoperative pain and stiffness in open anterior inguinal hernia repair. The discussion about a similar benefit for endoscopic repair is ongoing, but concerns exist about higher recurrence rates.

Objective: The aim of the randomized clinical trial was to compare the two years clinical outcomes of a lightweight (Ultrapro®) versus a heavyweight (Prolene®) mesh for endoscopic total extraperitoneal (TEP) inguinal hernia repair.

Methods: Between March 2010 and October 2012 male patients who presented with a primary, reducible unilateral inguinal hernia who underwent day-case TEP repair were eligible. Outcome parameters included chronic pain, recurrence, foreign body feeling and quality of life (QOL) scores.

Results: During the study period, 950 patients were included. One year postoperatively the presence of relevant pain (Numeric Rating Score 4-10) was significantly higher in the lightweight mesh group (2.9%) compared to the heavyweight mesh group (0.7%) (p=0.01), and after two years this difference remained significant (p=0.03). There were 4 (0.8%) recurrent hernias in the heavyweight mesh group and 13 (2.7%) in the lightweight group (p=0.03). No differences in foreign body feeling or QOL scores were detected.

Conclusion: In TEP hernia surgery there was no benefit of lightweight over heavyweight meshes observed two years postoperatively.

INTRODUCTION

Tension free mesh repair has become the standard technique in inguinal hernia surgery.[1,2] Use of mesh had led to low recurrence rates and less chronic pain compared to suture techniques, although chronic inguinal pain and discomfort are still reported after mesh use.[3,4,5] The mesh itself may contribute to these side effects. While the inflammatory reaction and subsequent fibrosis induced by the mesh are essential for optimal fixation and incorporation of the biomaterial in the abdominal wall, the foreign body reaction may also result in exaggerated fibrosis and the development of chronic inguinal pain.[6]

The inflammatory reaction to the foreign material correlates with the amount and pore size of the mesh material used.[7,8] So-called lightweight meshes have been developed and their use resulted in less pain and foreign body feeling when used in open anterior inguinal mesh repair.[9] This benefit has not been demonstrated in endoscopic repair and there is no consensus which type of mesh is optimal in these procedures.[10] In addition, there is concern about the incidence of recurrences when lightweight meshes are used in endoscopic repair, although data regarding prolonged follow-up are scarce.[11]

The prospective double blinded randomized TULP-trial was set up to compare the incidence of pain according to the definition of chronic pain described by the International Association for the Study of Pain (IASP)[12] three months postoperatively, hypothesizing it would be lower after implantation of a lightweight mesh compared to a heavyweight mesh. These results have been published previously and showed no significant differences between lightweight mesh and heavyweight mesh regarding pain, foreign body feeling, QOL score or recurrence rate after three months.[13] When studying chronic pain, others consider a follow-up of at least six months more appropriate, since this allows any mesh-related inflammatory response reaction, as a causative factor of pain, to cease.[14] Our analysis focuses on the occurrence of chronic pain, mesh awareness, quality of life and recurrence in patients after TEP hernia repair with a lightweight or heavyweight mesh up to two years postoperatively.

METHODS

Male patients over 18 years of age with a primary, reducible, unilateral inguinal hernia and no contraindications for TEP repair were eligible to participate in the study. Patients with collagen or connective tissue disorders as well as patients deemed unlikely to cooperate during follow-up (for example owing to language difficulties or without fixed address) were

excluded. After screening for eligibility, informed consent was obtained. All patients were operated in one hernia center, by one of four surgeons with a minimum experience of 500 TEP procedures per surgeon. The study was approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, The Netherlands) and the local Ethic Board of the hospital. The study is registered in the Dutch Trial Register (NTR2131).[15]

Randomization was done in the operating room after administration of general anesthesia by computerized block randomization of 8. Perioperative care and surgical technique were standardized. All procedures were performed under general anesthesia, the operative details of the TEP technique have been described previously.[16] In particular, we did not use any fixation device or glue. We performed a complete dissection of the preperitoneal space including an overview of the symphysis of the pubic bone, dissection of the spermatic cord and testicular vessels, visualization of the psoas muscle and the transversus abdominus muscle. The operative technique was similar in all patients. A 10 x 15 cm, polypropylene-poliglecaprone monofilament lightweight mesh with large pores (3-4 mm), weighing 55 g/m^2 (after absorption of poliglecaprone 28 g/m^2) (Ultrapro®, Ethicon, Johnson & Johnson company, Amersfoort, The Netherlands) or a 10 x 15 cm polypropylene monofilament heavyweight mesh with small pores (0.8-1.2 mm), weighing 80 g/m^2 (Prolene®, Ethicon, Johnson & Johnson Company, Amersfoort, The Netherlands), was used according to the randomization. The mesh selected by randomization was not mentioned in the operating chart. Prior to surgery, at the time of operation, at six weeks and three months postoperatively, pain and QOL scores were measured by validated questionnaires. Perioperative complications and functional results after three months have been published previously.[13]

Follow-up took place in a standardized manner according to a fixed schedule. Pain was measured (by questionnaires) after one and two years using the Numeric Rating Scale (NRS, 0 = no pain, 10 = extremely painful, Dutch version) and pain intensity was categorized as mild (NRS 1-3), moderate (NRS 4-6) or severe (NRS 7-10). Moderate and severe pain (NRS 4-10) were considered clinically relevant and therefore categorized as clinically relevant pain in the present study.[17] The Inguinal Pain Questionnaire (IPQ, Dutch version[18]) and the Carolinas Comfort Scale (CCS, Dutch version[19]) were used to assess the impact of pain on daily life activities. Pain related to sexual function and ejaculatory pain was measured using the Pain related to Sexual Function questionnaire (PSF), a Dutch translation of the questionnaire described by Aasvang et al.[20] IPQ, CCS and PSF questionnaires were filled in at one year and two years.

All patients were examined physically after one year in the outpatient department by one of the specialized hernia surgeons. After two years, patients reporting complaints of pain,

discomfort or a bulge in the groin in the questionnaires, were contacted by the hernia center by telephone and were administered some questions. Patients with complaints of pain or swelling in the groin during these follow-up conversations were offered an outpatient appointment for clinical examination. A reservation regarding the effectiveness of follow-up without physical examination has been suggested as a possible limitation to the validity of this study. A recent publication analyzing the accuracy of postoperative follow-up after inguinal hernia repair by phone concluded this was a reliable tool to detect both symptomatic and asymptomatic recurrences.[21] In cases of unclear inguinal pain or complaints suggestive of a recurrent hernia, ultrasound of the groin or MRI scan was performed. In cases of clinically relevant pain, patients received a multidisciplinary protocolled treatment. The patient, coordinating investigator and surgeon involved in the follow-up of enrolled patients were blinded for the allocated mesh.

The current analysis focuses on relevant pain (NRS 4-10) after one and two years. Additional outcome measures are any pain (NRS 1-10), foreign body feeling measured by CCS and IPQ, impact of pain and foreign body feeling on daily activities (IPQ and CCS) and hernia recurrences after one and two years. Data were prospectively collected on indigenously developed software and converted to SPSS software (SPSS, Chicago, IL, USA) for analysis.

Power calculation and statistical analysis

The power calculation of the TULP trial was based on the hypothesis that the incidence of pain three months after operation was lower after implantation of a lightweight mesh compared to a heavyweight mesh. According to the literature at the time of the initiation of the study and based on a pilot study in our hospital, a reduction of 7.5% in the incidence of pain was expected.[9] With a two-sided alpha of 0.05 and a power of 0.80, a total of 429 patients were required in each allocation group.

All data were analyzed on an intention-to-treat basis. Descriptive statistics were used for baseline data. The incidence of pain and recurrence for lightweight mesh and heavyweight mesh at 1 and 2 years was compared by means of Chi-square analysis. To correct for potential confounding factors for the association between mesh type and pain at one year, a binary logistic regression analysis was performed including the following factors: age, body mass index, operation time, surgeon, hernia type, severe pre-operative pain (NRS 8-10) and recurrence. The same analysis was used to assess the effect of the mesh on recurrences after 2 years, correcting for the following confounding factors: body mass index, operation time, surgeon and hernia type. For other endpoints, the Student's *t*-test (normally distributed continuous), Mann-Whitney analysis (not normally distributed continuous), or Chi-square analysis (categorical variables) were used. Effect estimators were

described with 95% confidence intervals. For the comparison of the incidence of pain, a Bonferroni correction was applied to correct for the repeated testing. Thus a p-value of 0.025 was considered significant for these results. For all the other tests, significance was set at a level of $p \leq 0.05$.

RESULTS

From March 2010 to October 2012, 978 male patients with a unilateral primary reducible inguinal hernia planned to undergo TEP repair, were enrolled in the study (Figure 1). After inclusion, 28 patients were not randomized because they did not meet the criteria, cancelled their operation or failed to be randomized. The study population comprised 950 patients, 478 patients were allocated to the lightweight mesh group and 471 to the heavyweight mesh group. After randomization, one patient was excluded because the allocated type of mesh was unknown. Demographic details, pre-operative pain, operation time and peri- and postoperative complications were similar in the two groups (Table 1). Complete one year follow-up information was available of 894 patients and two year follow-up data of 867 patients. At two years 440 (92%) patients in the lightweight group and 427 (91%) patients in the heavyweight mesh group could be analyzed.

At the one year postoperative point, the difference in reported relevant pain (NRS 4-10) was statistically significant between the two groups: 3 (0.7%) patients in whom a heavyweight mesh was used compared to 13 (2.9%) patients in whom a lightweight mesh was used (p=0.01). After two years this difference persisted: 4 (0.9%) and 13 (3.0%) patients reported relevant pain in the heavyweight and lightweight mesh group respectively (p=0.03). The number and proportion of patients reporting any pain (NRS 1-10) after one year was 48 (10.9%) with heavyweight and 52 (11.5%) with lightweight mesh and at two years 47 (11%) with heavyweight and 65 (14.8%) with lightweight mesh.

There were no differences between the groups with respect to foreign body feeling. After one year 54 (12.2%) patients in the heavyweight mesh group stated that they could feel the mesh in the groin compared to 60 (13.8%) patients in the lightweight group (p=0.49), hindrance of the mesh was reported by 9 (2.0%) versus 14 (3.2%) patients respectively (p=0.52). After two years these percentages were unchanged. There were no major differences in responses to the IPQ and CCS questionnaires (data not shown), neither regarding testicular pain and sexual related pain and discomfort.

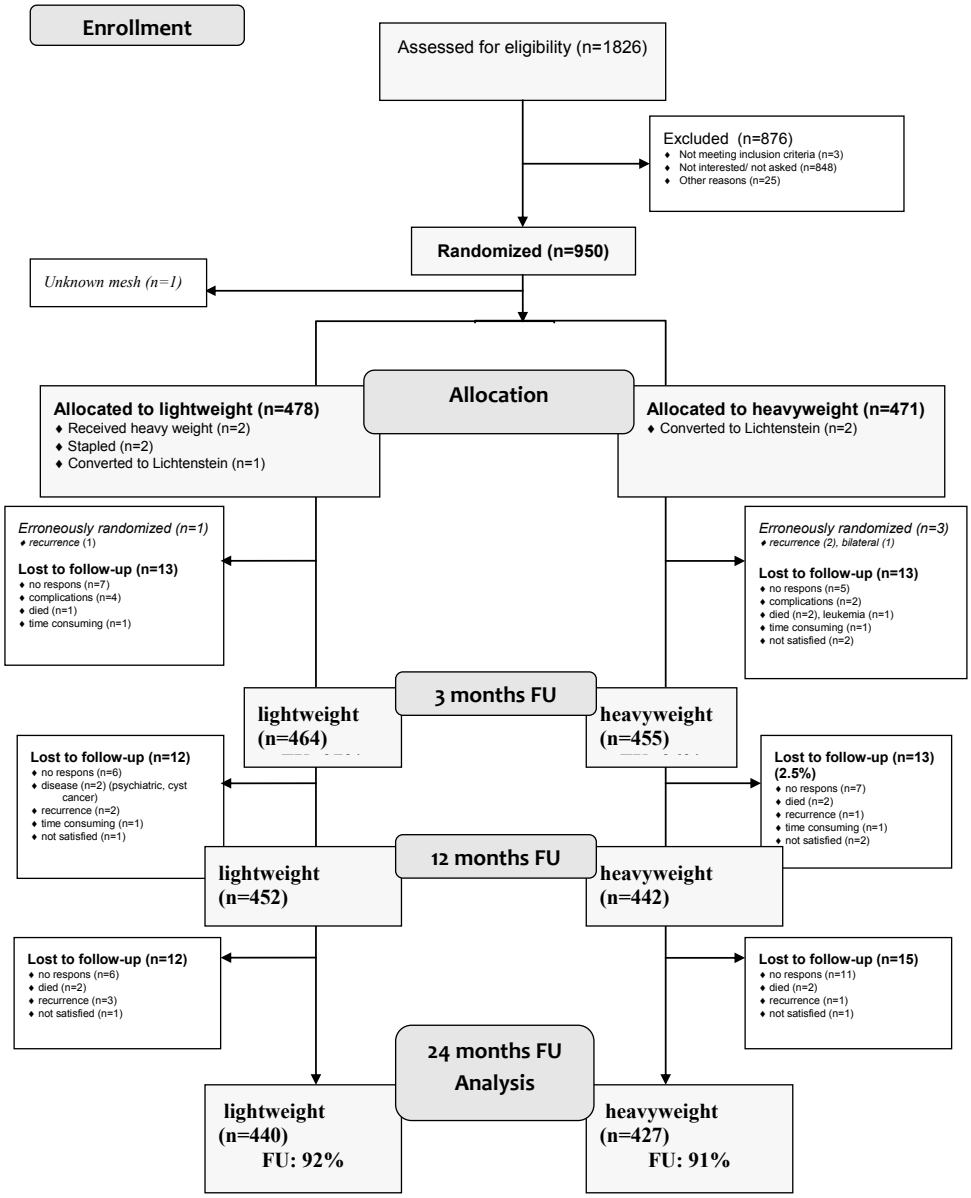

Figure 1. Flow chart

After three months, a total of 4 (0.4%) recurrences were reported, 2 in each group.[12] This figure increased to 11 (1.2%) after one year (8 (1.7%) with lightweight mesh and 3 (0.6%) with heavyweight mesh) and 17 (1.8%) recurrences after two years: 13 (2.7%) in the lightweight mesh group and 4 (0.8%) in the heavyweight mesh group (p=0.03). Five recurrent

Table 1. Baseline characteristics

	LW	HW
Total number of patients	478	471
Age (years), median (range)	55 (19-88)	55 (18-94)
BMI (kg/m^2), mean (SD)	25 (2.7)	25 (2.6)
Paid work	335 (70)	320 (68)
Side		
Left	215 (45)	193 (41)
right	263 (55)	278 (59)
Preoperative pain NRS		
NRS 0	138 (29)	136 (29)
NRS 1-3	204 (43)	215 (46)
NRS 4-7	118 (25)	105 (22)
NRS 8-10	18 (4)	15 (3)
Preoperative testicular pain	139 (29)	122 (26)
Preoperative ejaculatory pain	12 (2.5)	9 (1.9)
Preoperative pain during sex	186 (39)	179 (38)
Hernia type		
lateral	348 (73)	351 (75)
medial	128 (27)	118 (25)
femoral	2 (0.5)	2 (0.4)
Surgeon		
1	142 (30)	135 (29)
2	149 (31)	127 (27)
3	53 (11)	64 (14)
4	124 (26)	132 (28)
5 resident	10 (2)	13 (3)
Lipoma	173 (36)	161 (34)

LW = Lightweight , HW = Heavyweight
Percentages between parenthesis
BMI: Body Mass Index
NRS: Numeric Rating Scale (0 = no pain, 1-3 = mild pain, 4-7 = moderate pain, 8-10 = severe pain)

hernias were diagnosed clinically only. Eight were diagnosed clinically and confirmed by ultrasound. In four patients both methods were inconclusive and an MRI was performed additionally. After correcting for confounding factors (body mass index, operation time, surgeon and hernia type) the lightweight mesh was still associated with a significantly higher recurrence rate after two years follow-up (OR 3.30, 95% CI 1.06-10.29, p=0.04) (Table 2).

Since significantly more patients with a recurrent hernia reported pain (p<0.01), we analyzed the groups after exclusion of the 17 patients with a recurrence. The difference in the frequency of relevant pain after one year was 3 (0.7%) versus 11 (2.5%) patients (p=0.03) in the heavyweight and lightweight mesh group respectively. After two years the difference

Table 2. Multivariate analysis for recurrence at 2 years

		95% confidence interval		
	Odds ratio	Lower	Upper	p-value
Lightweight mesh	3.30	1.06	10.28	0.04
Body mass index ≥ 25 m^2/kg	1.68	0.63	4.51	0.31
Operation time	0.00	0.00	-	1.00
Surgeon	1.12	0.73	1.70	0.61
Nyhus IIIA	0.25	0.09	0.66	0.01

* All factors were simultaneously entered into the analysis.

was 4 (0.9%) versus 11 (2.5%) patients respectively (p=0.07, Table 3). After correcting for confounding factors (age, body mass index, operation time, surgeon, hernia type, severe pre-operative pain (NRS 8-10) and recurrence) a lightweight mesh was still associated with significantly more relevant pain after one year in a multivariate analysis (OR 3.96, 95% CI 1.10-14.23, p=0.04, Table 4).

