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# Inguinal Hernia Surgery in Men – Chronic Pain and Sexual Dysfunction

Nihad Gutlic, MD



DOCTORAL DISSERTATION

by due permission of the Faculty of Medicine, Lund University, Sweden.

To be defended at MFC Lilla Aulan, Skåne University Hospital, Malmö

on 5<sup>th</sup> June 2018 at 13:00.

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Associate Professor Jan Dalenbäck

University of Gothenburg, Sweden



# Inguinal hernia surgery in men – chronic pain and sexual dysfunction

Nihad Gutlic, MD



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*To my family  
Ida, Allan and Jasminka*

*Primum non nocere – "First do no harm"  
(Hippocrates medical policy)*

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# List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals

- I. Impact of Mesh Fixation on Chronic Pain in Total Extra-Peritoneal Inguinal Hernia Repair (TEP): A Nationwide Register-based Study.  
Gutlic N, Rogmark P, Nordin P, Petersson U, Montgomery A.  
*(2015) Annals of Surgery*
- II. A randomized controlled trial comparing Total Extra-Peritoneal (TEP) to Lichtenstein inguinal hernia repair concerning physical sequelae and quality of life at one year – the TEPLICH trial.  
Gutlic N, Rogmark P, Petersson U, Montgomery A.  
*Submitted*
- III. The relevance of sexual dysfunction related to groin pain after inguinal hernia repair – The SexIHQ short form questionnaire assessment  
Gutlic N, Petersson U, Rogmark P, Montgomery A.  
*(2018) Frontiers of Surgery*
- IV. A randomized control trial comparing Total Extra-Peritoneal (TEP) to Lichtenstein inguinal hernia repair concerning Sexual impairments at one and three years – TEPLICH trial.  
Gutlic N, Rogmark P, Petersson U, Montgomery A.  
*Manuscript*

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# Abbreviations

ASA	American Society of Anaesthesiologists
BMI	Body mass index
CI	Confidence Interval
CFL	Cutaneous Femoral Lateral Nerve
CPIP	Chronic Postoperative Inguinal Pain
EHS	European Hernia Society
GFN	Genitofemoral Nerve
HRQL	Health Related Quality of Life
HWM	Heavy Weight Mesh
IASP	International Association of the Study of Pain
IHR	Inguinal Hernia Repair
IIN	Ilioinguinal Nerve
IHN	Iliohypogastric Nerve
IH	Inguinal Hernia
IPQ	Inguinal Pain Questionnaire
IQR	Inter Quartile Range
Lich	Lichtenstein
LWM	Light Weight Mesh
MCS	Mental Component Score
OR	Odds Ratio
PCS	Physical Component Score
QoL	Quality of Life
RCT	Randomised Controlled Trial
SD	Standard Deviation
SexIHQ	Sexual Inguinal Hernia Questionnaire
SF-36	Short Form 36
SHR	Swedish Hernia Register
SPSS®	Statistical Package for the Social Sciences
TAPP	Trans-Abdominal Pre-Peritoneal repair
TEP	Totally Extra-Peritoneal repair
TIPP	Trans-Inguinal Pre-Peritoneal repair
VAS	Visual Analogue Scale

# Thesis at a Glance

Publication	Aim	Method	Results/Conclusion
<b>Paper I</b> Register based study: chronic postoperative pain after TEP repair	Compare the impact of fixation with non-fixation on chronic postoperative pain in men undergoing TEP repair for primary inguinal hernia	Men 30–75 years with primary inguinal hernia repaired by TEP and registered in SHR analysed regarding risk for chronic pain	TEP has relatively low (7.7%) occurrence of chronic pain without difference regarding chronic pain between fixed and unfixed mesh
<b>Paper II</b> RCT: pain and quality of life at one year after surgery comparing TEP to Lichtenstein	Analyse pain and quality of life at one year after surgery comparing TEP to Lichtenstein in a highly standardised setting for techniques and for surgical skills	482 men 30–75 years with primary unilateral inguinal hernia were randomised to TEP or Lichtenstein and analysed regarding risk for chronic pain	Both TEP and Lichtenstein provide good results with few recurrences and normalised QoL performed using standardized methods performed by hernia specialists
<b>Paper III</b> Register based study: sexual dysfunction after TEP repair	Introducing a new questionnaire SexIHQ, easy to use for large cohorts of patients, for inguinal hernia-related or postoperative pain-induced sexual dysfunction	Sexually Active Men 30–60 Years (cohort of Paper 1) with primary inguinal hernia repaired by TEP and registered in SHR analysed regarding risk for long term pain at sexual activity	Pain-related sexual dysfunction is more common than expected (6.1%). A postoperative complication is a risk factor for pain-related sexual dysfunction
<b>Paper IV</b> RCT: sexual dysfunction at one and three years after surgery comparing TEP to Lichtenstein	To compare the effect of hernia surgery on long term pain at sexual activity after TEP or Lichtenstein performed by hernia specialists according to a strict operative protocol.	Sexually Active Men 30–60 Years (cohort of Paper 2) with primary inguinal hernia randomized to TEP or Lichtenstein and analysed regarding risk for long term pain at sexual activity	QoL was preoperatively markedly reduced in patients with pain at sexual activity, but restored almost to norm levels at one and 3 years. Risk factors for postoperative pain were Lichtenstein op and preoperative pain.



# INTRODUCTION

As a young doctor, I was exposed to my first inguinal hernia operation, a Bassini repair, at the end of the 1980s. I could hardly understand the anatomy of inguinal canal that was so complex. At that time it felt unrealistic that I would spend so much time on research of this disease in the years to come.

Since then the development and fine-tuning of techniques for hernia repair surgery has come into focus and undergone major changes to enhance quality for the benefit of the patients.

The existence of an inguinal hernia was described already in Mesopotamia and Egypt around 1550 BC (135, 259). One of the first hernia treatments was described by Phoenicians 900 BC. The ancient Greeks (Hippocrates, 460–375 BC) also described men suffering from hernias.

The modern operative hernia repair was launched by Marcy in 1871, followed by Steele in 1874. Both performed a suture repair, including a reduction of the dilated orifice of the inguinal canal.

In 1884 Bassini was the first to perform a true suture reconstruction of the posterior wall of the inguinal canal. Bassini got famous for his invention and was the first to publish on the results in a large case series. This was the first step taken in hernia science.

Further technique developments were introduced by Halsted in 1903 and Kirschner in 1908 using a fascial grafts for reconstruction of larger defects.

McVay, Anson and Shouldice introduced in the 1940s a suture repair technique adding a fascial incisions to reduce tension (228). The Shouldice technique is still the gold standard for suture repair, even though several modifications have been adopted to the original version.

The mesh reinforcement techniques were introduced in the 1950s. Stock was early out in introducing an alloplastic mesh. Usher developed the first technique using an onlay position of a polypropylene mesh (253). Rives described in 1965 the open preperitoneal technique for mesh placement for unilateral hernias followed by Stoppa who introduced it in bilateral inguinal hernias using a larger mesh in 1968.

Irving Lichtenstein described the first tension-free repair in 1970 using an onlay Marlex<sup>®</sup> mesh. His technique has become gold standard of today's open onlay mesh repair (141). Parviz Amid was the co-founder of the Lichtenstein Hernia Institute, University of California in Los Angeles, that further defined the modern era of hernia surgery.

The laparo-endoscopic techniques, using the preperitoneal space for mesh placement, was introduced in the early 1990s. 1992 Dulucq performed first a totally extraperitoneal (TEP) approach (63) In 1992, Arregui (18) and Dion and Morin (62) performed transabdominal preperitoneal (TAPP) approach. Bittner from Germany was the first to publish a large case series of the TransAbdominal PrePeritoneal (TAPP) mesh repair technique (28). The mesh was put in the preperitoneal space through an intra-abdominal entrance by laparoscopy.

To avoid the intraabdominal rout, the Totally ExtraPeritoneal (TEP) technique was introduced (143). It uses the preperitoneal space for mesh placement leaving the abdominal compartment untouched. This technique was highly advocated by another German surgeon, dr Köckerling.

All techniques have pros and cons concerning different outcomes. Recurrence has for decades been regarded as the main outcome of inguinal hernia surgery being regarded as a failure of surgery most from a technical point of view. This



**Figure 1.** Reinhard Bittner, Stuttgart and Ferdinand Köckerling (Agneta Montgomery collection)

problem has diminished substantially after the introduction of mesh techniques. Two large internationally recognised RCTs has been performed by Swedish surgeons named SMIL I and SMIL II comparing Shouldice to TAPP and Lichtenstein to TEP during the early phase, after the introduction of the laparoscopic techniques (19, 68).

The reason to start this project was to enlighten and focus on quality of life issues from different perspectives after inguinal hernia surgery. Chronic pain, discomfort, pain at sexual activity and sexual impairments have come more into focus since these conditions are more commonly seen as a sequelae after surgery than former believed. The two most commonly used surgical techniques today in the western world are the Lichtenstein and the TEP procedures. There were indications of fewer problems following minimally invasive techniques.

Inguinal hernia surgery is the most commonly performed operation in men in all ages. Chronic sequelae after surgery could potentially alter the whole life and should by all means be prevented if possible.

There is a continuing search for an optimal technique for hernia treatment. The results are dependent on the constitution of the patient, the complexity of the hernia, the anatomical area to dissect with potential structures at risk for harm, the mesh material used for reinforcement, the fixation (if used) of the mesh and last but not least the performance of the surgeon.

Better outcomes are needed and possible. We have to further improve the inguinal hernia treatment to minimize the postoperative herniorrhaphy pain syndrome.

## Background

The definition of an inguinal hernia is a protrusion through the inguinal canal of abdominal content. The term groin hernia includes a protrusion through the femoral channel. The life time risk of suffering from a hernia is around 27% for males and 3% for females (113). Around 66% of patients have symptoms that could be from none to cosmetic or discomfort, to pain and incarceration. Bilateral hernias are seen in around 30% of all hernia patients.

The size of hernia could vary widely, as shown in Figure 2. The most common size is a local lump in the groin not protruding into the scrotum. Around 4% of male and 13% of female patients are operated in an emergency setting due to incarceration or strangulation, according to the SHR (243).



Hernia recurrence is to be regarded as a failure of surgery. It has been the main outcome measure for decades in hernia surgery (79). After the introduction of mesh techniques in the 1980–1990s this problem has diminished substantially.



**Figure 2.** A. Bilateral groin hernias with a recurrence on the right side (scar in the right groin). B. Right sided scrotal hernia dislocating the genital organs. C. Huge right-sided hernia with loss of domain of intestinal content down into the scrotum. (94)

Recurrence can usually be solved by a second operation with no further sequelae for the patient.

One of the most important issues of today is the problem of chronic postoperative pain that can be observed in up to 10–15% depending the definition of pain and instrument used for evaluation. Pain varies in frequency for different surgical techniques, type of mesh and type of fixation used. Experience of pain is subjective and it can be interpreted totally differently by different individuals. It is also difficult to compare pain levels since trials have used a variety of pain instruments. Several risk factors for the chronic pain have been identified such as extraordinary preoperative- and postoperative pain, young age, recurrent repair, and open hernia repair (82, 153).

Pain during sexual activity due to the hernia or after hernia surgery is a problem that has been sparsely discussed. This is a greater problem than formerly believed. Professor of Anaesthesiology, Henrik Kehlet, University of Copenhagen, has dedicated his life to study fast-track painless surgery in different fields. He has

together with his research group highlighted the problem of sexual impairment due to a hernia or following hernia surgery (22).



**Figure 3.** Professor Henrik Kehlet, Copenhagen University. An ikon for the development of fast track surgery and introducing the research of sexual impairment due to inguinal hernia surgery. (Agneta Montgomery collection)

### **Definitions, prevalence and risk factors**

The word *hernia* originate from the Greek word “hernios” which means “bulge”. Hernia is defined as a “protrusion of an organ or part of it (such as an intestine or fat) through connective tissue or through a wall of the cavity (as of the abdomen) in which it is normally enclosed”. An *inguinal hernia* is the protrusion through the inguinal channel (medial or lateral of the epigastric vessels). *Groin hernia* is a more global term as it also includes a protrusion through the femoral channel.

Inguinal hernia repair (IHR) is today one of the most commonly performed surgical procedures in adults in the western world. More than 20 million hernias are estimated to be repaired every year around the world (113). A total of 16 000 procedures are performed annually in Sweden according to the SHR. The comparative numbers are approximately 700 000 hernia repairs in the US and over 100 000 in the UK (214). The incidence of hernia repairs in Sweden is approximately 220 in 100 000 people annually.

The prevalence of inguinal hernia increases with age and are reported to be 47% at the age of 75 years for men. However, the lifetime risk of undergoing inguinal hernia repair is only 27% for men and 3% for women (113). This means that almost half of the men with an inguinal hernia do not require an operation during their lifetime (204).

A total of 30% of inguinal hernias are asymptomatic and up to 50% of the patients are unaware of their inguinal hernia (87). Inguinal hernia is eight times more common in males than in females. This is due to a gender difference in shape of the pelvis being more flat in females. The inguinal canal is broader in men as a consequence of the testicles moving down into the scrotum.

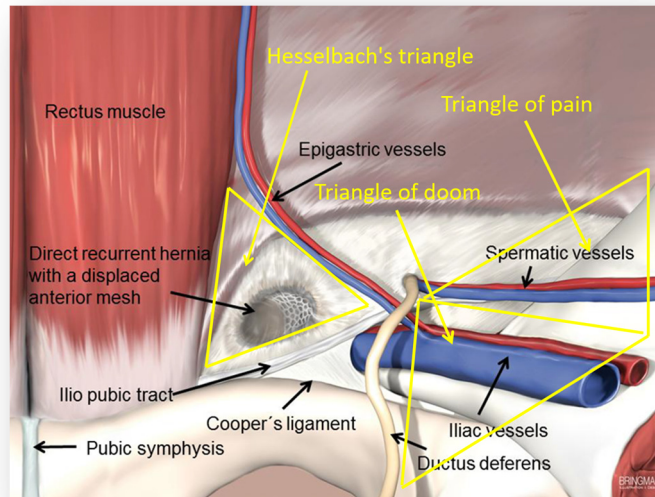
A recurrent IHR is performed in 9% in men and in 4% in females according to SHR. It could be a recurrent operation emanating from former surgery several years ago. The incidence of a recurrent operation in females have decreased the last years according to SHR. This could be the effect of an increased use of preperitoneal techniques in females, in line with recommendations.

There are several risk factors described for having an inguinal hernia like smoking, connective tissue disorder, defect closure of inguinal canal during embryonic life, family history of hernia disease, family history of hernias, low BMI and age (58, 212). After prostatectomy, particularly open, there is a three to fourfold risk increase (147, 177). Open appendectomy has also been described as risk for development right-sided groin hernia (17). This is probably due to nerve injury caused at the grid incision. A family history is also a risk factor if more than two relatives or a first degree relative having had hernias (144). People with low BMI are at risk due to the lack of intraabdominal visceral fat that could protect the weak areas (277).