Table 3. Number of patients with relevant pain (NRS >3) postoperative

	All patients				Patients without recurrent hernia			
	total	HW	LW	p	total	HW	LW	p
1 year	894	3 (0.7)	13 (2.9)	0.01	886	3 (0.7)	11 (2.5)	0.03
2 years	867	4 (0.9)	13 (3.0)	0.03	858	4 (0.9)	11 (2.5)	0.07

NRS = Numeric Rating Scale

Percentages between parenthesis

HW = Heavyweight, LW = Lightweight

Table 4. Multivariate analysis for pain at 1 year*

		95% confidence interval		
	Odds ratio	Lower	Upper	p-value
Lightweight mesh	3.96	1.10	14.23	0.04
Body mass index ≥ 25 m^2/kg	1.40	0.50	3.90	0.52
Operation time	2.06	0.25	16.65	0.50
Surgeon	0.95	0.63	1.47	0.81
Nyhus	1.69	0.48	5.93	0.41
Severe preoperative pain (NRS 8-10)	4.52	0.93	22.07	0.06
Recurrence	20.37	3.31	125.42	0.001
Young age (<30 years)	-	-	-	1.00

NRS = Numeric Rating Scale

* All factors were simultaneously entered into the analysis.

- No odds ratio could be calculated; the confidence interval for age reached from 0.00 to ∞

DISCUSSION

In this double-blinded randomized controlled trial, lightweight meshes were associated with a higher incidence of chronic pain, an equal rate of mesh awareness and discomfort and a higher risk of recurrence one and two years after TEP inguinal hernia repair.

The strength of this study is the large patient population. Data was collected prospectively, patients and surgeons performing the follow-up were blinded for the mesh to be used and follow-up was complete for more than 90% of patients after two years. This study has a few limitations. One limitation is the small number of patients reporting relevant pain after one and two years. Although this may limit our ability to draw definitive conclusions regarding the superiority of one type of mesh over the other, our data show the use of a lightweight mesh (Ultrapro®) does not render benefit in terms of the occurrence of chronic pain and suggests inferiority of the lightweight mesh regarding recurrence rates. Another limitation of the study is its single country population excluding women. Although the patient population corresponds to those described in several other European studies in terms of sex, age, mean BMI and the proportion of different hernia types, the generalizability to women and to patients on other continents is unclear. A third limitation is the single institution setting. Surgeons with less experience have higher incidence rates of minor complications, conversions and a longer operation time. However, the multivariable analysis in this study showed neither the operation time nor surgeon influenced pain or recurrence rates. A final limitation is the fact the two year follow-up was performed by written questionnaires, which could impair the reliability of the recurrent rates. All patients with any complaints of pain, discomfort or swelling were contacted by phone and asked to visit the surgeon for physical examination, and the reliability of this method is recently supported in literature.[21]

This is the first study showing an increase of relevant chronic pain with lightweight meshes compared to heavyweight meshes in endoscopic repair after two years follow-up. In a previous report of the short term results of this trial, no statistically significant differences in pain three months after TEP repair were observed between the lightweight and heavyweight mesh groups.[13] Since the inflammatory response continues three months postoperative and the subsequent fibrotic changes that lead to postoperative pain may occur later, it was hypothesized the increased fibrotic reaction from the use of heavyweight meshes would be accompanied by a higher frequency of chronic pain.[20] The current literature regarding lightweight and heavyweight meshes shows no significant differences regarding chronic pain at one year after endoscopic repair, while the present study observed even higher rates of relevant chronic pain one and two years postoperatively.[11,22]

The explanation for the increase of pain with lightweight Ultrapro® meshes after one and two years follow-up reported in this study remains to be determined. First, it should be underscored that the overall incidence of was very low, irrespective of the mesh used. This overall low incidence of chronic pain after endoscopic hernia repair is explained by placing the mesh in the preperitoneal anatomic plane. In this plane, direct nerve contact is avoided. As incidences of chronic pain are low, the sample sizes of previous studies were possibly too low to show a difference in pain based on the type of mesh used. One factor contributing to the increase of chronic pain with lightweight meshes could be the weakness of the lightweight mesh itself. Lightweight meshes contain less material and have larger pores, and may not have sufficient strength to avoid bulging, mainly in large defects. Bulging of the abdominal tissue creates pressure that might cause pain after surgery. Pain associated with hernia recurrence was more frequent in the lightweight mesh group, and supports this idea. Lightweight Ultrapro® mesh contains poliglecaprone (Monocryl®). The absorption of poliglecaprone by hydrolysis causes a different inflammatory response, possibly impairing fibrosis formation.[23]

In the present study, the incidence of a recurrent hernia was statistically higher in the lightweight mesh group and remained significant even after correcting for relevant confounding factors. Several studies reported higher recurrence rates after TEP repair with a lightweight mesh, although not significantly so.[11,24] To prevent recurrence, a mesh should have sufficient strength and stiffness, be of an appropriate size and must attain good tissue incorporation by initiation of fibrosis. In this study, the mesh size was similar in both groups and large enough to bridge the hernia defect. The intrinsic weakness of lightweight meshes and the decreased formation of fibrosis likely play a role in the increased risk of hernia recurrence after the use of a lightweight mesh. It is believed the formation of fibrosis hinges upon the intensity of the inflammatory response. The amount of the implanted material and its pore size were postulated as the main factors for the intensity of this reaction.[8,9] An analysis of 1000 explanted meshes confirmed less fibrosis formation in lightweight meshes.[25] Recent animal studies demonstrated that lightweight Ultrapro® meshes were correlated with the most intense tissue inflammatory response, but this response was an elevated, late inflammatory reaction. This is likely related to the hydrolysis of poliglecaprone, resulting in a low, irregular and heterogeneous collagen deposition and poorer mesh integration.[23,26,27] These erratic depositions may have insufficient strength to bridge large hernia defects and could contribute to the risk of a recurrent hernia. The increased risk of a recurrent hernia after lightweight mesh was confirmed in a study by Akeolar et al which concluded lightweight meshes should be fixated.[28] In our study, mesh was not routinely fixated and the observation of 0.8% recurrences in the heavyweight mesh Prolene® group makes the suggestion to fixate the mesh a questionable one in the heavyweight group. Hernia mesh repair without

fixation is in line with recent guideline recommendations that mesh fixation is considered unnecessary and should be avoided, since fixation itself may result in chronic pain[29]

CONCLUSION

In this study, lightweight Ultrapro® meshes for endoscopic inguinal hernia repair showed long-term disadvantages regarding chronic postoperative inguinal pain and recurrence rates. In addition, lightweight meshes are more expensive than standard heavyweight meshes. These findings indicate there is no benefit for lightweight Ultrapro® meshes and a conventional heavyweight standard polypropylene 10 x 15 mesh is recommended for endoscopic inguinal hernia repair.

REFERENCES

1. Lichtenstein IL, Shulman AG. Ambulatory outpatient hernia surgery. Including a new concept, introducing tension-free repair. *Int Surg* 1986; 71:1-4
2. Bay-Nielsen M, Kehlet H, Strand L, et al. Danish Hernia Database Collaboration (2001) Quality assessment of 26,304 herniorrhaphies in Denmark: a prospective nationwide study. *Lancet* 2001; 358:1124-1128.
3. M. P. Simons, T. Aufenacker, M. Bay-Nielsen et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2009: 13:343–403).
4. van Veen RN, Wijsmuller AR, Vrijland WW, et al. Long-term follow-up of a randomized clinical trial of non-mesh versus mesh repair of primary inguinal hernia. *Br J Surg* 2007; 94:506-510
5. EU hernia Triallist Collaboration. Endoscopic compared with open methods of groin hernia repair: systematic review of randomized controlled trials. *Br J Surg* 2000; 87:860-867
6. Klinge U, Conze J, Limberg W, et al. Pathofysiology of the abdominal wall. *Chirurg* 1996; 67:229-233
7. Klosterhafen B, Klinge U, Schumpelick V. Functional and morphological evaluation of different polypropylene-mesh modifictions for abdominal wall repair. *Biomaterials* 1998; 19:2235-2246
8. Greca FH, de Paula JB, Biondo-Simous ML et al. The influence of different pore sizes on the biocompatibility of two polypropylene meshes in the repair of abdominal defects. Experimental study in dogs. *Hernia* 2001; 5:59-64
9. Sajid MS, Leaver C, Biag MK, et al. Systematic review and meta-analysis of the use of lightweight *versus* heavyweight mesh in open inguinal hernia repair. *Br J Surg* 2012; 99:29-37
10. Currie A, Andrew H, Tonsi A, et al. Lightweight versus heavyweight mesh in endoscopic inguinal hernia repair: a meta-analysis. *Surg Endosc* 2012; 26:2126-2133
11. Chowbey PK, Garg N, Sharma A, et al. Prospective randomized clinical trial comparing lightweight mesh and heavyweight polylropylene mesh in endoscopic totally extraperitoneal groin hernia repair. *Surg Endosc* 2010; 24:3073-3079
12. International Association for the Study of Pain: Classification of chronic pain. Description of chronic pain syndromes and definitions of pain terms. Prepared by the International Association for the Study of Pain, Subcommittee on Taxonomy. *Pain* 1986, S1–226
13. Burgmans JP, Voorbrood CE, Schouten N, et al. Three-month results of the effect of Ultrapro or Prolene on post-operative pain and well-being following endoscopic totally extraperitoneal hernia repair (TULP trial). *Surg Endosc 2015*; Jan 1. [Epub ahead of print]
14. Kehlet H, Roumen RM, Reinpold W, et al. Invited commentary: persistent pain after inguinal hernia repair: what do we know and what do we need to know? *Hernia* 2013; 17:293-297
15. Schouten N, van Dalen T, Smakman N, et al. The effect of ultrapro or prolene mesh on postoperative pain and well-being following endoscopic Totally Extraperitoneal (TEP) hernia repair (TULP): study protocol for a randomized controlled trial. *Trials* 2012; 13:76
16. Langeveld HR, van 't Riet M, Weidema WF, et al. Total extraperitoneal inguinal hernia repair compared with Lichtenstein (the LEVEL-Trial): a randomized controlled trial. *Ann Surg* 2010; 251:819-824.
17. Loos MJA, Roumen RMH, Scheltinga MRM. Classifying postherniorrhaphy pain syndromes following elective inguinal hernia repair. *World J Surg* 2007; 31:1760–1765
18. Fränneby U, Gunnarsson U, Andersson M, et al. Validation of an Inguinal Pain Questionnaire for assessment of chronic pain after groin hernia repair. *Br J Surg* 2008; 95:488-493
19. Heniford BT, Walters AL, Lincourt AE, et al. Comparison of generic versus specific quality-of-life scales for mesh hernia repairs. *J Am Coll Surg* 2008; 206:638-644

20. Aasvang EK, Mohl B, Bay-Nielsen M, et al. Pain related sexual dysfunction after inguinal herniorrhaphy. *Pain* 2006; 122:258-263
21. van den Heuvel B, van Jarwaarde J.A., Wichers P, et al. *Surg Endosc* 2015 Jan 29 [Epub ahead of print].
22. Bittner R, Schmedt CG, Leibl BJ, et al. Early Postoperative and One Year Results of a Randomized Controlled Trial Comparing the Impact of Extralight Titanized Polypropylene Mesh and Traditional Heavyweight Polypropylene Mesh on Pain and Seroma Production in Endoscopic Hernia Repair (TAPP). *W J Surg* 2011; 35:1791–1797
23. Pereira-lucena CG, Artigiano Neto R, de Rezende DT, et al. Early and late postoperative inflammatory and collagen deposition responses in three different meshes: an experimental study in rats. *Hernia* 2014; 18:563-570
24. O'Dwyer PJ, Kingnorth AN, Molloy RG, et al. Randomized clinical trial assessing impact of a lightweight or heavyweight mesh on chronic pain after inguinal hernia repair. *Br J Surg* 2005; 92:166-170
25. Klinge U, Klosterhafen B. Modified classification of surgical meshes for hernia repair based on the analyses of 1,000 explanted meshes. *Hernia* 1012; 16:251-258
26. Pasqual G, Rodrigues M, Soromayor S, et al. Inflammatory reaction and neotissue maturation in the early host tissue incorporation of polypropylene prosthesis. *Hernia* 2012; 16:697-707
27. Pereira-Lucena CG, Artigiani Neto R, Frazao CVG et al. Experimental study comparing meshes made of polypropylene, polypropylene + polyglactin and polypropylene + titanium: inflammatory cytokines, histological changes and morphometric analysis of collagen. *Hernia* 2010; 299-304
28. Akeolar D, Kumar S, Khan LR et al. Comparison of recurrence with lightweight composite polypropylene mesh and heavyweight mesh in endoscopic totally extraperitoneal inguinal hernia repair: an audit of 1,232 repairs. *Hernia* 2008; 12:39-43
29. Miserez M, Peeters E, Aufenacker T, et al. Update with level 1 studies of the European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2014; 18:151-163

8

Female 'groin' hernia: totally extraperitoneal (TEP) endoscopic repair seems the most appropriate treatment modality

N Schouten
JPJ Burgmans
T van Dalen
N Smakman
GJ Clevers
PHP Davids
EJMM Verleisdonk
SG Elias
RKJ Simmermacher

Hernia 2012;16:387-392

ABSTRACT

Background: About 30% of all female 'groin' hernias are femoral hernias, although often only diagnosed during surgery. A Lichtenstein repair though, as preferred treatment modality according to guidelines, would not diagnose and treat femoral hernias. Totally Extraperitoneal (TEP) hernia repair, however, offers the advantage of being an appropriate modality for the diagnosis and subsequent treatment of both inguinal and femoral hernias. TEP therefore seems an appealing surgical technique for women with groin hernias.

Methods: This study included all female patients ≥ 18 years operated for a groin hernia between 2005 and 2009.

Results: A total of 183 groin hernias were repaired in 164 women. TEP was performed in 85% of women; the other 24 women underwent an open anterior (mesh) repair. Per-operatively, femoral hernias were observed in 23% of patients with primary hernias and 35% of patients with recurrent hernias. There were 30 cases (18.3%) of an incorrect preoperative diagnosis. Per-operatively, femoral hernias were observed in 17.3% of women who were diagnosed with an inguinal hernia before surgery. In addition, *inguinal* hernias were found in 24.0% of women who were diagnosed with a femoral hernia preoperatively. After a follow-up of 25 months, five patients had a recurrent hernia, two following TEP (1.4%) and three following open anterior repair (12.5%). Two of these three patients presented with a femoral recurrence after a previous repair of an *inguinal* hernia.

Conclusion: Femoral hernias are common in women with groin hernias, but not always detected preoperatively; this argues for the use of a preperitoneal approach. TEP hernia repair combines the advantage of a per-operative diagnosis and subsequent appropriate treatment with the known good clinical outcomes.

INTRODUCTION

Groin hernias, which include inguinal and femoral hernias, are rare in women compared to men, with an incidence of 0.3% in women and 2-5% in men. Femoral hernias, however, occur only in 2.4% of men, while in women they account for 34% of all groin hernias.[1-6]

According to the European Hernia Society (EHS) guidelines, an endoscopic approach is advocated for female patients with primary groin hernias (grade D recommendation), if expertise is available. This is based on the high frequency of femoral recurrence after conventional inguinal hernia repair in women, which argues for the use of a preperitoneal (endoscopic) approach.[2] Clinical examination mostly suffices to determine the preoperative diagnosis in case of an evident groin hernia, although it might not be completely clear whether it concerns an inguinal or a femoral hernia. Ultrasonography may be a useful non-invasive adjunct to physical examination in case of clinical occult groin hernia and/or obscure groin pain.[2] It is, however, unreliable to ensure accurate classification of the different hernia types (i.e. direct/indirect/femoral).[7]

Whereas a TEP approach essentially allows for a repair of either an inguinal or a femoral hernia, the original Lichtenstein approach does not diagnose and treat the latter entity. A recurrence of the 'groin' hernia after a Lichtenstein repair, therefore, might in fact often be a previously undiagnosed and subsequently untreated original femoral hernia.[3] So far, there is little evidence regarding the optimal treatment for groin hernias in female patients.[4,8] It is questionable whether a Lichtenstein repair should be the preferred operative treatment in women.[2] Mesh placement through a preperitoneal approach offers the advantage of being an appropriate modality for per-operative diagnosis and subsequent treatment of both inguinal and femoral hernias. In addition, endoscopic hernia repair is associated with less postoperative pain and earlier return to normal activities.[9-11] Therefore Totally Extraperitoneal (TEP) repair seems an appealing surgical technique for women with groin hernias.

The aim of the present study was to evaluate the abovementioned aspects of groin hernia surgery in a cohort of female patients treated in a single institution having experience with the TEP repair. We hypothesize that femoral hernias are under-diagnosed in women and that TEP should be the preferred operative treatment modality to avoid unnecessary operations for recurrent (femoral) hernias.