### **Inguinal anatomy**

The anatomy of the groin is complex. Knowledge of the anatomy is essential if you are to repair a hernia and to understand the mechanism for having chronic pain after hernia repair.

The inguinal canal in adult men has the form of a cylinder. It begins at the internal ring located laterally to the inferior epigastric vessels and is extended from the transversalis fascia. The inguinal canal ends at the external ring where the aponeurosis of the external oblique muscle continue. The anterior wall of the canal consists of external oblique muscles. The posterior wall consist of the internal oblique and transverse abdominal muscles. These muscles are connected medially to form the conjoined tendon. Peritoneum is behind the transverse fascia.



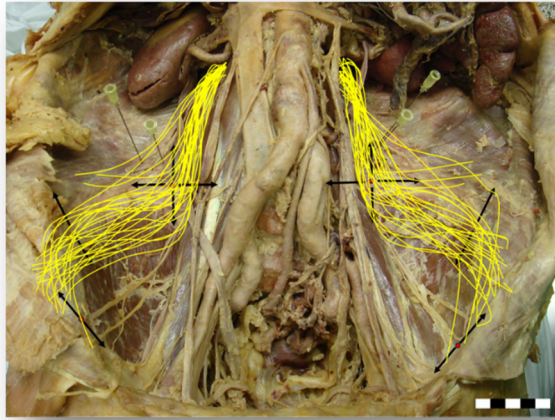
**Figure 4.** Anatomy from the inside, the right groin of the abdominal wall. The triangle of doom, the triangle of Hesselbach and the triangle of pain are demonstrated. With permission of ©Hanna Bringman Ljungqvist

The spermatic cord in men (and the round ligament of the uterus in women) passes through the inguinal canal. The spermatic cord contains vas deferens, testicular vessels, and the genital branch of the genitofemoral nerve.

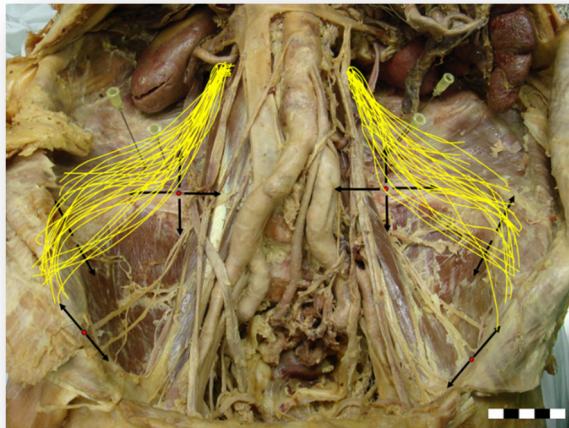
There are three areas where the femoral vessels and spermatic cord leave the abdominal cavity, Figure 4. These form the medial, lateral and femoral triangles (71). A medial (direct) hernia bulge through the medial (Hesselbach's) triangle between inferior epigastric vessels laterally and rectus muscle medially. A lateral (indirect) hernia protrudes laterally to the inferior epigastric vessels. A femoral hernia is located in the femoral canal below the inguinal ligament medial to the femoral vein.

A lateral hernia is the most common type of hernia and is present in 54%, while a medial hernia is present in 39% of all groin hernias in the SHR. It is almost impossible by physical examination alone to distinguish between a medial or lateral hernia as well as to differentiate between a femoral and an inguinal hernia.

The three main nerves in the groin are the ilioinguinal (IIN), iliohypogastric (IHN), and the genitofemoral (GFN) nerves. They all run retroperitoneal over the quadratus lumborum and the psoas muscles. Anteriorly they penetrate the transverse abdominal muscle and enter the inguinal canal, Figures 5–7.



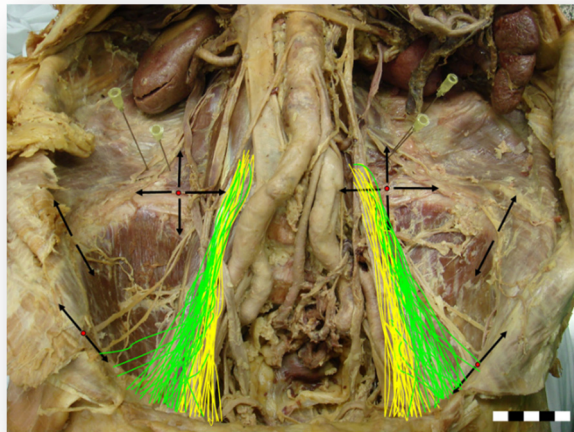
**Figure 5.** Retroperitoneal courses of the IIN (dots between arrows reference points, arrows direction of measurements, lines IINs, scale 1U = 1 cm). (205). With permission from Springer.



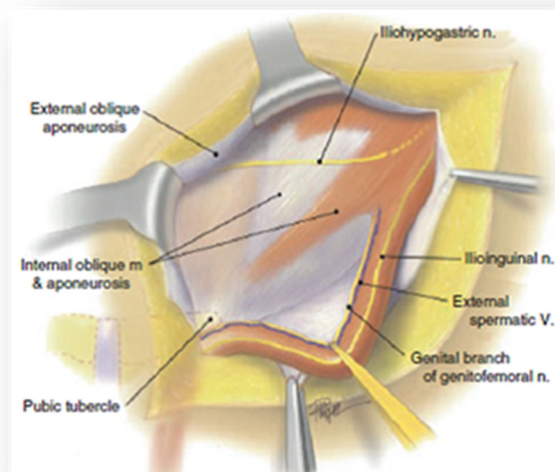
**Figure 6.** Retroperitoneal courses of the IHN (dots reference points, arrows direction of measurements, lines IHNs, scale 1U = 1 cm (205). With permission from Springer.

With the laparoscopic technique the target area for the nerves are behind the Gerotas fascia where the nerves run retro-peritoneally over the quadratus lumborum and psoas muscles, Figures 5–7. This fascia should always be kept intact during endoscopic dissection in the groin. The lateral femoral cutaneous

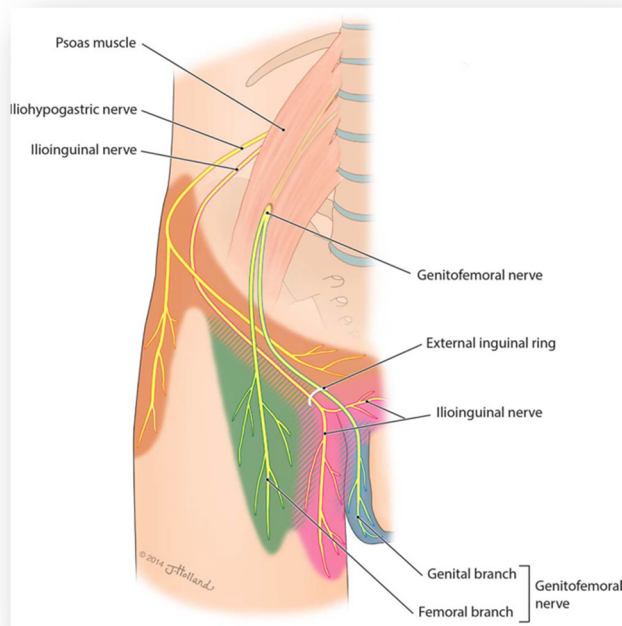
nerve which comes from the first and second lumbar roots runs more laterally but could also come in conflict laterally if mechanical mesh fixation is used.