METHODS

Since 2005 our hospital delivers a special groin hernia service with earmarked theatre programs, principally providing a TEP repair by four experienced surgeons. Simultaneously an institutional hernia register was established, prospectively collecting demographic data, hernia type, method of repair, operative times and complications and information regarding short term outcome (6 weeks post-operatively). The operative technique has been described in detail previously, allowing patients to be discharged the same day.[10] The mesh is not fixated, since it reduces operative time, saves costs and avoids possible entrapment neuralgia.[12,13] Patients who are deemed unfit for TEP repair are operated by an open (mostly anterior, that is, Lichtenstein) approach. In the present study, the most important reasons to exclude patients for TEP repair were relevant co-morbidity preventing general anesthesia and (before 2007) previous abdominal operations.[14,15] If an open anterior repair was performed in patients with preoperatively diagnosed or preoperatively suspected femoral hernia, the fascia transversalis was opened to explore the femoral canal, followed by a preperitoneal mesh placement and a subsequent repair of the fascia transversalis.

Preoperative work-up of a groin hernia is done in accordance with the EHS guidelines. In case of an evident groin hernia, clinical examination suffices. The clinical diagnosis of a femoral hernia is based on the neck of the swelling appearing lateral and below the pubic tubercle.[16] Cases of obscure pain and/or a doubtful swelling in the groin require radiological evaluation; ultrasound was used in case of a doubtful swelling, when necessary a subsequent MRI was the preferred technique.[2] Demographic characteristics, hernia occurrence (primary or recurrent) and hernia type (inguinal or femoral) are recorded preoperatively. Operative time, hernia type and perioperative complications are registered on a standard form in the operating room. Up until now, the classification according to Nyhus is used to describe hernia types. Postoperatively, hospital stay, postoperative complications, time to return to daily activities, and short term recurrences are registered by filling out forms by the patients at the 6-weeks follow-up visit.

Between November 2009 and February 2010, all female patients, who had been operated for a groin hernia in an elective setting, received questionnaires asking for symptoms suggestive of a recurrent hernia and the presence of chronic postoperative pain. Nonresponders received a new questionnaire after 8 weeks. The questionnaire was similar to the one previously described by Franneby *et al.*[17] and integrated visual analog scales (VAS) were used to assess the presence of chronic postoperative pain. Patients with moderate to severe persistent postoperative pain (VAS ≥ 4; pain scores implied: 0= no pain, 1-3= mild pain, 4-6= moderate pain and 7-10= severe pain)[18] or complaints suggestive of hernia

recurrence were invited for an examination at the outpatient clinic; 100% of the patients with complaints completed the visit. Patients with symptoms suggestive for a recurrent hernia underwent radiologic evaluation (Ultrasound and/or CT). VAS scores were used to assess the severity of pain (VAS ≥ 4 was considered to represent moderate to severe pain) and the Inguinal Pain Form (Dutch: Liespijnformulier) was used to classify postoperative pain.[17]

Statistical analysis

Statistical analyses were performed using SPSS version 17.0 (SPSS, Chicago, Illinois, USA). The Mann-Whitney *U* test was used to compare groups with regard to non-normal distributed continuous variables, whereas the *t* test was used for normal distributed continuous variables. The Fisher's Exact Test was used for analysis of categorical data. Significance was set at a level of 0.05 (two-sided). The occurrence of groin hernia recurrences and the interval between the primary repair and the recurrence were used to calculate the cumulative recurrence rate. Kaplan Meier statistics were used and differences in recurrence rates in relation to the operative technique were explored univariably by a log-rank test.

RESULTS

Between January 2005 and December 2009, 3.543 male and 167 female consecutive patients were operated for a groin hernia. Only female patients ≥ 18 years of age were included in this study (n=164). Their median age was 52.3 (range 18-91) years. Nineteen patients (11.6%) had bilateral hernias and 17 patients (10.4%) were operated for a recurrent hernia after an open anterior hernia repair. In addition to the clinical examination, radiological evaluation was performed in forty patients (24.4%); ultrasound in 36, subsequent MRI in three and CT in one patient (in the latter, an MRI could not be done due to claustrophobia).

A TEP hernia repair was done in 85.4% of the patients. The remaining patients were treated by an open anterior (mesh) repair (n= 24) for several reasons, including patient or anesthesiological preference for epidural anesthesia (Table 1). Three patients < 20 years of age underwent a herniotomy, and in the other patients, a Lichtenstein repair was done.

A total of 183 hernias were repaired. Indirect inguinal hernias occurred most often (62.3%), followed by femoral (24.6%) and direct inguinal hernias (13.1%). In patients who were operated for a recurrent hernia after an open anterior (mesh) repair in the past, femoral hernias were more common (35.3%), compared to patients with primary hernias (23.5%), albeit this was not statistically significant (P=0.373).

Table 1. Indications for an open hernia repair

Reasons to perform an open hernia repair	Number of patients (n)
Previous abdominal surgery (laparotomy and/or caesarean in combination with appendectomy)	7
Patient preference for epidural anesthesia	6
Anesthesiological preference for epidural anesthesia (relevant co-morbidity in patients > 80 years of age)	4
Age under 20 (herniotomy)	3
Recurrence after previous preperitoneal open repair	3
Morbid obesity	1
Total	24

Preoperatively, 139 (84.8%) women were diagnosed with an inguinal hernia and 25 (15.2%) with a femoral hernia. During surgery, however, there were 30 cases (18.3%) of an incorrect preoperative diagnosis. In 24 of the 139 patients (17.3%) who were diagnosed with an *inguinal* hernia, a femoral hernia was found, while in eight of these patients (33.3%) ultrasonography had 'confirmed' the preoperative diagnosis. In addition, in six of the 25 patients (24.0%) who were diagnosed with a *femoral* hernia preoperatively, inguinal hernias were found during hernia repair. In three patients (50%) an ultrasonography was done preoperatively.

In two patients who underwent TEP, a bladder laceration occurred, which was treated with a urinary catheter during 5 days. Further postoperative course was uneventful in these two patients. The mean time for return to normal daily activities was 9 days (SD±7.1) for women who underwent TEP repair and 12 days (SD±8.2) for women who underwent an open repair *(P= 0.09)*. Questionnaires regarding the long-term follow-up were returned by 148 (90%) of the patients (164 hernias). The median interval since the operation was 25 (range, 4-61) months, with no significant difference in response rate and follow-up interval between patients who underwent TEP and open hernia repair. Twenty-five patients reported moderate to severe pain (VAS 4-10) or had complaints suggestive for a recurrent hernia and were examined in the outpatient clinic.

Five recurrent hernias were observed (3.0% of the 164 hernia repairs, Fig. 1), two following a primary TEP repair (1.4%) and three following a primary open anterior mesh repair (12.5%; P=0.02). All patients with a recurrent hernia were re-operated; the patients with a recurrent hernia after TEP underwent an inguinal approach, with exploration of the femoral canal through the transversal fascia, the patients with a recurrent hernia after open anterior repair underwent a TEP. During the operation, one of the two patients with a recurrent hernia following TEP repair had an inguinal recurrence; the other patient

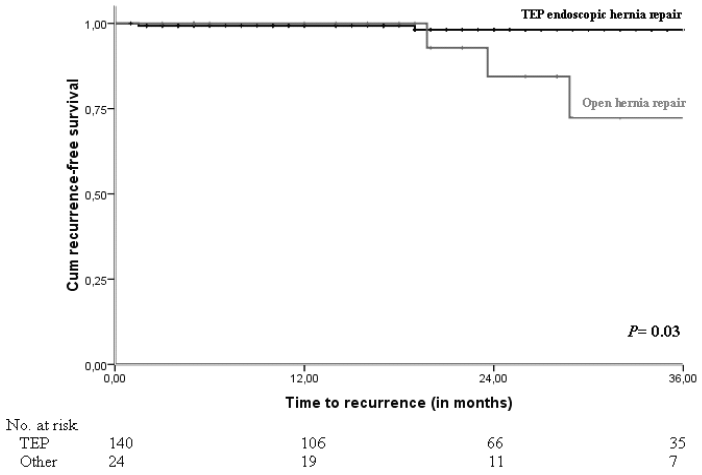

Figure 1. Recurrences after TEP and open hernia repair

had a femoral recurrence (after TEP for a femoral hernia). On the other hand, two of the three patients with a recurrent hernia following open anterior mesh repair had a femoral recurrence. Both patients were diagnosed with an *inguinal* hernia preoperatively (before the primary operation), without further radiological evaluation. The third patient had an *inguinal* recurrence (after anterior mesh repair for an *inguinal* hernia).

Persisting postoperative pain, scored as moderate to severe (VAS 4-10), was reported by eight of 125 patients (6.4%) who underwent TEP hernia repair (with only one patient reporting severe pain (VAS 7-10) and by five of 23 patients (21.7%) who underwent open hernia repair (P= 0.03). There was no difference in the incidence of persisting postoperative pain between patients operated for a primary or a recurrent hernia (p=0.25).

DISCUSSION

This study supports the hypothesis that a preperitoneal TEP repair seems the most appropriate approach for female patients with groin hernias in order to correct preoperative diagnostic errors and avoid subsequent mistreatment.

The high frequency of femoral hernias observed in this cohort is in accordance with the literature. We found femoral hernias in 23% of women with primary hernias, and Kark et al.[16] reported femoral hernias in 21% of women with primary hernias. As in the literature,

femoral hernias were also more often observed in patients with recurrences after previous open anterior hernia repair. In our study, femoral hernias were observed in 35% of patients, while others found femoral hernias in up to 41% of the women treated for a recurrence.[4]

The observed recurrence rate was 1.4% after TEP, which compares favorably to the recurrence rate following our open hernia repair (12.5%).[3,4,19] Bay-Nielsen et al.[4] reported a reoperation for recurrence rate of 4.3% in a population-based study in more than 3.600 women after (predominantly open anterior) hernia repair. They also observed a lower risk of reoperation for a recurrent hernia when endoscopic preperitoneal repair was performed (1.8%).

The reported high frequency of femoral hernias in women and the even higher proportion of femoral hernias in women with recurrent hernias suggest that high recurrence rates in women may be attributable to a preoperative diagnostic problem in groin hernias in women. Being unaware of the high prevalence, femoral hernias may be overlooked during the primary operation, as hypothesized by others as well.[3,19] In addition, in the registry study of Bay-Nielsen, which excluded primary femoral hernias, 41.5% of the (female) patients with primary *inguinal* hernias, repaired by an open approach, recurred with femoral hernias.[4] Together with the observation in the large population-based study by Koch (> 6.000 female hernia repairs) that Lichtenstein and Shouldice repair in women are associated with a twofold higher risk of recurrence in comparison with preperitoneal mesh repair,[3] it is conceivable that a primary open anterior *inguinal* hernia repair might contribute to the development of a subsequent femoral hernia.

The good results of endoscopic TEP hernia repair in women (regarding recurrences) are explained by advantages that are inherent to a preperitoneal approach. Preoperative discrimination between hernia types may be difficult, particularly so in obese patients.[16] In the present study, there were 30 cases (18.3%) of a “mistaken” preoperative clinical diagnosis; six groin lumps were diagnosed as femoral hernias and proved to be inguinal at the operation; 24 were diagnosed as inguinal and proved to be femoral. Preoperatively, an ultrasound (in addition to the clinical examination) was done in respectively 50% and 33% of these patients. As confirmed in studies with (predominantly) male patients, a correct preoperative diagnosis is not only difficult in women, but also in men. Crawford et al.[20] observed an erroneous preoperative diagnosis in 17.8% of the patients (243 male and 10 female) with unilateral hernias, whereof 8.2% consisted of ‘unsuspected’ femoral hernias. In another study by Renzulli et al.[7], the sensitivity of a correct preoperative clinical diagnosis varied between 61% (correct Nyhus classification) and 71% (discrimination between a direct and indirect hernia). In addition, they found a sensitivity and specificity of

respectively 54 and 43% for diagnosing the correct hernia type (according to Nyhus) with ultrasonography, which corroborates our findings that ultrasonography does not ensure accurate discrimination between the different hernia types (i.e.direct/indirect/femoral hernia).

A preperitoneal (endoscopic) approach allows for easy discrimination between the three hernia types (direct, indirect and femoral) intraoperatively, which makes a correct preoperative diagnosis less needed. Subsequently, a preperitoneal approach will enable a proper treatment of all of these hernia types, by covering the complete myopectineal orifice with a mesh. Finally, endoscopic hernia repair is associated with less postoperative pain and earlier return to normal activities compared to open hernia repair[9-11], which was confirmed in this study as well. Conceptually, the transabdominal preperitoneal (TAPP) approach offers similar advantages as the TEP technique. TAPP is frequently used and also advocated for complicated hernias (sliding or incarcerated inguinal hernias) and hernias following previous abdominal or pelvic surgery (prostatectomy). Then again, TAPP has in general been criticized for exposing intra-abdominal organs to potential complications and is associated with higher rates of port-site hernias compared to TEP.[2]

Admittedly, the present study has the limitations of a cohort study, and data regarding recurrences and chronic pain were collected by means of questionnaires. Although all patients with complaints visited the outpatient clinic, a questionnaire can never replace clinical examination. In addition, a minimum of 4 months follow-up may be insufficient to discover recurrent hernias. Furthermore, endoscopic hernia repair is an operative technique with a long learning curve,[9,10] making it an unappealing operative technique for a common disorder. However, groin hernias in women have a high risk of strangulation and the already discussed higher risk of recurrence than in men. This may be a reason to refer female hernia patients to centers where endoscopic inguinal hernia repair is routinely done.

In accordance to the literature, this study showed that the incidence of moderate-to-severe pain after TEP repair (6.4%) compared favorably to the incidence (21.7%) after open anterior repair.[2] Still, the incidence of chronic pain was higher than reported by others (i.e., 2-5% after endoscopic repair [9,17] and 10-12% after open repair[2]). This may be explained by the fact that this study comprised a cohort of female patients, who have a documented higher risk of developing chronic pain compared to men.[2,21]

In conclusion, a preperitoneal approach allows for a "one-step repair" of all groin hernias in women, where a preoperative diagnosis might be difficult or incorrect. TEP endoscopic

hernia repair combines the advantages of a preperitoneal approach with good clinical outcomes and it is therefore, in our hospital, the treatment of choice in women with (primary) groin hernias.

REFERENCES

1. Schumpelick V, Klinge U. Epidemiologie. In: Schumpelick (eds) Hernien, Georg Thieme Verlag, Stutgartt. 2000; pp 36-38
2. Simons MP, Aufenacker T, Bay-Nielsen M, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2000; 13:343-403
3. Koch A, Edwards A, Hapaniemi S, et al. Prospective evaluation of 6895 groin hernia repairs in women. *British Journal of Surgery* 2005; 92:1553-1558
4. Bay-Nielsen M, Kehlet H. Inguinal herniorrhaphy in women. *Hernia* 2006; 10:30-33
5. Weber A, Valencia S, Garteiz D, et al. Epidemiology of hernia in the female. In: Bendavid R, Abrahamson J, Arregui M, Flament J, Philips E (eds) Abdominal wall hernias, Springer, New York, 2001; pp 613-619
6. Nilsson E, Kald A. Hernia surgery in a defined population: a prospective three year audit. *Eur J Surg* 1997; 163:823-829
7. Renzulli P, Frei, E, Schäfer M, et al. Preoperative Nyhus classification of inguinal hernias and type-related individual hernia repair. A case for diagnostic laparoscopy. *Surg Lap Endosc* 1997; 7:373-377
8. Glassow F. Inguinal and Femoral hernia in women. *Int Surg* 1972; 57:34-36
9. Eklund A, Rudberg C, Smedberg S, et al. Short term results of a randomized clinical trial comparing Lichtenstein open repair with totally extraperitoneal laparoscopic inguinal hernia repair. Br J Surg 2006; 93:1060-1068
10. Lau H, Patil NG, Yuen WK. Day-case endoscopic totally extraperitoneal inguinal hernioplasty versus open Lichtenstein hernioplasty for unilateral primary inguinal hernia in males: a randomized trial. *Surg Endosc* 2006; 20:76-81
11. Langeveld HR, Riet M. van 't, Weidema WF, et al. Total Extraperitoneal Inguinal Hernia Repair compared with Lichtenstein (the LEVEL-Trial): A randomized Controlled Trial. *Ann Surg* 2010; 251: 819-824
12. Spitz JD, Arregui ME. Sutureless laparoscopic extraperitoneal inguinal herniorrhaphy using reusable instruments: two hundred three repairs without recurrence. *Surg Laparosc Endosc Percutan Tech* 2000; 10:24-29
13. Koch CA, Greenlee SM, Larson DR et al. Randomized prospective study of totally extraperitoneal inguinal hernia repair: fixation versus no fixation of mesh. *JSLS* 2006; 10:457-460
14. Dulucq JL, Wintringer P, Mahajna A. Totally extraperitoneal (TEP) hernia repair after radical prostatectomy or previous lower abdominal surgery. Is it safe? A prospective study. *Surg Endosc* 2006; 20:473-476
15. Elshof JWM, Keus F, Burgmans JPJ et al. Feasibility of right-sided total extraperitoneal procedure for inguinal hernia repair after appendectomy: a prospective cohort study. *Surg Endosc*; 2009: 23:1754-1758
16. Kark AE, Kurzer M. Groin hernias in women. *Hernia* 2008; 12:267-270
17. Fränneby U, Gunnarsson U, Andersson M, et al. Validation of an Inguinal Pain Questionnaire for assessment of chronic pain after groin hernia repair. *Br J Surg* 2008 ; 95: 488-493
18. Loos MJ, Roumen RM, Scheltinga MR. Classifying post-herniorrhaphy pain syndromes following elective inguinal hernia repair. *World J Surg* 2007; 31: 1760-1765 (16)
19. Mikkelsen T, Bay-Nielsen M, Kehlet H. Risk of femoral hernia after inguinal herniorrhaphy. *Br J Surg* 2002; 89:486-488
20. Crawford DL, Hiatt JR, Phillips EH. Laparoscopy identifies unexpected groin hernias. *Lap hern* 1998; 64: 976-978
21. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaesth* 2005; 95:69-70

9

Summarizing discussion, conclusion and future perspectives

SUMMARIZING DISCUSSION, CONCLUSION AND FUTURE PERSPECTIVES

Inguinal hernia is a common surgical disorder worldwide. The discussion about the most optimal operative technique to repair an inguinal hernia is on going as several postoperative sequelae still need attention. From 1890 till the late sixties of the former century, techniques focusing on closing the defects at the triangle of Fruchaud by suturing repairs were standard.[1] Recurrences, probably due to insufficient healing of the traumatized tissue, were an important adverse event with rates up to 30 %.[2] Suturing with tension in a nerve-ridden area was also commonly associated with considerable pain, although precise data on this subject in that era are lacking. A recent study analysing chronic pain after suturing repair showed high percentages of patients with groin pain after one and two years of 63% and 54% respectively. After two years, the pain still interfered with daily life activities in more than 10% of the patients.[3]

After the introduction of mesh repair techniques, recurrence rates dropped to low rates and the focus of interest shifted to persisting postoperative pain and other sequelae affecting quality of life.[4-6] The first mesh repairs using an anterior approach were associated with post-operative pain-rates of up to 43 %, [6-8] and while much of the postoperative pain subsides in the first six weeks, chronic postoperative inguinal pain after three months (CPIP) was present in 12 % of the patients.[9-12] Introduction of the posterior approach, commonly using endoscopic-assisted techniques, reduced the rate of CPIP, but did not eliminate it. In the preperitoneal space, iatrogenic damage to one or more of the three inguinal nerves is conceptually less likely to occur. TEP (Totally Extraperitoneal) repair, as the most widely used preperitoneal technique, is associated with a reduction of CPIP and has better outcomes regarding time to return to normal activities and work compared to open anterior techniques.[5,14,15] An invaluable side-effect of the endoscopic retromuscular technique is the unprecedented overview of the area involved in groin hernia pathology, and all hernia subtypes can be identified and treated during this operation. In experienced hands, recurrences are rare and patient satisfaction is high. Hence, many surgeons consider TEP repair as the preferable technique at present.