**Figure 7.** Retroperitoneal course of the GFN (dots between arrows reference points, arrows direction of measurement, lateral lines femoral branches, medial lines genital branches, scale 1U = 1 cm) (205) . With permission from Springer.



**Figure 8.** Anterior identification of the inguinal nerves in the inguinal canal. With permission from Springer (94).



**Figure 9.** Dermatomes of the nerves in the groin.  
With permission from John Wiley and Sons.

Several anatomical studies have been performed to clarify the course of these nerves. There are variations in the distribution pattern. Common variations include a single proximal common trunk for the IHN and IIN, the appearance of the GFN through the psoas muscle as two single branches. There is a variation in cutaneous innervation by the IIN and genital branch (GB) of the medial thigh, pubic and scrotal/labial region (205).

In the Lichtenstein operation there is a risk of injury to any of the three nerves that are sensory and motor nerves. The nerve anatomy is demonstrated in Figure 8. The dermatomes for innervation of the three nerves are demonstrated in Figure 9.

### **Classification**

Several classifications for inguinal hernias have been introduced by different surgeons using their own names as a brand mark like Casten, Halverson, McVay, Gilbert, Nyhus, and Zollinger. The most commonly used was the Nyhus classification (184) grouping hernias after anatomical type (I–III) adding a recurrent hernia as a type as IV.

EHS Groin Hernia Classification	Primary		Recurrent		3	x
	0	1	2	3		
L						
M						
F						

**Figure 10.** The EHS groin hernia classification.  
With permission from Springer (162).

The European Hernia Society (EHS) has developed and introduced a classification system based on localisation of the hernia, size of hernia orifice (by number of fingers) and difference between recurrent and primary hernia (162). This classification uses a simple grid that describes also if it is a combined. If there is a diffuse bulge of the inguinal wall, which cannot be accurately identified for localisation, then it is marked as x in the classification. This classification assists when comparing different hernia trials for outcomes after surgery.

### Indication for operation

There is no strict guide in the literature on when to recommend an operation or not. Treatment strategies are also not uniform. There is a variation within the surgical community from both a cultural and individual surgeon's perspective as well as from the influence of mesh companies and the reimbursement systems. It is however important to focus on the patient's perspective and give thorough information on pros and cons when recommending hernia repair or when not. What is there to gain or lose? What are the risks of a worst case scenario, a lifelong suffering from chronic pain?

The studies on "wait and see" has brought more knowledge on what happens over time in patients with minimal hernia symptoms. It has been concluded that it is safe for men to have a watchful waiting perspective when symptoms are minimal. Only 2.4% of patients required an emergency operation over a 10 year period in an RCT performed in US (59, 78). Another study showed similar result with a cumulative incidence of an emergency surgery in the watchful waiting group of 2.5% (46). Both studies show that 62–79% of the watchful waiting



patients after seven to ten years will eventually switch to surgical treatment due to the development of symptoms.

Watchful waiting has become questionable by others since patients can be exposed to a risk of suffering a complication (96). In a recent study from The Netherlands the results were not as favourable. Already after 2 years 35% of the patients in the watchful waiting group received an operation and 2.3% were operated on in an emergency setting due to strangulation or incarceration (59). However, the authors still conclude that watchful waiting seems safe.

The International guidelines for groin hernia management also recommend watchful waiting in cases of asymptomatic or minimally symptom particularly in older patients who have comorbidities and risks of anesthesia (93). The Swedish National Indications For Groin Hernia Surgery document concurs in recommending watchful waiting in men with minimally symptomatic hernias.

Symptoms from an inguinal hernia differ in magnitude from asymptomatic to worst pain ever experienced. Most of inguinal hernias increase in size over time and might also cause mechanical problems. In a worst case scenario a hernia could be obstructed and result in acute incarceration. Such patients must be immediately operated on to diminish the risk of developing a strangulation of blood supply leading to necrosis and perforation of an affected intestine (230). Femoral hernias have a high predisposition for incarceration and operative treatment is recommended even if symptoms are minor or absent (55). One should bear in mind that a femoral hernia diagnose is difficult to distinguish from an inguinal hernia both at X-ray and at clinical examination.

Elective groin hernia surgery is a low-risk operation even in elderly patients with co-morbidity. Symptomatic elderly patients should be considered for operation. Quality of life in elderly has been shown to improved significantly after repair (199).

Operation is recommended to male patients in Sweden if they suffer from discomfort or pain or if the hernia has a tendency to enlarge over time. All female patients are strongly recommended for surgery to hopefully prevent emergency treatment, even in the absence of symptoms (35, 93)

# Meshes

*“if we could artificially produce tissues of the density and toughness of fascia and tendon, the secret for the radical cure of hernia would be discovered”*

— Theodor Billroth 1878

## Mesh materials

Great efforts have been made to create or invent a product that could strengthen the host tissue in the abdominal wall. The lack of good quality collagen of is one of the most important causes for the development of hernias (102). The high recurrence rate was a serious problem in hernia surgery before meshes for reinforcement were introduced (25). In the beginning autologous body tissue was used to strengthen the hernia area. Marcy was the first to use a foreign material. He used kangaroo tendons as reinforcement material already in 1887 (101). Halsted and Kirschner treated large defects using fascia grafts at the beginning of the twentieth century.

The first use of synthetic material was tantrum gauze. It was abandoned in the 1940s due to a very high infection rate. Silver filigrees and stainless steel were also tried without any greater success.

The first synthetic mesh from nylon (polyamid) was describes by Melick in 1942 (101). Stockings were used as alloplastic mesh in 1950s. Usher was the first to describe the polyethylene mesh (Marlex<sup>®</sup>) in 1958 (253). This mesh material is still in use today. Marlex<sup>®</sup> is a trademarked name for crystalline polypropylene and high-density polyethylene. The Bard company marketed in 1963 a Marlex<sup>®</sup> polypropylene (PP) mesh which was more stretchable and temperature resistant. Modulations of the mesh structure of PP are still in common use like Surgipro<sup>®</sup> and Prolene<sup>®</sup>.

In the meantime, other non-absorbable synthetic materials have been developed like polyethyleneterephthalate (PET), polyvinylidenedifluoride (PVDF) and polytetrafluoroethylene (ePTFE).

Absorbable materials have been introduced for intraabdominal use or to be used in contaminated situations. The most known absorbable materials are polycaprolactone (PCL), polylactide (PLA), polydioxanone (PDO) and polyglycolic acid (PGA) (97, 279).

## Mesh properties

All meshes can be distinguished by their mechanical and biological properties like material, weight, pore size, strength, elasticity, degradability and design(47). There is a high demand on meshes that are to be placed intraabdominally for primary ventral and incisional hernias using the laparoscopic route for hernia reconstruction.

The ideal mesh

- provides good reinforcement of the abdominal wall
- is strong enough not to burst
- maintains the abdominal wall elasticity
- causes minimal inflammatory reaction
- is not too robust to cause inconvenience to the patient
- is easy to handle for the surgeon
- does not induce adhesion (to avoid fistulation)
- is easy to cut without fraying
- is inexpensive

Special demands are required for mesh characteristics as memory of shape after inserting through port at laparoscopy, visual permeability for secure fixation and an antiadhesive surface facing the abdominal cavity and a good attachment towards the abdominal wall for ingrowth. All these properties are not necessary in the groins where the mesh can be placed in the preperitoneal space, used in both TEP and TAPP.

Shrinkage of mesh or contraction from ingrowth in the abdominal wall is an important property and occurs due to inflammatory response and formation of scar tissue. “Mesh shrinkage” up to around 20% is dependent on mesh type and host tissue reaction. Inflammation and shrinkage is more pronounced if the amount of polypropylene material is large, like in a heavy weight type of mesh (185).