Although TEP repair theoretically could reduce CPIP rates to close-to-zero, the incidence of debilitating CPIP is still reported and ranges between two and five percent.[9,10,12,16] CPIP impairs daily life activities and treatment is often required. Despite numerous publications about the treatment of CPIP, a clear work-up algorithm to assess the type of pain and to subsequently treat it accordingly is currently not available. Due to the variety of presenting

symptomatology of CPIP the work-up of CPIP is challenging. But to treat this condition appropriately, finding a correct diagnosis is a important.

Neuropathic pain, nociceptive pain and a recurrent hernia are considered as the three causative factors of CPIP.[17] Neuropathic pain predominates as a causative factor and it is assumed to play a role in about 50% of the patients with CPIP.[18,19] Several treatment options to treat neuropathic CPIP exist, with a wide range of reported success rates and agreement regarding the most effective treatment is currently lacking.[5,20-21] Medical treatment alone is insufficient in the majority of patients while surgical neurectomy shows favourable results, although long-term outcome data are scarce.[19,22-23] Simple nerve infiltrations and peripheral nerve stimulation (PNS) modalities are less invasive and have demonstrated promising results without the drawback of remaining numbness as reported after surgical neurectomy.

The possibility to treat neuropathic pain is important for those patients who have CPIP due to nerve injury. However, distinction between neuropathic and nociceptive pain may be difficult. A multidisciplinary approach by a hernia surgeon, a pain specialist and a dedicated radiologist could help to find the cause of CPIP, select the proper selection of patients with neuropathic pain and apply an appropriate treatment. Hitherto, a protocolled multidisciplinary work-up was not described before.

In **Chapter 2** we analysed the outcome of an algorithm designed by the departments of hernia surgery and anaesthesia in a hernia clinic. The presented algorithm enabled us to filter out the diagnosis of neuropathic pain in more than one third of the patients with CPIP. These patients reported significant pain relief after protocolled treatment that consisted of ultrasound-guided nerve blocks as an initial treatment and peripheral nerve stimulation if long-term pain reduction proved inadequate. The cumulative success rate of this protocolled treatment was 83%. Data regarding the success rate of minimally invasive injection therapy are limited. In some studies success rates up to 90% are described.[24,25] The advantage of injection therapy is represented by the ease of its application. In this study simple injections with a local anaesthetic resulted in pain relief in 62% of the patients with neuropathic CPIP and may be recommended as a simple first line treatment. In case of refractory pain after these nerve blocks, patients were offered PNS and 6 out of 7 patients became pain free. These results compare favourably to the outcomes reported by others.[26-28] Despite these promising results some reservations are justified regarding the implementation of PNS. Until now, the effectiveness was only reported in small case series and PNS has the potential side effect of erosion and migration of the stimulation lead.[29] A recent publication by Schu et al. demonstrated promising results of a new neuromodula-

tion system stimulating the dorsal root ganglion, but this upcoming technique has been inadequately studied so far.[30] The multidisciplinary approach described in a clear protocol might indeed improve pain relief in CPIP, but further testing of the described algorithm in the setting of a randomized controlled trial including the option of dorsal root ganglion stimulation, is recommended.

The need for guidelines regarding the management of CPIP has been emphasized by Lange and other experts, and an international consensus algorithm for the management of CPIP has been published.[31] The authors stress the importance of a multidisciplinary approach including a pain management team and referral to dedicated hernia centres.[31] The strategy to adopt an observation phase of three months before starting any treatment seems wise. A limitation of this consensus algorithm is the advocation of surgical neurectomy as one of the treatment options early in the algorithm. Based on the aforementioned drawbacks, we propose caution towards operative treatment of neuropathic pain before injections or PNS techniques have been tried.

As stated before, the incidence of clinically relevant CPIP is lower after endoscopic repair compared to open anterior repair. The cause of the pain after (endoscopic) preperitoneal mesh repair is thought to be less related to neuropathic pain as the nerves involved are theoretically left untouched intraoperatively. Inflammation-mediated nociceptive pain appears to be the prevailing pathophysiology. Our algorithm **(Chapter 2)** contained only a small number of patients with post-TEP neuropathic pain. Data regarding a systematic assessment of CPIP specifically after TEP are limited and it is unclear whether the diagnostic tools used are appropriate and therefore useful. In the diagnostic work-up of CPIP after TEP, history and physical examination can enable us to identify a recurrent hernia, neuropathic pain or other disorders such as tendinitis, bursitis or arthrosis of the hip. Ultrasound can be used to confirm the clinical diagnosis or to detect other postoperative conditions including seroma, hematoma or meshoma. Possible “nociceptive” soft tissue changes caused by the operation itself and fibrosis due to the inflammatory response initiated by the surgical damage and/or the use of a mesh is more difficult to distinguish. Other pathology around the groin mimicking groin pain should be excluded too.

MRI is known to be useful to diagnose soft tissue pathology and its role is well established in diagnosing a primary inguinal hernia in clinically unclear cases.[5,32-36] However, MRI has rarely evaluated causes of CPIP after TEP. In times of reducing medical costs one has to be critical to implement such expensive (radiological) examinations. On the other hand, the costs of MRI may be counterbalanced by multiple visits by concerned patients to their surgeon, second opinion, or pain clinic. The results in **Chapter 3** show that MRI may well

offer reassurance of the patient by showing adequate position of the mesh. In 40% of the patients with clinically relevant CPIP three months after TEP this reassurance by MRI and the fact that no abnormalities other than minor fibrosis were found, led to acceptance of a wait and see policy while the majority of patients eventually became pain free. In another 15% of the patients, MRI revealed conditions other than hernia-operation-related that were responsible for the persisting groin pain. MRI was of little help to distinguish between a recurrent hernia or bulging and to identify a specific cause of inguinal hernia repair-related pain. A suggested relation between the degree of inflammatory response with its subsequent fibrosis formation on MRI and CPIP after TEP was not observed. Although exaggerated fibrosis appeared more prevalent in patients with chronic pain, this was not significantly so. In addition, fibrosis was also found in pain free groins. Moreover, in most patients with moderate to extensive fibrosis, the pain diminished over time with or without treatment.

Spontaneous pain reduction after TEP repair has been described previously and may be explained by the hypothesis that CPIP after TEP is mainly caused by inflammation-mediated nociceptive pain.[5,37-39] It is assumed that this inflammatory reaction diminishes over time, generally within three to six months postoperatively.[21] Accordingly, nociceptive CPIP is basically a self-limiting condition. However, detailed and well-designed data assessing the natural time course of groin pain after endoscopic inguinal hernia repair are limited. Only one study described the inguinal pain course during the first year after TEP in detail.[40] Such information is important to design appropriate algorithms for the assessment and treatment of CPIP after TEP. In **Chapter 4** the incidence and course of inguinal pain over time following TEP hernia repair was described in detail. Pain was recorded preoperatively and up to one year postoperatively at different time points. This study confirmed the self-limiting character of clinically relevant CPIP after TEP. Although a relatively high percentage of patients experienced any pain symptoms (NRS 1-10) in the first six weeks (26%) to three months (19%) after TEP repair, relevant pain (NRS >3) was reported in only 3% of the patients after six weeks and 0,6% after three months. Less than 1 % of the patients reported moderate pain (NRS 4-7) at one year postoperatively. Postoperative pain scores were higher and lasted longer in patients with severe pain pre-operatively. In this unprecedented study the time courses of pain in the first year after TEP in patients without pain preoperatively compared to patients with substantial preoperative pain were significantly different. These data are helpful to inform patients more adequately about their prognosis and to reset patients' expectations regarding recovery. The low risk of recurrence after TEP in experienced hands was confirmed in this study: only two patients (0,4%) developed a non-painful recurrent hernia. Due to the self-limiting time course of CPIP and the low risk of hernia recurrence in patients with inguinal pain, (surgical) re-intervention or diagnostic

re-examination (MRI) are presumably not indicated before the twelfth month postoperatively. Remarkably, in this study postoperative pain was often localized at the scrotal or genital region, while inguinal pain was seen more frequently pre-operatively. Most patients complained of testicular pain rather than scrotal skin pain. Genital or scrotal skin pain may be caused by injury to the genital branch of the genitofemoral nerve.[41] The mechanism responsible for post-TEP orchialgia is more complex, hypothesized to be related to injured nerve fibres originating from the hypogastric plexus, rather than to direct injury of the (genital branch) of the genitofemoral nerve.[42] Testicular pain resolved over time in 96% of patients in our study. In a study analysing ipsilateral orchialgia after laparoscopic donor nephrectomy, testicular pain spontaneously disappeared after about six months.[43]

Orchialgia and sexual-related pain is another important issue. Few studies have dealt with sexual function after inguinal hernia repair, and those that did merely focused on general sexual function such as erectile disorders.[44-46] Moreover, no studies evaluated the incidence of painful sexual activity and impairment of sexual function before and after TEP repair. The primary objective of **Chapter 5** was to quantify pain during sexual activity before and after TEP. Sexual activity as a quality of life parameter appears to be greatly affected by the presence of an inguinal hernia. Painful sexual activity was present in one third of the patients with inguinal hernias. In the majority of patients this improved after TEP repair. Only 2.3% of the patients with no prior history sexual-related pain experienced pain postoperatively. The frequency of relevant painful sexual activity preoperatively decreased from 21 to 3% after TEP, serious impaired sexual function decreased from 6 to 1%. This improvement in postoperative sexual functioning compares favourably with the results of the study reported by Aasvang et al.[47] Patients without pre-operative pain probably develop postoperative pain after trauma of the spermatic cord, post-operative scarring or fibrosis formation after implantation of the mesh. To prevent orchialgia and probably sexual impairment overzealous dissection of the cord should be avoided.

Fibrosis is the result of the operation and the insertion of a mesh. Meshes should prevent recurrences and have become the golden standard for inguinal hernia repair. The adverse effect of their use is the induced inflammatory response. The meshes used originally were heavy-weight and it was felt that the amount of synthetic material was related to the extent of fibrous reaction. Consequently, during the last decades, lightweight meshes were developed to reduce the inflammatory response and prevent excessive fibrosis formation. Hypothetically, the inflammatory response should be decreased after the implantation of meshes with less material and larger pores. This was confirmed in animal studies, [48,49] and in open anterior repair the use of lightweight meshes reduced CPIP and stiffness and guidelines recommend the use of a lightweight mesh for the Lichtenstein repair.[50,51] For endoscopic

repair evidence about this benefit is not available.[52] In addition, there is concern about higher recurrence rates after the use of lightweight meshes.[40,52] Several RCT's comparing lightweight and heavyweight meshes for endoscopic repair have been published but many studies were hampered by insufficient powering and a short follow-up.[52] In two studies with large patient groups and a follow-up of at least one year, a small benefit of lightweight meshes regarding comfort were found, mainly in the early post-operative period.[40,53] Thus, the discussion which mesh is better for TEP is on-going. In **Chapter 6 and 7** we analysed 950 patients with a primary unilateral inguinal hernia undergoing a TEP repair with either a lightweight Ultrapro® or a heavyweight Prolene® mesh. This study is the largest RCT to date. Potential biases were avoided by large patient groups, double blind evaluation, validated questionnaires and a follow-up rate of more than 90%. Three months after TEP repair, there were no significant differences between the lightweight and heavyweight mesh regarding the incidence of CPIP, mesh feeling or any other endpoint. This may be explained by the preperitoneal position of the mesh. This space consists of two layers, separated by a thin fascia acting as a protector of the genitofemoral and femoral nerves.[42] The extent of the inflammatory response and the resulting swelling and fibrosis should have a limited influence in this space. Fibrosis on the other hand is deemed essential for fixation and incorporation of the mesh in the abdominal wall to bridge the defect of the weak inguinal floor. The results of our study showed a significantly higher incidence of recurrences after two years when using a lightweight Ultrapro® mesh (2.7%), as compared to heavyweight Prolene® mesh (0.8%). This can be explained in three ways: 1. by the weakness of the mesh itself, 2. by the fact that lightweight meshes induce an insufficient inflammatory response creating less fibrosis and 3. by the special characteristic of Ultrapro meshes containing Monocryl®. The latter resolves by hydrolysis thus creating a different inflammatory response. This response seems to occur later and lasts longer and the formation of collagen is less organized and weaker compared to the collagen formation after Prolene meshes.[54] At one and two years postoperatively we also observed a higher incidence of clinically relevant pain in the lightweight mesh group compared to the heavyweight group. This difference remained significant after multivariate analysis to adjust for the differences in recurrence rates. It is unclear if the reaction emanating from the hydrolysis of the Monocryl has influence on the development of CPIP. It should be stressed that the overall incidence of CPIP was very low. Therefore, the ability to draw firm conclusions regarding the superiority of Prolene meshes is limited. Then again, the data do show that lightweight Ultrapro meshes do not render any benefit in terms of CPIP and mesh awareness and even suggests inferiority regarding the risk of hernia recurrence.

Despite the implementation of mesh repair in inguinal hernia surgery, recurrences still occur, and the risk is associated with surgical expertise. In experienced hands, recurrence rates are extremely low after endoscopic surgery. Additionally, an important advantage of endoscopic preperitoneal repair is the ability to oversee the entire inguinal floor enabling the surgeon to identify otherwise missed simultaneous inguinal defects, in particular femoral hernias. In women femoral hernias are observed in up to 25% of primary repairs and in up to 40% in cases of recurrent hernias.[55,56] In **Chapter 8** we studied the frequency of different hernia subtypes in women. The study showed that the diagnosis of the correct hernia type is difficult preoperatively and confirmed a high incidence of femoral hernias in women. As endoscopic hernia repair offers the opportunity to identify all hernia subtypes intra-operatively, this technique is recommended as the most appropriate treatment and, in the meantime , is now advocated as such in the EHS guidelines.[5]

CONCLUSIONS

The following conclusions may be drawn from the studies presented in this thesis:

- Using a standardized assessment of inguinal pain and a protocolled treatment sequence including nerve infiltrations and peripheral nerve stimulation, an 82% reduction of CPIP can be attained. (Chapter 2)
- For patients with CPIP after TEP, MRI is useful to confirm a correct flat mesh-position and to identify possible non-operation-related causes of groin pain. (Chapter 3)
- Patients with moderate-to-severe groin pain preoperatively, have a higher risk of CPIP. In most cases the pain fades out and the overall incidence of clinically relevant CPIP one year after TEP is less than 1%. (Chapter 4)
- The presence of an inguinal hernia may limit a patient's sexual function, a beneficial effect of TEP hernia repair on sexual function being observed in the majority of patients (Chapter 6)
- The expected benefit regarding pain and comfort of a lightweight Ultrapro mesh compared to a heavyweight Prolene mesh could not be demonstrated during the first three months after TEP repair (Chapter 7)
- Lightweight Ultrapro meshes are associated with increased recurrence rates and CPIP at one and two years after TEP inguinal surgery. (Chapter 8)
- In female patients with a groin hernia an endoscopic technique should be advocated as preoperative assessment of the origin of the hernia is often inconsistent. (Chapter 9)

FUTURE PERSPECTIVES:

Improving Patient Selection for TEP hernia repair.