Large pore (greater than 1 mm) meshes can reduce inflammatory reaction and minimizing shrinkage (117). Meshes with large pores still remain as strong as a small pore mesh regarding recurrence (116).

## Mesh types

The boundary between heavy (HWM) and lightweight (LWM) meshes is not clearly defined (34). Coda et al (47) recommends the classification on mesh weight: Ultra-light <35 g/m<sup>2</sup>, light 35–70 g/m<sup>2</sup>, standard 70–140 g/m<sup>2</sup> and heavy ≥140 g/m<sup>2</sup>. Currently a mesh weight over 80 g/m<sup>2</sup> is interpreted as heavy, and less than 50 g/m<sup>2</sup> as a lightweight (254).

It has been demonstrated in an animal study (115) that shrinkage was 34% in LWM and 46% in HWM in 46%. LWM shows less postoperative pain with comparable recurrence rates (217). The more foreign material, the more inflammation, and therefore the LWM has advantages over HWM (103).

In a meta-analysis and a systematic review comparing HWM to LWM including nine RCTs there was no difference in recurrence between HWM and LWM in open mesh repair techniques, but LWM reduced the incidence of chronic groin pain (216).

There are more than 160 different meshes available for hernia surgery. A classification regarding meshes, also including biological and clinical response, have been suggested by Klinge et al (119).

#### **Mesh classification (119)**

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<b>Class I</b>	Large pore meshes
<b>Class II</b>	Small pore meshes
<b>Class III</b>	Porous meshes with special features
<b>Class IV</b>	Meshes with films (no porous)
<b>Class V</b>	Three-dimensional meshes (plugs, etc.)
<b>Class VI</b>	Biologicals

Biological meshes were introduced to be used in a contaminated field (183). Porcine biological meshes (the most commonly used) are produced from dermis or pericardium from animal cadavers. They are of acellular tissue and contain growth factors. The idea was that they were to induce the production of new collagen in the patient that should replace the temporary scaffold. Collagen cross-linking was introduced to prolong the lifetime of the scaffold. This was to the price of a more heavy inflammatory reaction. One of disadvantages of the biological meshes is that they will resorb over time eventually, leaving the patient with a new hernia. They are also very costly (88).

The latest “cheaper” generation of meshes are the bio-synthetic collagen meshes which breakdown within 6 to 7 months (209). Biological and biosynthetic meshes have not been accepted for standard hernia repairs where synthetic meshes are still preferred (121).

#### **Meshes used in this thesis**

Stapling of the mesh to the abdominal wall when using the preperitoneal space may cause nerve entrapments or inflammatory reactions and is also costly. Due to these potential side effects, the TEP without any mesh fixation was developed. Mesh stability in the groin can be accomplished without any fixation of the mesh

using a preperitoneal placement through the “sandwich effect” where intraabdominal pressure on the peritoneum will keep the mesh in place. A stationary position of the mesh has been confirmed by re-laparoscopy in connection with TEP surgery using hip flexion on the operating table (45). Groin-shaped meshes designed to fit the anatomical shape of the pelvis and the dissected preperitoneal pocket facilitates mesh positioning even further, prohibits wrinkling, and keeps the mesh in place without fixation.

We used the cup-shaped Bard® 3D Max Mesh 10.8x16.0 cm in the TEP group and a flat mesh Parietene Light® Covidien mesh 10x15 cm in the Lichtenstein group. Both meshes are polypropylene meshes. The Bard mesh is a HWM 148 g/m<sup>2</sup> and the Parietene a LWM 48 g/m<sup>2</sup>.

## Surgical techniques

The optimal surgical technique should have:

- a low risk of complications, early and late (pain and recurrence)
- fast recovery
- easy to learn
- cost effective

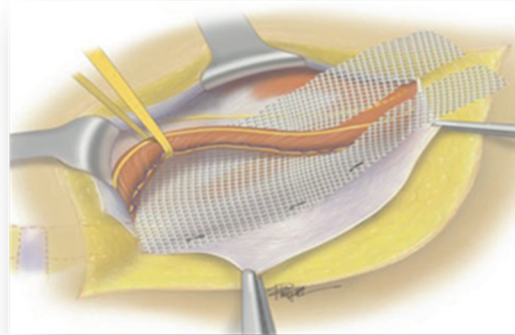
Sutured techniques were worldwide the most commonly used techniques up to the 1990s. Hernia surgery came into focus when dedicated hernia surgeons realised that recurrent hernia rates were unacceptable high when the “ordinary” surgeon performed a sutured hernia repair. Dedicated centres, already present since long, where the Shouldice clinic in Canada advocating suture repair, and the Lichtenstein centre in California advocating mesh repair.

Mesh use today varies from 0% in some low-resource countries up to 99% in high resources countries like Sweden.

### **Lichtenstein technique**

Irving Lichtenstein was the first to introduce mesh for reinforcement in hernia repair in 1970 in the Lichtenstein Institute in California, Los Angeles. Outcome was favourable concerning recurrence. The method using Marlex® mesh (a high density polyethylene) was described and published in 1989 (141). Further development of the technique was reported by Amid, who was the successor at the Lichtenstein institute (14). Several studies have confirmed that the Lichtenstein procedure is superior to the non-mesh sutured Shouldice procedure regarding recurrence (178, 225, 230).

The Lichtenstein technique seems easy to learn having a short learning curve where non-experts and supervised residents can reach outcomes comparable to experts. (56, 164). Other advantages are low costs for mesh and that it can be safely performed under local anesthesia (179).



**Figure 11.** Lichtenstein repair using an onlay mesh. The overload of mesh laterally is cut.  
Textbook of Hernia, W. Hope, Springer company (with permission)

A major drawback is the high rate of postoperative pain compared to endoscopic techniques both in short and long run with frequencies of 10–30% (68, 93, 220, 230). It can be caused by the handling of the nerves at dissection or inadvertently entrapping a nerve it when suturing. By careful dissection and identification of all three nerves the incidence of chronic pain may be reduced.

#### **Other open techniques**

There are several other mesh techniques but none has gained popularity as the Lichtenstein technique. Open preperitoneal mesh plug placed through the hernia defect was promoted by Gilbert and further developed by Rutkow adding an onlay patch on the top (213).

Preperitoneal or retromuscular mesh repairs were originally introduced by Rives and Stoppa in France (206) and Wantz in the USA (262). Kugel made a mesh with a plastic ring to be inserted blindly in the preperitoneal space through an incision above the inguinal canal (127). Gilbert designed the Prolene Hernia System (PHS) as a bilayer polypropylene mesh with an connected underlay and overlay part later developed in a LWM design, the Ultrapro Hernia System® (UHS). Trans-inguinal pre-peritoneal repair (TIPP) (196), transrectus pre-

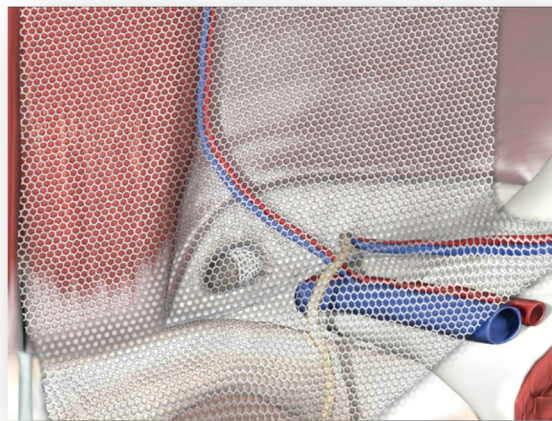
peritoneal approach (TREPP) (123), and the Onstep (151) approach are other preperitoneal versions to be mentioned.

### **Endoscopic preperitoneal techniques**

Total Extra Peritoneal (TEP) and Trans Abdominal Pre-Peritoneal (TAPP) are the most important preperitoneal techniques in use currently. The use of the preperitoneal techniques varies between countries and local traditions. Sweden is a TEP country, Denmark a TAPP country and Germany a mixed country both TEP and TAPP (50/50). The laparoscopic-endoscopic frequencies varies being 55% in Australia, 40% in Switzerland, 45% in the Netherlands and 28%.in Sweden.

Indications for laparoscopic operations used to be bilateral, recurrent and femoral hernia according to EHS recommendations. In the current guidelines it is up to the surgeons' choice and competence to also include primary hernias (93).

TEP has some disadvantages compared to TAPP concerning a longer learning curve, while TAPP has a higher risk for intra-abdominal organ injuries (64, 168, 255).



**Figure 12.** Right groin viewed from the inside, mesh placed preperitoneally according TEP covering all three openings. With permission from ©Hanna Bringman Ljungqvist,

Some studies show no differences between laparoscopic and open technique concerning recurrence rates (158, 230) while others found a higher recurrence rate after laparoscopic than after the Lichtenstein repair (67, 69, 168). TEP has been deemed more technically difficult, and therefore provides a longer learning curve

compared to Lichtenstein (230). About 50–100 TEP operations are required to become an independent TEP surgeon (44, 193).

Laparo-endoscopic techniques are dependent on general anaesthesia but could easily be done as day-case surgery. The patient recovers fast and several studies have shown shorter sick leave compared with the open techniques (19, 145, 220).

### **Causes of chronic pain**

#### *Neuropathic pain*

A mesh can be fixed with sutures, clips or titanium spiral tackers, i.e. mechanical fixation. Mechanical fixation can be associated with higher prevalence of chronic postoperative pain. Stapling is a critical step of the operation that requires attention to avoid injury to surrounding nerves and blood vessels. The most commonly injured nerves are the femoral branch of genitofemoral nerve and lateral femoral cutaneous nerve (pain on the outside of the thigh). Nerve damage may lead to painful neuralgia.

#### *Nociceptive pain*

Staples during laparoscopic surgery or sutures during open surgery in Cooper's ligament and pubic bone can cause osteitis with nociceptive pain in the pubic and suprapubic area. A total of 237 pain patients were operated for persistent pain after groin hernia operations and 13% of them had a pubic tubercle suture removal (156). Another study found that 12% of chronic post-herniorrhaphy pain belonged to the pubic pain (148). Deep mesh fixation to the pubic bone should be avoided since it is related to an increased incidence of CPIP and operative staples or suture removal must be considered.

#### *Risk factors for pain*

A risk factor for postoperative pain can be the attachment of the mesh. A periosteal inflammatory reaction, or traction in attachment points due to shrinkage of the tissue around the mesh, can cause discomfort or pain. This mechanism can be seen after both open and laparoscopic surgery. At the TEP operation, small titanium screws (Tackers) have frequently been related to chronic pain. This problem might occur several months after the operation due to dragging at the attachment points due to shrinkage of mesh (247).

It has been thought that mesh fixation is only needed temporarily until the tissue is incorporated into the mesh through cell ingrowth during the first two weeks as well as by collagen deposition during the following two months.



Studies have shown that it is safe regarding recurrence not to fixate the mesh (247). This may be an advantage to avoid traction and attachment points thus perhaps reducing chronic pain.

It has been confirmed in a meta-analysis that risk of recurrence does not increase using a unfixated mesh (215, 245, 249). There is no difference either between glue and staples/tacks concerning the risk for recurrence (109, 218). The same statement is confirmed for mesh weight (54, 217).

Mechanical fixation should only be used under special circumstances like a large hernia (defect size >3 cm), especially with a large medial defect or if sufficient overlap cannot be achieved. There is no consensus on the “best” fixation method. Fibrin sealant or cyanoacrylate may reduce postoperative early and chronic pain. Fibrin glue fixation or no fixation is recommended because it is possibly related to less cost, less postoperative and chronic pain, and still equal recurrence rate (30).

### **Nerve handling**

Surgeons can either recognize or overlook the courses of the inguinal nerves during open repair. The IHN and IIN can be seen directly after opening of the external aponeurosis. The GB is running with the cremaster vessels behind the spermatic cord and would be identified at a later stage of dissection. Several methods of handling of the nerves are described; nerve preservation, prophylactic neurectomy and pragmatic neurectomy if nerve injury occur during operation.

A prospective multicentre study in open mesh repair compared preservation versus division of the inguinal nerves showing moderate-to-severe pain in 4.7% in division/no nerves identified group and 0% in identified and preserved nerves group six months postoperatively (9). Similar results were reported by Izard (99), however, both were observational studies of “low” grade quality.

Three meta-analyses reported no differences in chronic pain and numbness at 6 and 12 months postoperatively between groups in which the IIN was prophylactically neurectomized in one group and saved in the other. However, increased sensory loss was reported after IIN resection (95, 100, 272).

Two studies comparing IHN neurectomy with IHN preservation reported no differences in the incidence of CPIP or sensory loss one year postoperatively (106, 192).

During open inguinal hernia repairs it is recommended to identify and preserve all three nerves resulting in reduced chronic pain to less than 1%. In case of an injured nerve it should be totally removed (9, 10) Recommendation also given by the International guidelines (93).

In case there is close contact between a mesh edge and the nerve a small opening at the edge of the mesh is recommended to reduce contact area between mesh and nerve.

One study involved 364 Lichtenstein operation compared pragmatic neurectomy, if nerve injury occur or interfere with mesh position preoperatively, with a routine nerve preservation. Pragmatic neurectomy caused less CPIP (232).

Pragmatic neurectomy of the ilioinguinal nerve and/or the iliohypogastric nerve is suggested (10).

## International guidelines

International guidelines for groin hernia management were published in *Hernia* in the beginning of 2018 (93). This was an international project joining 50 hernia experts from all continents around the globe for evidence-based statements and recommendations for inguinal hernia treatment. The work took two years to complete.

A total of 166 key questions were formulated and an evidence-based literature search was performed and graded using the Oxford SIGN and Grade



**Figure 13.** The group of the project “HerinaSurge”. The International Hernia Guidelines of inguinal hernia working (Maarten Simmons Collection)

methodologies. A total of 136 statements and 88 recommendations were agreed on. Recommendations were graded as *strong* (recommendations) or *weak* (suggestions). The AGREE II instrument was used to validate the guidelines and an external review was performed. Some of the recommendations that might be of clinical use are summarized in the list below.

*Hernia Surge recommendations and suggestions:*

- Risk factors for inguinal hernia: family history, previous contra-lateral hernia, male gender, age, abnormal collagen metabolism, prostatectomy and low body mass index
- Peri-operative risk poor surgical techniques, low surgical volumes, surgical inexperience and local anaesthesia
- Symptomatic groin hernias should be treated surgically
- Asymptomatic or minimally symptomatic male IH patients may be managed with “watchful waiting”. The majority will eventually require surgery
- Surgical treatment should be tailored to the surgeon’s expertise, patient- and hernia-related characteristics and local/national resources
- Mesh repair is recommended as first choice, either by an open procedure or a laparo-endoscopic repair technique
- One standard repair technique for all groin hernias does not exist – surgical services that provide both anterior and posterior approach options is recommended
- Lichtenstein and laparo-endoscopic repair are best evaluated
- Laparo-endoscopic techniques have faster recovery times, lower chronic pain risk and are cost effective
- After appropriate discussions with patients concerning results, tissue repair (first choice is the Shouldice technique) can be offered
- Day surgery is recommended for the majority
- Surgeons should be aware of the intrinsic characteristics of the meshes
- Use of LW mesh may have slight short-term benefits like reduced postoperative pain and shorter convalescence, but are not associated with better longer-term outcomes like recurrences and chronic pain
- The incidence of erosion seems higher with plug versus flat mesh. It is suggested not to use plug repair techniques
- In almost all cases, mesh fixation in TEP is unnecessary
- In both TEP and TAPP it is recommended to fix mesh in M3 hernias (large medial) to reduce recurrence risk.