Specifically in Western countries, inguinal hernia surgery has become a specialisation of the "general surgeon". Dedicated hernia surgeons require a wide acquaintance of possible groin pathology and different treatment options for the individual patient. Tailored treatment is necessary for women. Given the relatively low incidence of female inguinal hernia and the difficulty to distinguish the type of hernia preoperatively, an endoscopic approach for women seems to be mandatory. The success of an endoscopic technique is strongly correlated with experience indicating that women with groin hernia primarily should be treated by experienced hands, such as available in a hernia center.

Another group that may benefit from a more tailored treatment are older patients with a primary inguinal hernia. Concurrent with the rise in global life expectancy and age of the population, the number of older patients will increase. It is important to evaluate which octogenarian would benefit from a surgical inguinal hernia repair and which would not. The hernia surgeon should balance possible operation-related harms with the benefits of reducing hernia related symptoms. Treating elderly patients with an endoscopic repair may be appropriate, but has not been evaluated so far. Several issues need to be resolved in this regard. Firstly, the discussion about the harm of general anaesthesia is unsolved. Secondly, in our ageing world the number of patients with prostatic cancer will increase. Today it is not clear if the incidence of per- and postoperative prostatectomy complications is higher after a previous TEP repair. Finally, anterior repair under local anaesthesia is a good second option and watchful waiting is advised if an operation is assumed too risky. Geriatric consultation is increasingly used for treatment decisions in older oncological patients. It is therefore conceivable that a geriatric evaluation for older patients with an inguinal hernia would become standard in the nearby future.

The treatment of a so-called sportsman hernia was not the subject of this thesis, but active sportsmen with groin pain constitute a growing group of patients their treatment being a challenge requiring attention in future trials. There are several publications reporting good outcome after a diversity of operation techniques. Hypothetically, sportsmen may have a weakened inguinal floor and this could be improved by an inguinal repair with mesh. A multidisciplinary approach and a systematic evaluation of the pain including different diagnostic tools, may very well contribute in solving this problem.

Ways to improve long term functional outcome

If surgical treatment of an inguinal hernia is indicated, unwanted sequelae must be kept to a minimum. Since recurrences, due to the use of meshes, are at low levels nowadays, CPIP is the most important side effect after inguinal repair. During the last decades knowledge about the pathophysiology of CPIP after TEP has improved, but its mechanism is still not fully understood. Literature suggests that preperitoneal techniques and high volume are important factors to minimize CPIP. Hence, hernia surgery may benefit from concentration of care in hernia centres and from hernia surgeons. The type of mesh for TEP repair has negligible influence on CPIP. In fact, in this thesis we showed that the risk of CPIP and a recurrent hernia after lightweight Ultrapro meshes is increased. Hence our advice that surgeons should use (less expensive) Prolene meshes. The fact that there are still some recurrences after TEP performed by skilled hernia surgeons in high volume centres using Prolene meshes should be explored. After analysis of these rare recurrences, further recommendations to prevent them should evolve.

High volume dedicated hernia centres are confronted with a considerable number of second opinions of patients with unexplained groin pain. Dedicated teams including a hernia surgeon, an experienced radiologist, a pain specialist and optionally an orthopaedic surgeon, neurologist and urologist are needed. This multidisciplinary approach is even more important for patients with complex pathology, usually following previous and repeated surgery. It is particularly challenging to find the best treatment strategy for these patients with CPIP after several inguinal repairs. Inherent to the caseload of this subset of complex patients, experimental treatment algorithms for diagnostic and therapeutic management of these patients may be addressed.

Addressing quality of hernia care: a plea for clinical auditing

To further improve the outcome of hernia repair, new promising preperitoneal techniques like TREPP and TIPP will be evaluated. To justify the implementation of those techniques, uniformity in the definition and the assessment of the outcome of these techniques is imperative. In the current literature, the incidence of CPIP and the impairment of daily life activities is very low after TEP in experienced hands. However, a clear comparison between different papers remains difficult. Therefore, we must adopt one definition of CPIP and a simple, similar method to assess CPIP and other sequelae. Validated questionnaires so far contain multiple questions. In practice, these comprehensive questionnaires are time-consuming and only a few items are truly useful. The most important issue concerns any limitation in work or daily life activities including sex and sports. If limitations are encountered, their level and duration need to be clarified as well. In this light I plea to develop one uniform simple questionnaire, for international use. Although randomised controlled

trials remain the source of best evidence, limitations are described more and more. Proof is hindered by the delay between surgery and the development of possible complications and when slight modifications of techniques or materials are studied. To prevent this bias, registry of hernia repair is necessary. National Scandinavian registries have demonstrated that they improve outcome and hopefully the international platform for registration and outcome measurement of hernia operations provided by the EuraHS will quickly come into effect. In the meantime, hernia surgeons should register their results themselves using it as audit of their own performance.

REFERENCES

1. W.Y. Lau. History of treatment of groin hernia. *World J Surg.* 2002; 26:748-759
2. Bekker J. Keeman JN, Simons MP et al. A brief history of the inguinal hernia operation in adults. *Ned Tijdschr Geneeskd*. 2007; 151:924-931
3. Cunningham J, Temple WJ, Mitchell P, et al. Cooperative hernia study. Pain in the postrepair patient. *Ann Surg*. 1996; 224:598-602
4. Lichtenstein IL. Local Anesthesia for Hernioplasty. Immediate ambulation and return to work: a preliminary report. *Calif Med* 1964; 100:106-109.
5. Simons MP, Aufenacker T, Bay-Nielsen M et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2009; 13:343-403.
6. Kehlet H. Chronic pain after groin hernia repair. *Br J Surg* 2008; 95:135-136.
7. Kuhry E, van Veen RN, Langeveld HR, Steyerberg EW, Jeekel J, Bonjer HJ. Open or endoscopic total extraperitoneal inguinal hernia repair? A systematic review. Surg Endosc 2007; 21:161-166
8. O'Reilly EA, Burke JP, O'Connell PR. A meta-analysis of surgical morbidity and recurrence after laparoscopic and open repair of primary unilateral inguinal hernia. Ann Surg 2012; 255:846-853
9. Bay-Nielsen M, Perkins FM, Kehlet H. Pain and Functional Impairment 1 Year After Inguinal Herniorrhaphy: A Nationwide Questionnaire Study.2001; *Ann Surg*; 233: 1–7
10. Poobalan AS, Bruce J, Cairns W et al. A Review of Chronic Pain After Inguinal Herniorrhaphy. *Clin J Pain;* 2003; 19:48–54
11. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaest* 2005; 95: 69–76
12. Ferzli GS, Edwards ED, Khoury GE. Chronic Pain after Inguinal Herniorrhaphy. *Am Coll Surg* 2007; 205: 333–341
14. Dahlstrand U, Gabriel Sandblom G, Ljungdahl M. TEP under general anesthesia is superior to Lichtenstein under local anesthesia in terms of pain 6 weeks after surgery: results from a randomized clinical trial *Surg Endosc* 2013; 27:3632–3638
15. Westin L, Wollert S, Ljungdahl M, et al. Less Pain 1 Year After TEP Compared with Lichtenstein Using Local Anesthesia: Data from a Randomized Controlled Clinical Trial. *Ann Surg* 2015; Jun 15. [Epub ahead of print]
16. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaesth* 2005; 95: 69–76
17. Aasvang EK, Brandsborg B, Christenen B, et al. Neurophysiological characterisation of postherniotomy pain. *Pain* 2008; 137:173-181
18. Loos MJA, Roumen RMH, Scheltinga RMR. Classifying Postherniorrhaphy Pain Syndromes Following Elective Inguinal Hernia Repair. *World J Surg* 2007; 31:1760–1765
19. Amid PK. Causes, prevention, and surgical treatment of postherniorrhaphy neuropathic inguinodynia: Triple neurectomy with proximal end implantation. *Hernia* 2004; 8:343–349
20. Kehlet H, Roumen RM, Reinpold W, et al. Invited commentary: persistent pain after inguinal hernia repair: what do we know and what do we need to know? *Hernia* 2013; 17:293-7
21. Alfieri S, Amid PK, Campanelli G, et al. International guidelines for prevention and management of postoperative chronic pain following inguinal hernia surgery. *Hernia* 2011; 15:239-49
22. Hakeem A, Shanmugam V. Current trends in the diagnosis and management of postherniorrhaphy chronic groin pain. *W J Gastrointest Surg*. 2001; 27:73-81

23. Bischoff JM, Koscielniak-Nielsen ZJ, Kehlet H, et al. Ultrasound-guided ilioinguinal/iliohypogastric nerve blocks for persistent inguinal postherniorrhaphy pain: a randomized, double-blind, placebo-controlled, crossover trial. *Anesth Analg* 2012; 114:1323-9
24. Carr DB. Local Anesthetic Blockade for Neuralgias: "Why Is the Sky Blue, Daddy?". *Anesth and analg* 2011; 112:1283-85
25. Palumbo P, Minicucci A, Nasti AG, et al. Treatment for persistent chronic neuralgia after inguinal hernioplasty. *Hernia* 2007; 11:527-31
26. Weiner RL. Peripheral nerve stimulation. Neurosurg Clin N Am 2003;14:401-8.
27. Carayannopoulos A, Beasley R, Sites B. Facilitation of percutaneous trial lead placement with ultrasound guidance for peripheral nerve stimulation trial of ilioinguinal neuralgia: a technical note. *Neuromodulation* 2009; 12:296-301
28. Stinson LW, Roderer GT, Cross NE, et al. Peripheral Subcutaneous electrostimulation for Control of Intractable Post-operative Inguinal Pain: A Case Report Series. *Neuromodulation* 2001;4:99-104.
29. Stuart RM, Winfree CJ. Neurostimulation techniques for painful peripheral nerve disorders. *Neurosurg Clin N Am* 2009; 20:111–120.
30. Schu S, Gulve A, Eldabe S, et al. Spinal cord stimulation of the dorsal root ganglion for groin pain – a retrospective review. *Pain Pract* 2014 April 1 [Epub ahead of print]
31. Lange JF, Kaufmann R, Wijsmuller A.R. et al. An international consensus algorithm for management of chronic postoperative inguinal pain. *Hernia* 2015; 19:33-43.
32. Van den Berg JC, de Valois J, Rosenbusch G. Detection of groin hernia with physical examination, ultrasound and MRI compared with laparoscopic findings. *Invest Radiol* 1999; 34:739-743.
33. Van den Berg JC, Go PM, de Valois J, et al. Preoperative and postoperative assessment of laparoscopic inguinal hernia repair by dynamic MRI. *Invest Radiol* 2000: 35: 695-698.
34. Leander P, Ekberg O, Sjoberg S, et al. MR imaging following herniography in patients with unclear groin pain. *Eur Radiol* 2000; 10:1691-1696.
35. Amid PK. Radiologic images of meshoma: a new phenomenon causing chronic pain after prosthetic repair of abdominal wall hernias. *Arch Surg* 2004; 139:1297-1298.
36. Barile A, Erriquez D, Cacchio A, et al. Groin pain in athletes: role of magnetic resonance. *Radiol Med* 2000; 100: 216-222
37. Van der Pool AEM, Harlaar JJ, den Hoed PT, et al. Long-term follow-up evaluation of chronic pain after endoscopic total extraperitoneal repair of primary and recurrent inguinal hernia. 2010; *Surg Endosc* 24: 1707-1711
38. Aasvang E, Bay-Nielsen M, Kehlet H. Pain and functional impairment 6 years after inguinal herniorrhaphy. *Hernia* 2006; 10:316-32
39. Singh AN, Bansal VK, Misra MC, et al. Testicular functions, chronic pain, and quality of life after laparoscopic and open mesh repair of inguinal hernia: a prospective randomized controlled trial. *Surg Endosc* 2012; 26:1304-1317
40. Chowbey PK, Garg N, Sharma A, et al. Prospective randomized clinical trial comparing lightweight mesh and heavyweight polylropylene mesh in endoscopic totally extraperitoneal groin hernia repair. *Surg Endosc* 2010 24:3073-3079
41. Ducic I, Dellon AL. Testicular pain after inguinal hernia repair: An approach to resection of the genital branch of genitofemoral nerve. *J Am Coll Surg* 2004; 198:181-184
42. Amid PK, Hiatt JR. New understanding of the causes and surgical treatment of postherniorrhaphy inguinodynia and orchalgia. *J Am Coll Surg* 2007; 205(2): 381-385

43. Kim FJ, Pinto P, Ming Su L, et al. Ipsilateral orchialgia after laparoscopic donor nephrectomy. *J Endourol* 2003; 17:405-409
44. Pokorny H, Klinger A, Scheyer M, et al. Postoperative pain and quality of life after laparoscopic and open inguinal hernia repair: results of a prospective randomized trial. *Hernia* 2006; 10: 331-337
45. El-Awady SE, Elkholy AAM. Beneficial effect of inguinal hernioplasty on testicular perfusion and sexual function. *Hernia* 2009: 13:251-258
46. Zieren J, Beyersdorff D, Beier KM, et al. Sexual function and testicular perfusion after inguinal hernia repair with mesh. *Am J Surg* 2001; 181:204-206
47. Aasvang EK, Gmaehle E, Hansen JB, et al. Predictive risk factors for persistent postherniotomy pain. *Anesthesiology* 2010; 112:957-969
48. Klosterhafen B, Klinge U, Schumpelick V. Functional and morphological evaluation of different polypropylene-mesh modifictions for abdominal wall repair. *Biomaterials* 1998; 19:2235-2246
49. Greca FH, de Paula JB, Biondo-Simous ML et al. The influence of different pore sizes on the biocompatibility of two polypropylene meshes in the repair of abdominal defects. Experimental study in dogs. *Hernia* 2001; 5:59-64
50. Sajid MS, Leaver C, Biag MK, et al. Systematic review and meta-analysis of the use of lightweight *versus* heavyweight mesh in open inguinal hernia repair. *Br J Surg* 2012; 99:29-37
51. Miserez M, Peeters E, Aufenacker T, et al. Update with level 1 studies of the European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* 2014; 18:151-163
52. Currie A, Andrew H, Tonsi A, et al. Lightweight versus heavyweight mesh in laparoscopic inguinal hernia repair: a meta-analysis. *Surg Endosc* 2012; 26:2126-2133
53. Bittner R, Schmedt CG, Leibl BJ, et al. Early Postoperative and One Year Results of a Randomized Controlled Trial Comparing the Impact of Extralight Titanized Polypropylene Mesh and Traditional Heavyweight Polypropylene Mesh on Pain and Seroma Production in Laparoscopic Hernia Repair (TAPP). *W J Surg* 2011; 35:1791–1797
54. Pereira-lucena CG, Artigiano Neto R, de Rezende DT, et al. Early and late postoperative inflammatory and collagen deposition responses in three different meshes: an experimental study in rats. *Hernia* 2014; 18:563-570
55. Bay-Nielsen M, Kehlet H. Inguinal herniorrhaphy in women. *Hernia* 2006; 10:30-33
56. Kark AE, Kurzer M. Groin hernias in women. *Hernia* 2008; 12:267-270

10

Nederlandse samenvatting, discussie en toekomstperspectieven

NEDERLANDSE SAMENVATTING, CONCLUSIES EN TOEKOMSTPERSPECTIEVEN

Een liesbreuk is een frequent voorkomende aandoening en het operatieve herstel ervan is een van de meest uitgevoerde operaties ter wereld. Er bestaan verschillende technieken om een liesbreuk te herstellen. Elke techniek kan leiden tot complicaties of andere nadelige gevolgen en de optimale techniek is geen uitgemaakte zaak. Tot eind jaren zestig van de vorige eeuw was het herstellen van een liesbreuk gericht op het sluiten van het buikwanddefect met hechtingen. Deze hechttechnieken, waarbij het weefsel onder spanning werd gesloten, resulteerden in hoge percentages recidieven en chronische pijn.

In 1960 werd de kunststofmat (meshprothese) ingevoerd met als doel de zwakke achterwand van het lieskanaal te versterken in plaats van alleen te hechten en de weefselschade te beperken. Met deze spanningsloze plastiek volgens Lichtenstein daalde het recidiefpercentage van 30% naar 2-4% en werd het gebruik van een mat voor het herstellen van een liesbreuk de gouden standaard. Tot die tijd was er weinig aandacht voor andere gevolgen van liesbreuk operaties, maar door het stabiele lage percentage recidieven werden andere postoperatieve complicaties, met name pijn, belangrijker. Sindsdien wordt verdere verbetering van de kwaliteit van liesbreukchirurgie met name gezocht in het voorkomen van chronische liespijn (CPIP: chronic postoperative inguinal pain). Daarnaast wordt geprobeerd om het zogenaamde “matgevoel” in de lies te beperken en de impact, die pijn en matgevoel hebben op de kwaliteit van het dagelijks leven, tijdens het herstel na een liesbreukoperatie te reduceren.