- Antibiotic prophylaxis in average-risk patients in low-risk environments is not recommended in open surgery. In laparo-endoscopic repair it is never recommended
- Local anaesthesia in open repair has many advantages, and its use is recommended provided the surgeon is experienced in this technique
- General anaesthesia is suggested over regional in patients aged 65 and older as it might be associated with fewer complications like myocardial infarction, pneumonia and thromboembolism.
- Perioperative field blocks and/or subfascial/subcutaneous infiltrations are recommended in all cases of open repair.
- Patients are recommended to resume normal activities without restrictions as soon as they feel comfortable.
- Provided expertise is available, it is suggested that women with groin hernias undergo laparo-endoscopic repair in order to decrease the risk of chronic pain and avoid missing a femoral hernia
- Watchful waiting is suggested in pregnant women as groin swelling most often consists of self-limited round ligament varicosities
- Timely mesh repair by a laparo-endoscopic approach is suggested for femoral hernias provided expertise is available
- Overall, the incidence of clinically significant chronic pain is in the 10–12% range, decreasing over time.
- Debilitating chronic pain affecting normal daily activities or work ranges from 0.5 to 6%.
- Chronic postoperative inguinal pain (CPIP) is defined as a bothersome moderate pain impacting daily activities and lasting at least 3 months postoperatively and decreasing over time
- CPIP risk factors include: young age, female gender, high preoperative pain, early high postoperative pain, recurrent hernia and open repair.
- For CPIP the focus should be on nerve recognition in open surgery and, in selected cases, prophylactic pragmatic nerve resection (planned resection is not suggested)
- It is suggested that CPIP management be performed by multi-disciplinary teams.
- It is also suggested that CPIP be managed by a combination of pharmacological and interventional measures and, if this is unsuccessful, followed by, in selected cases (triple) neurectomy and (in selected cases) mesh removal.

- For recurrent hernia after anterior repair, posterior repair is recommended. If recurrence occurs after a posterior repair, an anterior repair is recommended.
- After a failed anterior and posterior approach, management by a specialist hernia surgeon is recommended
- Risk factors for hernia incarceration or strangulation include: female gender, femoral hernia and a history of hospitalization related to groin hernia.
- It is suggested that treatment of emergencies be tailored according to patient- and hernia-related factors, local expertise and resources
- Probably about 100 supervised laparo-endoscopic repairs are needed to achieve the same results as open mesh surgery like Lichtenstein
- It is suggested that case load per surgeon is more important than centre volume
- It is recommended that minimum requirements be developed to certify individuals as expert hernia surgeon. The same is true for the designation *Hernia Centre*
- From a cost-effectiveness perspective, day-case laparoscopic IH repair with minimal use of disposables is recommended.
- The development and implementation of national groin hernia registries in every country (or region, in the case of small country populations) is suggested

*Conclusions:*

The HerniaSurge Group has developed these extensive guidelines for the management of adult groin hernia patients with the hope to bring better outcome for the patients. More knowledge and better training is needed for standardised care of our patients. The guidelines are also there to identify gaps in knowledge to provide ideas for future research work.

## The Swedish Hernia Register

There was a growing interest in the early 1990s in decreasing recurrence rate. Standardized techniques for inguinal hernia repair were introduced in Sweden. The five year recurrence rate decreased from 25% to 3% after the implementation of a standardized Shouldice repair compared to a “non-specified” Bassini repair in a county hospital setting (25).

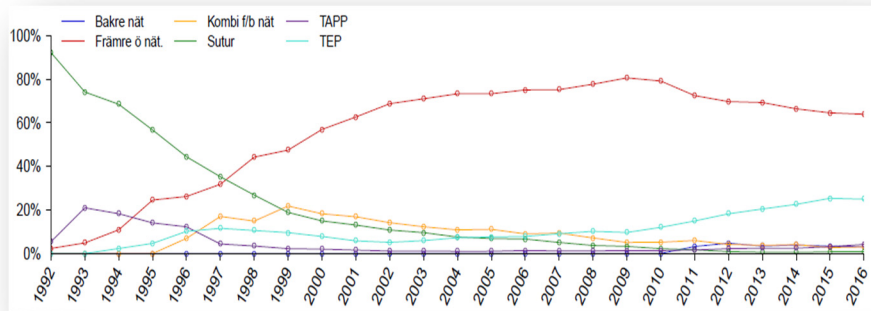


**Figure 14.** Professor Erik Nilsson, the founder of the Swedish Hernia Register SHR in 1991.  
(Agneta Montgomery collection)

All Swedish citizens have a personal identification number which is used in all health care systems. The patient can be followed over time from operation, to reoperation, to death. The SHR was started in 1992 by Professor Erik Nilsson in eight hospitals with the intention of collecting and analysing all hernia operations performed in these initial hospitals in order to improve the surgical quality. The number of surgical units that joined grew over time and in 2003 a total of 83 units had joined. Participation is not mandatory for neither the hospitals nor for the patients. Today are 96% of all inguinal hernia operations are registered voluntary in patients older than 15 years performed in the country including 93 hospitals.

SHR uses a standard protocol for registration on-line and patient data together with preoperative, peri-operative and postoperative data are recorded prospectively. Around 16 000 inguinal hernia operations are registered annually and approximately 300 000 hernia operations are currently recorded since 1992.

Variables registered at operation are patient characteristics (age, gender and body mass index (BMI)), operation date, hernia type, method of repair, prosthetic material used, operating time, intra-operative complications, anaesthesia, operating unit and surgeon. Since 1999, a reoperation for chronic pain is also included in the registers. A 30 day follow up by chart review is performed to identify short term complications. Since 2016 a one year web-based (or letter) enquire on basic outcomes of QoL and pain are recorded with a follow up frequency of 72%.



**Figure 15.** Report from the Swedish Hernia Register on different surgical techniques over time in men since the start of the register in 1992. With permission från the SHR.

The next step is to include health-related quality of life (QoL) in order to plan new studies and report on chronic postoperative disorders such as chronic pain and sexual impairment (7).

Quality checks of source data are performed in 10% of participating hospitals annually. Five independent external investigators check validity of registered data in randomly chosen surgical units.