De gerapporteerde incidentie van CPIP na een liesbreukcorrectie varieert tussen 2 en 43%. De grote spreiding van deze incidentiecijfers wordt niet alleen veroorzaakt door een reële spreiding van de pijnklachten, maar ook door het gebrek aan een uniforme definitie van CPIP en het ontbreken van goede gevalideerde vragenlijsten. Er zijn diverse pogingen gedaan om dit laatste op te lossen, maar het gebrek aan consistentie blijft vooralsnog bestaan. Dat maakt het lastig om de resultaten van verschillende studies te vergelijken en exacte incidentiecijfers te bepalen. De meest gebruikte definitie van CPIP (pijn in de lies, die langer dan drie maanden na de ingreep aanhoudt) wordt in dit proefschrift gehanteerd. De mate van CPIP wordt uitgedrukt door middel van een VAS (visuele pijnscore) of een NRS (numerieke pijnscore). Uit studies blijkt dat de laatste nauwkeuriger is. Er kan onderscheid gemaakt worden in geen (NRS=0), milde (NRS=1-3), matige (NRS=4-7) en ernstige (NRS=8-10) pijn.

De kennis omtrent de oorzaken van CPIP is de laatste jaren toegenomen. Naast een recidief liesbreuk, wordt zenuwletsel (neuropathische pijn) en een door de mat en de operatie geïnduceerde ontstekingsreactie (nociceptieve pijn) als belangrijkste verklaringen gevonden. Door meer aandacht voor het intra-operatief identificeren en zo mogelijk sparen van de drie inguinale zenuwen is de kans op neuropathische pijn na een Lichtensteincorrectie verminderd. Bij een Lichtensteinplastiek wordt de kunststof mat via een directe (anterieure) benadering van voren aan de achterwand van het lieskanaal gehecht. Op die plaats verlopen ook de inguinale zenuwen. Door het positioneren van de mat via een benadering aan de achterzijde van de buikwand: in de preperitoneale ruimte, is de kans op zenuwschade lager. Deze techniek wordt sinds het einde van de vorige eeuw steeds vaker toegepast.

De endoscopische preperitoneale TEP (Totale Extra Peritoneale) techniek is de meest gebruikte preperitoneale techniek van de laatste 10 jaar. Na een TEP blijkt de kans op CPIP lager en de hersteltijd tot normale dagelijkse activiteiten, werk en sport in vergelijking met open anterieure technieken korter te zijn. Een ander voordeel van de TEP techniek is het verkrijgen van een totaal overzicht van de anatomie van het liesgebied, waarbij alle subtypes liesbreuken duidelijk herkend en adequaat behandeld kunnen worden. Indien de chirurg voldoende ervaring heeft, is de kans op recidieven en complicaties laag, vandaar dat veel chirurgen op dit moment een voorkeur hebben voor de TEP als behandeling van een liesbreuk.

Hogere kosten, algehele anesthesie en een lange leercurve worden beschouwd als belangrijkste nadelen van een TEP. Hoge kosten zouden veroorzaakt worden door het benodigd endoscopisch materiaal en het gebruik van algehele narcose. In diverse studies, waarbij de opbrengsten van de korte herstelperiode ook zijn meegenomen, blijken de kosten na TEP gelijk of zelf lager vergeleken met die van de open anterieure technieken. Algehele narcose kan bij ernstig pulmonaal gecompromitteerde patiënten gecontra-indiceerd zijn, maar de vermeende nadelen met betrekking tot de cognitie bij de oudere patiënt zijn discutabel. Om algehele narcose toch te vermijden en de voordelen van het preperitoneaal positioneren van de mat te behouden, worden momenteel nieuwe technieken zoals de TIPP (Trans Inguinale PrePeritoneale techniek) en de TREPP (TransREctus PrePeritoneale techniek) onderzocht. De resultaten zijn echter nog te prematuur om conclusies te kunnen trekken. De lengte van de leercurve van de TEP wordt gedefinieerd als de periode, die een chirurg nodig heeft (meestal uitgedrukt in het aantal ingrepen) om optimale uitkomsten en acceptabele operatietijden te bereiken voor een bepaalde procedure. Zoals beschreven in de Europese richtlijnen is de kans op ernstige complicaties en recidieven het grootst tijdens de eerste de 30 tot 50 TEP procedures en wordt aanbevolen de eerste 50 ingrepen onder supervisie van een gespecialiseerd TEP-chirurg (proctoring). te verrichten Na deze

introductie kan de chirurg, die met het uitvoeren van de TEP-techniek begint, de kans op perioperatieve complicaties en conversies verder beperken door vooral relatief jonge (<60 jaar) en slanke patiënten met een unilaterale liesbreuk zonder eerdere abdominale chirurgie te opereren. Zo kan de verlengde leercurve (tot 400 procedures) veilig, efficiënt en zonder frustratie doorlopen worden.

De endoscopische preperitoneale liesbreukcorrectie is conceptueel een excellente operatietechniek. In de praktijk blijven echter nog enkele problemen onopgelost. Het percentage patiënten met CPIP na een TEP is lager dan na een open voorste benadering, maar ook niet volledig tot nul gereduceerd. CPIP kan invaliderend zijn en behandeling is vaak nodig. Ondanks talrijke publicaties over de behandeling van CPIP na alle types liesbreukchirurgie, is er tot op heden geen goede strategie om deze pijn te evalueren en vervolgens te behandelen. Het vinden van de juiste oorzaak is van belang om CPIP adequaat te kunnen behandelen. Na het uitsluiten van een recidief liesbreuk, of andere oorzaken van liespijn die mogelijk niet in de lies gelokaliseerd zijn, moet een onderscheid gemaakt worden tussen neuropathische en nociceptieve pijn. Het differentiëren tussen deze twee is lastig. De klassieke presentatie van neuropathische pijn uit zich in verschillende typen sensorische veranderingen in het operatiegebied: hypo- en hyperesthesie, allodynie en paresthesie. Bij nociceptieve pijn zijn de symptomen veel vager, het pijngebied diffuser en zijn deze klassieke sensorische afwijkingen afwezig.

Bij ongeveer 50% van alle liesbreukpatiënten met CPIP is er sprake van neuropathische pijn. Er bestaan verschillende opties om deze pijn te behandelen, maar het slagingspercentage varieert en er bestaat geen consensus over de meest effectieve behandeling. In de meerderheid van de patiënten is medicamenteuze behandeling niet voldoende. De resultaten van chirurgische neurectomie lijken goed, maar lange termijn-gegevens zijn nauwelijks beschikbaar. Een belangrijk nadeel hiervan is de blijvende gevoelloosheid van de liesregio. Dit nadeel is na eenvoudige zenuwinfiltraties met anesthetica niet aanwezig. Tot op heden zijn resultaten met betrekking tot het succes van deze minimaal invasieve injectietherapie beperkt. In sommige studies zijn succespercentages tot 90% beschreven. Het belangrijkste voordeel van injecties is de eenvoud van de therapie en lijkt het verstandig om deze behandeling als eerste keuze toe te passen. De resultaten van perifere zenuwstimulatie (PNS) zijn veelbelovend, maar nog onvoldoende onderzocht.

Zoals eerder beschreven start de behandeling van CPIP met het stellen van de juiste diagnose. Omdat dit in de praktijk zeer lastig blijkt, zou een multidisciplinaire aanpak door een liesbreukchirurg, een pijnspecialist en een toegewijde radioloog kunnen bijdragen.

In **Hoofdstuk 2** wordt een algoritme beschreven, ontwikkeld door liesbreukchirurgen en pijnspecialisten van een liesbreukcentrum en werden de resultaten hiervan geanalyseerd. Het doel van het algoritme is het selecteren van patiënten met neuropathische pijn, gevolgd door de behandeling van deze groep met behulp van een geprotocolleerd schema. Na analyse bleek dat bij meer een derde van de patiënten met CPIP, de diagnose neuropathische pijn kon worden gesteld. Deze patiënten rapporteerden na hun behandeling een substantiële vermindering van de pijn met een cumulatief succespercentage van 83%. Van de patiënten met neuropathische pijn was bij 62% pijnreductie succesvol na perifere zenuwblokkade. Zes van de zeven patiënten bij wie de klachten na zenuwblokkade persisteerden, werden na het plaatsen van een perifere zenuwstimulator (PNS) pijnvrij. Ondanks deze gunstige resultaten, zijn er ook nadelen beschreven van de PNS zoals erosie en/of migratie van de lead. Enige reserve ten aanzien van het standaard aanbieden van deze behandeling is dus gepast. Nieuwe technieken van neuromodulatie via de dorsale wortels (DRS) hebben deze nadelen mogelijk in mindere mate. Het beschreven algoritme en het toepassen van dorsale wortel ganglion-stimulatie zal in andere (gerandomiseerde) studies geanalyseerd moeten worden.

De incidentie van klinisch relevante CPIP is lager na endoscopische preperitoneale benadering ten opzichte van een anterieure Lichtensteinplastiek techniek. De lagere kans op neuropathische pijn na een (endoscopische) preperitoneale ingreep lijkt vooral gerelateerd te zijn aan de kleinere kans op beschadiging van de betrokken inguinale zenuwen tijdens deze operatie. De oorzaak van CPIP na TEP lijkt vooral terug te voeren op ontstekingsgerelateerde nociceptieve pijn. Ons algoritme (**Hoofdstuk 2**) bevatte slechts een klein aantal patiënten met neuropathische pijn na een TEP (circumstantial evidence). Er zijn nauwelijks gegevens bekend over het systematisch beoordelen van CPIP specifiek na TEP en het is onduidelijk of de gebruikelijke diagnostische methodes voor het onderzoeken van CPIP dan ook geschikt zijn voor patiënten na een TEP operatie. In de gebruikelijke diagnostische work-up van CPIP is het mogelijk na anamnese en lichamelijk onderzoek een recidief liesbreuk, de aanwezigheid van neuropathische pijn of andere aandoeningen, zoals tendinitis, bursitis of arthrose van de heup te identificeren of uit te sluiten. Een echografie kan worden gebruikt om een gestelde klinische diagnose te bevestigen of andere postoperatieve gevolgen van de operatie waaronder seroom, hematoom of meshoom te detecteren. Het blijft echter lastig om mogelijke “nociceptieve” weefselveranderingen na TEP te onderscheiden of om de mate van fibrose als gevolg van de ontstekingsreactie aan te tonen. Een MRI scan is nuttig voor het identificeren van afwijkingen aan de weke delen en om een klinisch onduidelijke primaire liesbreuk te diagnosticeren. Het gebruik van MRI om eventuele oorzaken van CPIP na TEP te evalueren is zelden geëvalueerd.

In **Hoofdstuk 3** werden de uitkomsten van MRI-scans van 53 patiënten met relevante CPIP (NRS 4-10) na TEP geëvalueerd. De beelden werden beoordeeld door twee geblindeerde radiologen door middel van een checklist van mogelijke afwijkingen in de lies, die de pijn kunnen verklaren, terwijl hierbij ook naar identificatie en positionering van de mat gevraagd werd. Op deze manier werden 106 liezen van 53 patiënten geanalyseerd: 55 geopereerde liezen met CPIP, 12 geopereerde liezen zonder CPIP en 39 niet-geopereerde liezen. Van de mogelijke oorzaken van CPIP na TEP, bleek geen enkele oorzaak significant vaker voor te komen bij de groep geopereerde liezen met CPIP. Hoewel ernstige fibrose vaker bij CPIP-liezen gerapporteerd werd, was dit niet significant. Daarnaast werd fibrose ook bij de geopereerde liezen zonder CPIP geobserveerd. Het aantonen van fibrose toonde een redelijk goede interobserver overeenkomst. De MRI bleek betrouwbaar om een recidief of bulging aan te tonen(κ=0.74), maar het onderscheid tussen een echt recidief of bulging was niet goed mogelijk. Bij 40% van de patiënten met CPIP na TEP bleek er sprake van een goede ligging van de mat en werden er behalve milde tot matige fibrose geen andere afwijkingen op de MRI zichtbaar. Het observeren van een adequate vlakke ligging van de mat toonde een zeer goede interobserver betrouwbaarheid (κ=0.88). Deze patiënten konden worden gerustgesteld en accepteerden een expectatief beleid, waarbij de pijn in de loop van de tijd meestal geheel verdween. Bij 15% van de patiënten werden niet-operatie gerelateerde oorzaken voor CPIP gevonden.

Spontane pijnreductie na TEP is eerder beschreven en wordt verklaard door de hypothese dat de pijn voornamelijk door ontstekings-gemedieerde nociceptieve pijn veroorzaakt wordt. Over het algemeen wordt aangenomen dat deze ontstekingsreactie binnen drie tot zes maanden na de operatie spontaan verdwijnt. Gedetailleerd onderzoek naar het precieze verloop van pijn in de lies na endoscopische liesbreukcorrectie is beperkt. Er is slechts één studie beschreven, waarbij de incidentie en het beloop van pijn gedurende het eerste jaar na TEP in detail beschreven zijn.

In **Hoofdstuk 4** werden van 473 patiënten de incidentie en het beloop van pijn gedurende het eerste jaar na TEP tot in detail beschreven. Pijnscores werden tot een jaar na de operatie op verschillende tijdstippen gemeten en bevestigden dat pijn na TEP zelflimiterend is. Ondanks een relatief hoog percentage patiënten met pijn (NRS 1-10) in de eerste zes weken (26%) tot drie maanden (19%) na TEP, blijkt dat slechts 3% van de patiënten na zes weken en 0.6% na zes maanden relevante pijn (NRS> 3) aangeeft. Na een jaar rapporteerde minder dan 1% van de patiënten matige CPIP (NRS 4-7) en geen enkele patiënt ernstige CPIP. Relevante postoperatieve pijn kwam vaker voor bij patiënten met preoperatief ernstige liespijn. Ook hadden patiënten met ernstige pijn preoperatief een ander beloop van pijn in het eerste jaar na TEP. Dergelijke informatie is van belang om patiënten beter te informeren

over hun prognose en om eventuele verwachtingen ten aanzien van postoperatief herstel bij te stellen. Bovendien is deze informatie van belang voor het ontwikkelen van het juiste protocol voor het beoordelen en behandelen van CPIP na TEP. Zoals eerder beschreven in de analyse van CPIP na liesbreukchirurgie is een periode van afwachtend beleid tot in ieder geval drie maanden postoperatief aangewezen. Vanwege het zelflimiterende karakter van CPIP na TEP, de relatieve mildheid van pijn en de lage kans op een recidief, zou deze periode van afwachtend beleid na een TEP ook tot één jaar verlengd kunnen worden. Opvallend was dat chronische pijn na TEP relatief vaak in het scrotum gelokaliseerd was, terwijl preoperatieve pijn in de lies werd aangegeven. Genitale of scrotale pijn kan door schade aan het genitale tak van de nervus genitofemoralis veroorzaakt worden. Het mechanisme, dat verantwoordelijk is voor post-TEP orchialgie is complexer, en wordt verondersteld veroorzaakt te worden door neuropraxie van zenuwvezels afkomstig van de plexus hypogastricus rond het vas deferens. Deze orchialgie verdwijnt na verloop van tijd spontaan bij 96% van de patiënten in onze studie.

Orchialgie en andere uitingen van CPIP hebben impact op het dagelijks functioneren en de kwaliteit van leven, waarbij seksueel functioneren een relatief onbesproken onderwerp is. Slechts enkele studies beschrijven de impact van pijn op het seksueel functioneren. Deze studies behandelen met name erectiestoornissen of ejaculatieproblemen na open anterieure liesbreukchirurgie. Prevalentiecijfers betreffende de impact van pijn op seksuele functie ten gevolge van een liesbreuk en het effect van een TEP-operatie zijn niet bekend.

Het doel van de studie beschreven in **Hoofdstuk 5** is het kwantificeren van pijn tijdens seksuele activiteit en de impact daarvan op het seksueel functioneren voor en na TEP met een follow-up van twee jaar. Preoperatief ervaart 32% van de patiënten pijn tijdens seksuele activiteit, postoperatief daalt dit naar 9%. Ruim twee jaar na een TEP bedroeg de prevalentie van matig tot ernstig pijn (NRS 4-10) nog 3.4% ten opzichte van 21% preoperatief. Bij slechts 2,3% van de patiënten zonder pijn preoperatief ontstond seksueel-gerelateerde pijn na de operatie. Een negatief effect op het seksleven vanwege liesbreuk-gerelateerde pijn daalde van 6% preoperatief naar 1% na TEP.

Fibrose ontstaat als gevolg van een ontstekingsreactie ofwel vreemdlichaamreactie, die optreedt na inbrengen van een kunststofmat. Fibrose is nuttig om de zwakke achterwand van het lieskanaal te verstevigen en de mat te integreren. Overmatige fibrose zou echter de kans op CPIP kunnen verhogen. De ernst van de ontstekingsreactie blijkt onder andere afhankelijk van het type mat. Daarom zijn er gedurende de laatste jaren matten met minder materiaal en grotere poriën ontwikkeld. In dierexperimentele studies werd de hypothese bevestigd dat na implantatie van een dunnere en lichtere mat, de ontstekingsreactie

minder heftig is. Inmiddels zijn er ook aanwijzingen dat het gebruik van een lichtgewicht mat voor het herstellen van een liesbreuk met een Lichtensteinplastiek, de kans op CPIP en matgevoel vermindert. Dat het gebruik van een lichtgewicht mat ook voordeel heeft bij een endoscopische liesbreukcorrectie is niet aangetoond. De kwaliteit van de meeste studies is beperkt door kleine patiëntaantallen en een korte follow-up. Desondanks bepleiten veel chirurgen het gebruik van een lichtgewicht mat bij alle technieken.

In **Hoofdstukken 6 en 7** worden de resultaten beschreven van een dubbelblind gerandomiseerde studie naar de resultaten van verschillende typen matten bij de laparoscopische liesbreukcorrectie. In deze studie werden 950 patiënten met een primaire unilaterale liesbreuk, die in aanmerking kwamen voor een TEP, tussen een lichtgewicht Ultrapro® of een zwaargewicht Prolene® mat gerandomiseerd. Er werd gebruik gemaakt van gevalideerde vragenlijsten om pijn, matgevoel en de impact van pijn en matgevoel op de kwaliteit van het dagelijks leven te evalueren.

In **Hoofdstuk 6** werden de resultaten na drie maanden geanalyseerd. De follow-up bedroeg 97% in beide groepen. Gedurende de gehele postoperatieve periode waren er geen significante verschillen in pijn, matgevoel of enig ander eindpunt. Het aantal recidieven na drie maanden bedroeg vier: twee in elke groep.

Hoofdstuk 7 beschrijft de analyse van de studie-populatie tot twee jaar na de operatie. De incidentie van klinische relevante pijn (NRS 4-10) na een en twee jaar was hoger in de Ultrapro® groep vergeleken met de Prolene® groep. Deze opmerkelijke resultaten zijn niet eerder beschreven. De verschillen waren significant, ook na multivariate analyse. Daarnaast waren er significant meer recidieven bij het gebruik van een Ultrapro® mat (2,7%) in vergelijking tot een Prolene® mat (0,8%) (p=0.03). Omdat de totale incidentie van relevante CPIP erg laag was (0.7% in de Prolene® groep en 2.5% in de Ultrapro® groep) is het niet mogelijk te concluderen dat een Prolene mat duidelijk superieur is in vergelijking met een Ultrapro mat. Echter, de hypothese dat een Ultrapro mat voordelen heeft ten aanzien van CPIP, kan verworpen worden. Daarnaast laten deze data zien dat een Ultrapro® mat de kans op een recidief vergroot.

De resultaten uit Hoofdstuk 7 zijn in lijn met gegevens uit de literatuur: na een TEP in ervaren handen is de kans op een liesbreukrecidief kleiner dan 1%. Ook de kans op CPIP na een TEP is minder dan 1%. Een ander voordeel van de endoscopische preperitoneale techniek is de mogelijkheid om alle potentiële buikwanddefecten goed te overzien en een eventueel klinische gemiste breuk te identificeren en behandelen. Met name de femoraalbreuk wordt bij lichamelijk onderzoek en tijdens een open anterieure liesbreukoperatie vaak gemist

en laat zich ook slecht via een Lichtensteinplastiek benaderen. Van alle liesbreuken bij mannen is maximaal 5% een femoraalbreuk, maar bij vrouwen is dit 25% en loopt op tot 40% bij vrouwen met een recidief liesbreuk. Met name bij vrouwen zou de preperitoneale benadering de kans op een recidief aanzienlijk kunnen verminderen.

In **Hoofdstuk 8** hebben we de frequentie van verschillende subtypen liesbreuken bij vrouwen onderzocht. Deze studie bevestigt de hoge incidentie van femoraalbreuken bij vrouwen en laat zien dat het stellen van een juiste diagnose preoperatief lastig kan zijn. Dit leidt tot een sterke aanbeveling om vrouwen met een liesbreuk via een endoscopische preperitoneale benadering te behandelen.

CONCLUSIES:

Uit de studies van dit proefschrift kunnen de volgende conclusies getrokken worden:

- De diagnostiek en behandeling van CPIP zijn lastig. Door een multidisciplinaire en gestandaardiseerde benadering van de klachten kunnen patiënten met neuropathische pijn worden geselecteerd, waarbij een geprotocolleerd behandelplan inclusief zenuwinfiltratie en perifere zenuwstimulatie succesvol is bij 85%. (Hoofdstuk 2)
- Een MRI is bij patiënten met CPIP nuttig om de juiste positie en vlakke ligging van de mat na een TEP operatie te bevestigen en om mogelijke niet-operatie-gerelateerde oorzaken van liesklachten uit te sluiten. (Hoofdstuk 3)
- CPIP na TEP verdwijnt meestal spontaan; minder dan 1% van alle patiënten rapporteert klinisch relevante CPIP één jaar na TEP. Patiënten die preoperatief matige tot ernstige pijn (NRS 4-10) in de lies aangeven, hebben een hoger risico op CPIP. (Hoofdstuk 4)
- Pijn ten gevolge van een liesbreuk kan leiden tot een beperking van seksueel functioneren. Bij het merendeel van de patiënten heeft een TEP operatie een gunstig effect. (Hoofdstuk 5)
- Het hypothetische voordeel van een lichtgewicht Ultrapro® mat vergeleken met een zwaargewicht Prolene® mat ten aanzien van pijn en matgevoel in de eerste drie maanden na een TEP kan niet worden aangetoond. (Hoofdstuk 6)
- Het risico op een recidief en op CPIP één en twee jaar na een TEP is groter na het plaatsen van een lichtgewicht Ultrapro® mat. (Hoofdstuk 7)
- De voorkeursbehandeling voor vrouwen met een liesbreuk is een endoscopische techniek om een foutieve preoperatieve diagnose te voorkomen en het aantal recidieven te beperken. (Hoofdstuk 8)

TOEKOMSTPERSPECTIEVEN:

Chirurgie op maat: verbetering van patiëntselectie.

In Westerse landen is de liesbreukoperatie uitgegroeid tot een specialisatie van de "algemeen chirurg". Dedicated hernia surgeons require a wide acquaintance of possible groin pathology and different treatment options for the individual patient. Een toegewijd liesbreukchirurg moet een brede kennis hebben van alle mogelijke pathologie in de lies en op de hoogte zijn van de diverse behandelopties voor de individuele patiënt. Tailored treatment is necessary for women.

Vrouwen met een liesbreuk: chirurgie op maat is noodzakelijk bij vrouwen met een liesbreuk. De incidentie van een liesbreuk bij vrouwen is relatief laag en het blijkt lastig om peroperatief de juiste diagnose te stellen. Een endoscopische benadering voorkomt een onjuiste diagnose en verlaagt daarmee de kans op een recidief. Derhalve lijkt het gepast om vrouwen met een liesbreuk voornamelijk door chirurgen met ruime expertise in de een endoscopische operatietechniek te behandelen.

Oudere patiënten: een andere groep die zou kunnen profiteren van een meer geïndividualiseerde behandeling is de oudere patiënt met een primaire liesbreuk. Het is van belang om bij een bejaarde patiënt af te wegen of hij/zij voordeel zal hebben van het herstellen van zijn/haar liesbreuk. De chirurg moet de mogelijke risico's van een operatie afwegen tegen de voordelen: het verminderen van de klachten en daardoor verbeteren van de kwaliteit van leven. De endoscopische benadering voor het herstellen van een liesbreuk bij de oudere patiënt is een optie, maar is tot op heden niet geëvalueerd. Een aanhoudend discussiepunt daarbij is de mogelijk nadelige (cognitieve) effecten van algehele narcose bij de oudere patiënt. Daarnaast zal in onze vergrijzende wereld het aantal patiënten met prostaatkanker toenemen en daarmee ook het aantal patiënten dat een prostatectomie zal ondergaan. Het is tot op heden niet duidelijk of de incidentie van per- en postoperatieve complicaties van deze ingreep hoger is na een eerdere TEP-operatie. Tenslotte is de anterieure benadering onder plaatselijke verdoving een goede tweede optie, die overwogen kan worden, als een operatie te riskant verondersteld wordt. Geriatrische evaluatie wordt steeds meer gebruikt bij de besluitvorming van de behandeling bij oudere oncologische patiënten. Het is denkbaar dat in de nabije toekomst ook vaker een geriater betrokken wordt bij de behandelkeuze van oudere patiënten met een liesbreuk.

De sportieve jongere: de behandeling van een zogenaamde sportersliesbreuk (sportsman hernia of inguinal disruption) was niet het onderwerp van dit proefschrift. Er is echter sprake van een steeds groter wordende groep sporters met liesklachten en de behandeling

daarvan krijgt steeds meer aandacht in de literatuur. Er bestaan verschillende publicaties met goede resultaten na uiteenlopende behandelingen en operatietechnieken. Hypothetisch kan er sprake zijn van een verzwakte achterwand van het lieskanaal, welke versterkt kan worden met een kunststofmat via een endoscopische benadering. Deze afwijking is echter nooit aangetoond. Het blijft onduidelijk in welke mate een actieve sporter met liesklachten van een dergelijke ingreep baat heeft en hoe we patiënten, die in aanmerking komen voor een chirurgische behandeling, het beste kunnen selecteren.

Technische verbeteringen van liesbreukchirurgie

Als de indicatie voor een chirurgisch herstel van een liesbreuk gesteld is, is het van belang eventuele complicaties tot een minimum te beperken. Momenteel is CPIP de belangrijkste complicatie na liesbreukchirurgie. Gedurende de laatste decennia is de kennis van de pathofysiologie van CPIP gegroeid, maar het precieze mechanisme is nog steeds niet volledig duidelijk. De literatuur suggereert dat naast preperitoneale technieken, hoog volume een belangrijke factor is om CPIP te minimaliseren. Daarom kunnen de uitkomsten van liesbreukchirurgie verbeteren door concentratie van zorg.

Het type mat, dat bij een TEP gebruikt wordt, heeft een verwaarloosbare invloed op CPIP. De hypothese, dat een lichtgewicht mat beter is, moet verworpen worden. In dit proefschrift bleek dat het risico op CPIP of een recidief liesbreuk na een TEP met een lichtgewicht Ultrapro® mat zelfs hoger is. Daarom adviseren wij het gebruik van een (goedkopere) Prolene® mat. Het feit, dat een klein aantal patiënten na een TEP met een Prolene® mat een recidief ontwikkelt, ook al wordt de ingreep door een ervaren liesbreukchirurg in een hoog volume centrum uitgevoerd, moet verder worden onderzocht. Analyse van de zeldzame recidieven kan mogelijk leiden tot technische aanbevelingen.

Expertise centra voor liesbreukchirurgie worden geconfronteerd met een toenemend aantal second opinions van patiënten met onverklaarbare pijn in de lies. Toegewijde teams waaronder een herniachirurg, een ervaren radioloog, een pijnspecialist en eventueel een orthopedisch chirurg, neuroloog en uroloog zijn dan wenselijk. Een multidisciplinaire benadering voor deze patiënten met lastig te duiden pathologie, die meestal na eerdere en herhaalde operaties resteert, is belangrijk. Het is een grote uitdaging om voor deze patiënten een goede behandelstrategie te vinden. Het hoge aantal van dergelijke patiënten vraagt om de ontwikkeling van een diagnostisch en therapeutisch algoritme

Kwaliteit van de liesbreukchirurgie: een pleidooi voor clinical audit

Nieuwe technieken worden onderzocht om de kwaliteit van liesbreukchirurgie verder te verbeteren. Momenteel worden preperitoneale technieken zoals TREPP en TIPP geëva-

lueerd. Deze technieken zijn mogelijk goedkoper en hebben een kortere leercurve vergeleken met de gangbare preperitoneale endoscopische technieken. Implementatie van deze technieken is pas gerechtvaardigd bij voldoende evidence van gunstige resultaten. Uniformiteit in de definitie en de beoordeling van de resultaten is vereist. In de huidige literatuur is de incidentie van CPIP na TEP in ervaren handen zeer laag, maar het vergelijken van de resultaten uit de diverse studies is door gebrek aan een eenduidigheid lastig. Het is van belang om één definitie van CPIP te gebruiken en een eenvoudige manier te kiezen om CPIP en andere gevolgen na liesbreukchirurgie te evalueren. Tot op heden zijn er meerdere gevalideerde vragenlijsten beschikbaar, die teveel vragen bevatten. In de praktijk blijken deze uitgebreide vragenlijsten tijdrovend, waarbij in feite slechts enkele vragen nuttig zijn. Een belangrijke uitkomstmaat van de kwaliteit van liesbreukchirurgie is de terugkeer naar werk en de duur van de beperking van dagelijkse activiteiten, seks en sport. Ook dergelijke uitkomstmaten moeten uniform worden beoordeeld, zowel nationaal als internationaal.

Gerandomiseerde studies leveren nog altijd het hoogste level of evidence, maar kennen ook beperkingen. Overtuigend bewijs vanuit RCT's wordt belemmerd, als de tijd tussen interventie (chirurgie) en het optreden van een eventuele complicatie lang is, maar ook als geringe modificaties van technieken of materialen worden bestudeerd. Een prospectieve registratie in de vorm van een klinische audit kan uitkomst bieden. Nationale registratie in Scandinavische landen, heeft inmiddels voldoende aangetoond dat de resultaten van liesbreukchirurgie door registratie zijn verbeterd. Vanuit de Europese Hernia Society is men bezig met het ontwikkelen van een internationaal platform voor het registreren en meten van uitkomsten van liesbreukchirurgie welke hopelijk op korte termijn in werking treedt. Tot die tijd is het van belang dat liesbreukchirurgen hun eigen resultaten registreren en als audit gebruiken om persoonlijke prestaties te verbeteren.

Het opleiden en certificeren van liesbreukchirurgen

Concentratie van hoog-complexe zorg is in Nederland een feit. Concentratie van laag-complexe zorg daarentegen leidt tot discussie. Liesbreukchirurgie wordt tot op heden door chirurgen met diverse subspecialisaties uitgevoerd. Toch blijkt dat ook voor liesbreukchirurgie de zorg verbetert als alleen chirurgen met ruime expertise dit type operaties doen.

Specialisatie binnen de chirurgie is een gegeven en de huidige chirurg differentieert tot een gecertificeerd vaatchirurg, oncologisch chirurg, GE (gastro-intestinaal) chirurg of traumachirurg. Met het verdwijnen van de "algemeen chirurg" is onduidelijk geworden wie zich toelegt op de vermeend "algemeen chirurgische" ingrepen. Buikwandchirurgie is één van de modules van GE-chirurgie. Deze indeling is vanuit opleidingsoogpunt weliswaar verdedigbaar, maar nog geen garantie dat de chirurg voldoende expertise kan opdoen.

Daarnaast wringt het dat deze chirurgie op termijn dan exclusief door GE-chirurgen zou kunnen worden uitgevoerd. Veel logischer lijkt het om buikwandchirurgie, waarbinnen liesbreukchirurgie, als deelgebied van de algemene heelkunde te erkennen en opleiding hierin in gecertificeerde hoog-volumecentra te honoreren met een deelcertificaat. In een beoogd opleidingsinstituut moet naast aandacht voor de chirurgische technieken ook aandacht zijn voor de organisatie van zorg, die een belangrijk onderdeel vormt van de kwaliteit van liesbreukchirurgie.

Appendices

PUBLICATIONS

Voorbrood CE, **Burgmans JP**, Van Dalen T, Breel J, Clevers GJ
Totally extraperitoneal endoscopic (TEP) hernia repair in elderly patients. *Hernia* 2015 [Epub ahead of print]

Haas LE, van der Ploeg RS, Quak JJ, **Burgmans JP**, Otten M. A Young Man With Severe and Disabling Complications of Septic Shock. *Am J Crit Care* 2015;24:450-2

Schiphorst AH, Ten Bokkel Huinink D, Breumelhof R, **Burgmans JP**, Pronk A, Hamaker ME. Geriatric consultation can aid in complex treatment decisions for elderly cancer patients. *Eur J Cancer Care* 2015 Jul 24[Epub ahead of print]
Voorbrood CE, **Burgmans JP,** Van Dalen T, Breel J, Clevers GJ, Wille F, Simmermacher RK. An algorithm for assessment and treatment of postherniorrhaphy pain. *Hernia* 2015;19:571-7

Burgmans JP, Schouten N, Clevers GJ, Verleisdonk EJ, Davids PH, Voorbrood CE, Simmermacher RK, Van Dalen T. Pain after totally extraperitoneal (TEP) hernia repair might fade out within a year. *Hernia* 2015;19:579-85.

Burgmans JP, Voorbrood CE, Schouten N, Smakman N, Elias S, Clevers GJ, Davids PH, Verleisdonk EJ, Hamaker ME, Simmermacher RK, van Dalen T. Three-month results of the effect of Ultrapro or Prolene mesh on post-operative pain and well-being following endoscopic totally extraperitoneal hernia repair (TULP trial). *Surg Endosc* 2015 Jan 1. [Epub ahead of print]

Voorbrood CE, **Burgmans JP**, Clevers GJ, Davids PH, Verleisdonk EJ, Schouten N, van Dalen T.
One-stop endoscopic hernia surgery: efficient and satisfactory. *Hernia* 2015;19:395-400.

Schouten N, Elshof JW, Simmermacher RK, van Dalen T, de Meer SG, Clevers GJ, Davids PH, Verleisdonk EJ, Westers P, **Burgmans JP**. Selecting patients during the “learning curve” of endoscopic Totally Extraperitoneal (TEP) hernia repair. *Hernia* 2013;17:737-43.

Schouten N, Simmermacher RK, van Dalen T, Smakman N, Clevers GJ, Davids PH, Verleisdonk EJ, **Burgmans JP**. Is there an end of the “learning curve” of endoscopic totally extraperitoneal (TEP) hernia repair? *Surg Endosc* 2013;27:789-94

Schouten N, van Dalen T, Smakman N, Elias SG, Clevers GJ, Verleisdonk EJ, Davids PH, **Burgmans IP.** The effect of ultrapro or prolene mesh on postoperative pain and well-being following endoscopic Totally Extraperitoneal (TEP) hernia repair (TULP): study protocol for a randomized controlled trial. *Trials* 2012;13:76

Schouten N, van Dalen T, Smakman N, Elias SG, van de Water C, Spermon RJ, Mulder LS, **Burgmans IP**. Male infertility after endoscopic Totally Extraperitoneal (Tep) hernia repair (Main): rationale and design of a prospective observational cohort study. *BMC Surg* 2012;21

Tekatli H, Schouten N, van Dalen T, **Burgmans I**, Smakman N. Mechanism, assessment, and incidence of male infertility after inguinal hernia surgery: a review of the preclinical and clinical literature. *Am J Surg* 2012;204:503-9

Schouten N, **Burgmans JP**, van Dalen T, Smakman N, Clevers GJ, Davids PH, Verleisdonk EJ, Elias SG, Simmermacher RK. Female 'groin' hernia: totally extraperitoneal (TEP) endoscopic repair seems the most appropriate treatment modality. *Hernia* 2012;16:387-92

Schouten N, van Dalen T, Smakman N, Clevers GJ, Davids PH, Verleisdonk EJ, Tekatli H, **Burgmans JP.** Impairment of sexual activity before and after endoscopic totally extraperitoneal (TEP) hernia repair. *Surg Endosc* 2012;26:230-4

Schouten N, de Lange DH, Wink D, **Burgmans JP**. Een beklemde 'blaashernia': casus en overzicht van de literatuur. *Ned Tijdschr v Heelk* 2001;Okt

Elshof JW, Keus F, **Burgmans JP**, Clevers GJ, Davids PH, van Dalen T. Feasibility of right-sided total extraperitoneal procedure for inguinal hernia repair after appendectomy: a prospective cohort study. *Surg Endosc* 2009;23:1754-8

Burgmans JP, Clevers GJ, Verleisdonk EJ, Davids PH. Endoscopische liesbreukchirurgie: minder chronische pijnklachten en een snellere re-integratie in het arbeidsproces. *TBV* 2008; okt

Madsen E, Gobardhan P, Bongers V, Albregts M, **Burgmans J**, De Hooge P, Van Gorp J, van Dalen T. The impact on post-surgical treatment of sentinel lymph node biopsy of internal mammary lymph nodes in patients with breast cancer. *Ann Surg Oncol* 2007;14:1486-92.

de Kanter AY, Menke-Pluymers MM, Wouters MW, **Burgmans I**, van Geel AN, Eggermont AM.

5-Year follow-up of sentinel node negative breast cancer patients. *Eur J Surg Oncol* 2006;32:282-6

Rooijens PP, **Burgmans JP**, Yo TI, Hop WC, de Smet AA, van den Dorpel MA, Fritschy WM, de Groot HG, Burger H, Tordoir JH. Autogenous radial-cephalic or prosthetic brachial-antecubital forearm loop AVF in patients with compromised vessels? A randomized, multicenter study of the patency of primary hemodialysis access. *J Vasc Surg* 2005;42:481-6

de Bruijne EL, **Burgmans JP**, Krestin GP, Pols HA, van den Meiracker AH, de Herder WW. Adrenal incidentaloma: a clinical problem related to imaging. *Ned Tijdschr Geneeskd* 2005;149:1821-6

Rooijens PP, Tordoir JH, Stijnen T, **Burgmans JP**, Smet de AA, Yo TI. Radiocephalic wrist arteriovenous fistula for hemodialysis: meta-analysis indicates a high primary failure rate. *Eur J Vasc Endovasc Surg* 2004;28:583-9
van der Klooster JM, Peters R, **Burgmans JP**, Grootendorst AF. Chronic tophaceous gout in the elderly. *Neth J Med* 1998;53:69-75.

Burgmans JP, van Erp EJ, Brimicombe RW, Kazzaz BA. Salmonella enteritidis in an endometriotic ovarian cyst. *Eur J Obstet Gynecol Reprod Biol* 1997;72:207-11. Review.

DANKWOORD

Naast alle patiënten die deelnamen aan mijn studies wil ik graag iedereen bedanken voor hun bijdrage aan het tot stand komen van dit proefschrift. Een aantal noem ik in het bijzonder.

Prof. Dr I.H.M. Borel Rinkes, beste Inne, ik heb je leren kennen als een snelle denker, positief en enthousiast. Dat werkt motiverend. Het is een eer dat je mijn promotor wilt zijn.

Prof. Dr J.F. Lange, beste Johan, zoals beklonken op de promotieborrel van Nelleke ben ook jij mijn promotor. Dat waardeer ik enorm. Als mijn opleider en leermeester van de TEP ben jij de basis van dit proefschrift.

Dr. Th. Van Dalen, beste Thijs, copromotor en maat. De combinatie is bijzonder, maar heeft gewerkt. De energie die jij hebt voor je patiënten, maar ook voor al het werk dat je daarnaast doet, bewonder ik. Wetenschap is jouw ding. Ik heb een hoop geleerd en kan nog veel meer leren. Het boek is af en dat heb ik voor een belangrijk deel aan jou te danken.

Dr. R.K.J. Simmermacher, beste Rogier, het boekje van deze jongedame is gedrukt. Dat was zonder jouw hulp niet gelukt. Jij, als buikwandexpert leverde een belangrijke bijdrage aan het niveau van de stukken. Tussen werk, congressen, cursussen en vergaderingen maakte jij tijd vrij. Ook de vanzelfsprekendheid van de steun die je me gaf buiten dit proefschrift heb ik heel erg gewaardeerd.

Prof. dr. J.T.A. Knape, Prof. dr. T. Leiner, Prof. dr. MR Vriens, Prof. dr. R.L.A.W. Bleys, Prof. dr. M. Miserez, Dr. R. Roumen, leden van de leescommissie, hartelijk dank voor het lezen en beoordelen van mijn proefschrift.
Beste Menno, ooit, heel even, was ik je baas, vandaag beoordeel je mij. Erg leuk dat je er bij bent.
Beste Ronald, dat jij de docentenprijs hebt gewonnen, is volledig terecht. Ik heb genoten en een hoop geleerd van je fantastische uitleg over de ontwikkeling en de opbouw van het lieskanaal. Dat waren inspirerende onderwijsdagen.
Beste Marc, dank voor je bereidwilligheid om naar Utrecht te komen. Jij bent in Europa een man van de TEP en een belangrijke inspirator binnen de European Hernia Society.
Beste Rudy, ons werk kent vele raakvlakken: chirurgische oncologie, liesbreukchirurgie en de interesse in de patiënt met chronische pijn. Je wetenschappelijke output is groot en ik ben vereerd dat jij als lid van de leescommissie aanwezig bent.

Dr N Schouten, beste Nelleke, jij hebt de basis gelegd voor het wetenschappelijk onderzoek van het Liesbreukcentrum en mijn en onze ideeën uitgewerkt wat heeft geleid tot meerdere publicaties en jouw proefschrift. Het waren erg gezellige jaren en ik ben trots op de manier waarop jij dat hebt gedaan, een onderdeel bent van de nieuwe World Guidelines of Hernia Surgery en inmiddels al als 3e jaars AIOS zelf een TEP kan doen. Veel van jou werk zit ook in mijn boek en wellicht schrijven we samen nog eens een stuk! Dank.

Drs CEH Voorbrood, beste Charlotte, als opvolgster van Nelleke nam jij het werk over en jij hebt inmiddels ook drie publicaties, een vierde stuk en een protocol geschreven. Daarmee heb jij ook een grote bijdrage geleverd aan het onderzoek binnen het liesbreukcentrum en met name de aan TULP studie en daarmee aan mijn proefschrift. Veel lol op donderdagmiddag met ".....", kakhiel of bij de Polen in Gdansk. Dank Charlotte, en het is fijn dat je erbij bent.

Dr. E.J.M.M. Verleisdonk, Dr G.J. Clevers en Dr P.H.P. Davids, mijn liesbreukmaten. Jullie hebben mij gestimuleerd om niet alleen te bedenken en te begeleiden, maar ook te doen. Niet om het gouden randje per se, maar wel als een bekroning van ons werk ben ik heel blij dat het boek er is.
Egbert Jan, wie anders dan jij kan mijn paranimf zijn. Hopelijk gaan we nog lang door als prins carnaval en moeke, want zonder feest geen vreugd!
Geert Jan, natuurlijk kreeg jij je gewilde rol om te mogen opponeren. Je rol binnen de maatschap is grootsch en de mogelijkheid met je te reflecteren op medisch inhoudelijk en persoonlijk vlak waardeer ik zeer.
Paul, je OK tijden zijn verbluffend en je resultaten net zo. Je bijdrage aan de data van dit proefschrift zijn groot, dank hiervoor en voor je enthousiasme voor de stukken, de voordrachten en de voortgang van het werk.

Dr C.I. Perre, Dr. A. Pronk, Dr. S.K. Nagesser, Dr. D.E.J.G.E. Dolmans en Dr N. Smakman, mijn andere maten. Dank voor de tijd die ik kreeg om soms wat extra meters te maken. Jullie zijn allemaal onderdeel van een bijzonder plezierige maatschap, onderhouden dus en voort met de club.
Kees, mijn onco maat, een poli op woensdag zonder jou is er geen. Mopperen, maar vooral veel humor. Dank voor alles wat ik tot nu toe van je geleerd heb, de vanzelfsprekendheid van je steun op vele gebied en het plezier op de werkvloer.
Niels, jij was nog assistent en we filosofeerden wat over twee matten. Zie hier! Erg plezierig dat je onze maat bent geworden. Dank voor je bijdrage aan dit boek.

Drs H Witjes, lieve Hille, erg leuk dat ik je de TEP heb mogen leren. Dank voor al die momenten dat jij stond te ploeteren op OK en ik zat te ploeteren achter de PC. Blij dat ik je ken.

Verpleegkundigen van afdeling ZB3, lieve meiden, dit boekje is ook een beetje van jullie. Minstens 80% van de patiënt tevredenheid komt voort uit jullie goede zorg. Dat is topzorg. Dank namens alle patiënten.

Iedereen van OK2 in Zeist, dank, voor jullie geduld, gezelligheid en hulp bij het uitvoeren van de TULP studie en van al die liesbreukoperaties. Soepele wissels, 100% NL, Guus Meeuwis, leuke verhalen, strakke matten, fijne endo-eye's en goed camerawerk. Zonder jullie geen data, geen wetenschap, geen proefschrift.

Dr. M. Hamaker, beste Marije, jij bood spontaan hulp aan toen je mij voorbijliep in de gang en zag dat ik met 'SPSS voor dummies' probeerde eenvoudige berekeningen uit mijn database te halen. Dat bleek goud waard. Dank voor de avonden bijles in statistiek, het bijschaven van de artikelen en het invliegen van experts in 'repeated measures' (dank Ellen Hamaker) of een native speaker die tijd vrijmaakt mijn moderate English te verbeteren in een excellente versie (thank you Rebecca Weel).

Mede auteurs van de artikelen in dit proefschrift, dank voor jullie werk en input. Sjoerd Elias, voor het meedenken bij het protocol van de TULP studie. Hilal Tekatli, voor je bijdrage aan Hoofdstuk 5. Jenny Breel en Frank Wille, voor het meedenken met de Chopin studie, de behandeling van de patiënten met CPIP en de bijdrage aan Hoofdstuk 2. Rob Boxhoorn, voor het opstarten van de MRI studie, Floris Sanders en Dick Naafs voor het blind beoordelen van alle MRI's en jullie bijdrage aan Hoofdstuk 3 en vooral ook de prettige samenwerking op de werkvloer.

Cees Haring, beste Cees, dank voor je tijd en bereidheid om de juiste gegevens uit die eindeloze database van Access te halen en om te zetten naar een bruikbaar SPSS bestand.

Secretaresses en oud-secretaresses van het Diak, Marianne en Martine, dank voor jullie inzet en de hulp bij het verzamelen van alle patiënt gegevens, het aansturen van inclusie, het versturen, ontvangen, ordenen van de vragenlijsten en het nabellen naar de patiënten. Atie, dank dat je mijn tweede brein bent.

Doktersassistentes van het Diak, dank voor jullie zorg voor de patiënten, het maken van alle afspraken en het goed laten lopen van overboekte poli's. Piema, zonder jou geen MAIN.

Esther van de Heeft, Harke Harkema en Jaqueline Jonker, dank voor jullie inzet voor het Liesbreukcentrum.

Maarten Jansen, dank voor je hulp bij de kaft, nhè, ni?

Alle ANIOS en AIOS chirurgie, NP-ers en PA-ers, werken in het Diak is leuker met jullie!

Frans Jasper, Caroline en Rienk, dank voor jullie spontane aanbod mijn feestcommissie te willen zijn. Ik voel mij zeer vereert en vergeet nooit die avond op de dorpsstraat.

Vrienden en Vriendinnen, dank voor jullie steun, en dank voor al die leuke en belangrijke momenten buiten het werk.
Lieve Tanja en Annie, lief en leed, humor en tranen. Vriendschap tot in het bejaardenhuis.

Manon Hillegers, mijn paranimf, vriendin. Blij dat je mij bijstaat. Dank voor je tips, je luisterend oor, en de memorabele momenten met jou, Maarten en de kinderen.

Schoonfamilie, Jaap, Ria, Ellen, Rinus, Cees, Odette, neefjes en nichten, dank koude kant voor jullie warmte en voor de gezelligheid als we elkaar zien.

Mijn familie, pap, mam, Ank en mijn twee grote nichten.
Lieve zus, afstand is lastig, drukte nog erger. Dank voor de mooie momenten die we moeten koesteren. Jij bent de beste masseur die ik ken. Lieve mam, trots als een pauw en bezorgd dat het wat teveel was. Lieve pap, *"ik wil, ik kan"* is het motto dat je me hebt meegegeven. Het kan een berg verzetten…… Ik wil jullie bedanken voor jullie onvoorwaardelijke liefde. Zonder jullie was ik niet zover gekomen en geworden wie ik nu ben.

Pleun, Toon en Huib, de liefste kinderen van het heelal. Ik ben super trots op jullie en zal nooit vergeten hoe lief jullie voor me waren als ik weer eens een weekend zat te werken aan het boekje. "Kom op mamma, het is bijna af!", latte macchiato's en veel knuffels. Toch fijn dat er weer meer tijd komt voor leuke dingen, maar eerst een feestje!

Johan, mijn liefste maatje. Eindelijk dat dankwoord. Er zijn veel grappen gemaakt over het aantal pagina's dat minimaal nodig is om in woorden te beschrijven hoe groot jouw bijdrage aan dit boek is. Zou nog een boek worden….. Ik ben je heel erg dankbaar voor je geduld, je positieve steun, je humor, je oprechte geïnteresseerdheid, de ruimte die je me altijd gaf als ik zo nodig moest werken, je relativeren, je goede zorg voor de kids en voor mij. Koffie? Dank dat jij er bent.

CURRICULUM VITAE

Ine Burgmans is geboren op 2 juni 1970 te Bergeijk. Na het behalen van haar VWO diploma aan het Rythovius College te Eersel (1988) studeerde zij geneeskunde aan de Universiteit van Rotterdam. Tijdens haar studie heeft zij gewerkt in een kinderziekenhuis in Recife, Brazilië en onderzoek gedaan naar de transmissie van HIV-2 tijdens zwangerschap in The Gambia. In 1996 behaalde zij haar artsexamen en werkte zij als AGNIO chirurgie in het Albert Schweitzer ziekenhuis te Dordrecht en vervolgens in het Clara Ziekenhuis te Rotterdam waar zij in 1998 startte met de opleiding tot algemeen chirurg (opleiders Dr. T.I. Yo en Prof. dr. J.F. Lange). In deze periode kreeg zij de mogelijkheid zich te bekwamen in de endoscopische liesbreukchirurgie. De opleiding werd voortgezet in het Dijkzigt ziekenhuis te Rotterdam (opleider Prof. dr. H.J. Bonjer) en werd na een stage van 8 maanden in de Daniel den Hoed Kliniek afgerond in het Reinier de Graaf Gasthuis te Delft (opleider Prof. dr. L.P.F. Stassen). Sinds 2004 is zij werkzaam als algemeen/oncologisch chirurg in het Diakonessenhuis met als aandachtsgebied liesbreukchirurgie (TEP) en mamma chirurgie. Ine Burgmans heeft vanaf de oprichting van het Liesbreukcentrum Nederland in 2005 een aanzienlijke bijdrage geleverd aan de organisatie van zorg binnen dit centrum. Vervolgens heeft ze zich vanaf 2010 actief bezig gehouden met onderzoek naar de uitkomsten en verbetering van de kwaliteit van de endoscopische liesbreuk operatie. In dit proefschrift zijn de uitkomsten van dit onderzoek beschreven. Ine woont in Zeist met Johan Klein en hun drie kinderen; Pleun (14 jaar), Toon (12 jaar) en Huib (9 jaar).