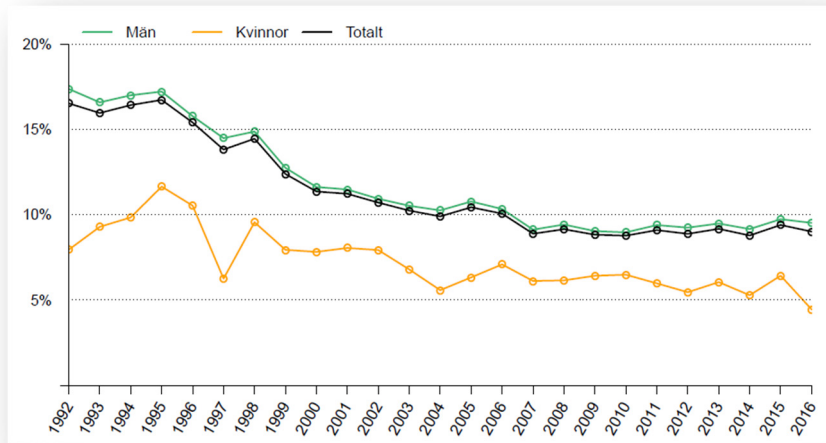
An annual report is sent to all participating hospitals with their own and national results as well as secret individual surgeons' data for quality control and hopefully for improvement of quality when needed. Information is available on the web for anyone interested: [www.svensktbrackregister.se](http://www.svensktbrackregister.se). The SHR is supervised by the SHR Board.

Around 60% of the patients, mainly primary unilateral inguinal hernia in men, are operated by the Lichtenstein technique. The laparo-endoscopic methods TEP and TAPP have increases reaching more than 25%, Figure 15.

Surgical techniques have changed from sutured to mesh repairs, currently being 99%. A re-operation for a recurrence has decreased substantially over time, Figure 16.

SHR has improved the results of hernia care in Sweden. A comparison between participating hospitals from 1992 and 1995 showed that both costs and quality have been improved in hospitals with long time participation (174). Most operations are today performed in a day-care setting.

More than 10 dissertations and 60 scientific publications are based on data from SHR.



**Figure 16.** Report from the Swedish Hernia Register on frequencies of recurrent operations over time in males (green) and females (yellow). With permission from the SHR

### Other hernia registers

Another well-known register is The Danish Hernia register that was founded in 2007 and have become internationally well-known for several important publications. It is mandatory in Denmark to participate in the register. The coverage is >95% (84)

The German hernia register HerniaMed enroll mainly German and Austrian hernia centers with interested surgeons. It covers around 15% of all hernia operations in Germany (237), about 200 000 patients during 2009–2016.

The European Hernia Society started the European Registry of Abdominal Wall Hernias (EurAHS) in 2015. It was to encourage European users not having their own national databases to collect data for quality outcomes. You can include patients for RCTs. This would enable having a standardized protocol for data (166). There are more registers coming up in Europe that are summarized in the Core project (129). The SHR which almost covers the complete country, reported for 2015 Lichtenstein 64%, TEP 25%, TAPP 3%, open pre-peritoneal mesh 3.3%, combined open and pre-peritoneal 2.7% and tissue repair in 0.8%. The German HerniaMed registry reported for 2009–2016: TAPP 39%, TEP 25%, Lichtenstein 24%, Plug 3%, Shouldice 2.6%, Gilbert PHS 2.5% and Bassini 0.2%.



# Register studies and RCTs

## Register studies

A registry is commonly based on a clinical task and includes large numbers of data from patients suffering the problem that fits in the inclusion criteria. Register studies are observational studies identifying problems found in everyday practice. The opportunity to detect rare adverse events, like serious complications and mortality, are important especially if new interventions or products are introduced (176).

Hernia registers, having a high coverage, have an exceptional possibility to investigate and reflect on outcomes in the routine daily clinical practice of unselected patients. A benefit is that registry studies contains a mixture of all treatment methods, surgeons on all different educational levels and an unselected patient cohort. The external validity in the registry studies are high as results are not limited to highly specialised centres. Results can be applied to all type of surgeons with different backgrounds and experience and not only to specialists. You can also study long-term results at low cost. Large size register study also allows analysis of uncommon adverse events with higher statistical effect than RCTs (128). Registry studies are a good complement to RCTs (146), Figure 17.

A disadvantage of registry based studies is the risk of incorrect data entry or missed data. It is of major importance that registry data should be continuously validated.

## Randomized controlled trial

RCTs are investigational studies and report the results in expert hands when treatment is optimally applied in selected patients (80). Randomized clinical trials compare groups that get different treatment options to see if the treated group perform better compared to the other. This method enables to get unknown factors equally distributed between groups. The randomization results in as equal groups as possible, composed of persons with the same characteristics. RCTs usually evaluate the effect of any factor that could differ between study groups. Randomization is the best method to find out if a particular treatment has an effect or not. RCTs insures a high internal validity (13, 23).

There is usually a loss of patients during the study. If this loss is high, or skewed, it may affect the outcome. Major loss in follow up may be due to the fact that the patient gets healthy so that he does not care for getting back for control, or is disappointed on treatment results. If loss is large, analysis is needed to see whether the loss can affect results. If patients know the treatment they have received, they can influence the outcome measurements in any direction. The same

goes for the surgeon. A blinded or double blinded study is recommended if possible, i.e. where the patient or both the patient and the researcher do not know what treatment is given.

RCTs are usually performed at specialised centres with selected patients having a specific problems (24, 60). All RCTs are required to report their results uniformly using the CONSORT instrument (223). The disadvantages of RCTs are high costs making long term follow up difficult in opposition to registry based studies.

## Surgical outcomes

### Chronic pain

Groin pain, although often minor, is frequently reported after hernia surgery but preoperative incidences are rarely reported. Chronic pain has come into focus as a central outcome variable during the last decade and has been shown to reduce QoL (10, 79, 105, 156).

It is mandatory to carefully evaluate preoperative pain to ensure that hernia is the cause of pain as well as to rule out other causes, which will need other treatment than repair of the hernia. Preoperative pain is reported with large variations between 30–70% in a few RCTs (165, 173). The potential gain of an operation is important to report. Postoperative pain is difficult to treat and every effort must be made to avoid pain to develop as a result of surgery. The patients should be informed about the risks of the different strategies Whether a “wait and see”-strategy could be considered as an alternative to operation for a patient with minor symptoms should be involved in the treatment decision.



**Figure 17.** The hypothetical coverage of patients operated for an inguinal hernia reported in a national register compared to those that participate in a randomized control trial. With permission of Springer (93)

### *Definition of chronic pain*

Pain is a subjective experience and it is difficult to uniformly define and measure. Postoperative pain is often minor and it is difficult to distinguish pain from discomfort (170). The time frame for the end of early postoperative pain due to normal healing and thereby the start point for chronic pain is also a matter of discussion. Consequently, definitions of chronic pain vary in the literature.

The most commonly used definition of postoperative chronic pain is the one by the International Association of the Study of Pain (IASP): pain persisting more than three months after surgery (98, 159). Three months is a minimum period for pain to be classified as chronic. It takes at least this period of time for the inflammatory reaction of the healing process to subside. Sometimes the healing process with inflammatory reaction around a mesh may continue much longer than 3 months and a time period of 6 months has been proposed as definition of chronic (1).

Grading pain is also important since the consequences of pain vary with severity. Cunningham et al graded pain as *mild* when pain does not limit daily activities and the patient can return to pre-hernia daily life; as *moderate* when pain prevents return to preoperative lifestyles; and *severe* pain as pain interferes with daily activities. (53)

In other studies postoperative pain has been defined as pain that differs from preoperative pain or if there is new pain that was not present before surgery (10). Sometimes it is difficult to distinguish whether postoperative pain differs from preoperative. It is therefore important to assess and describe pain preoperatively and to exclude other possible causes of pain before the hernia operation takes place.

Differential diagnoses to be considered in groin pain patients are orthopedic and vascular diseases like intervertebral disc herniation, tendinitis, coxartrosis, trochanteritis, sacroiliacal disorder, iliac or femoral aneurysm as well as diseases of retro- and intra-abdominal origin, neuralgia after previous abdominal surgery, malignancy and chronic infection. A modification of the definition of chronic postoperative pain has hence been suggested as postoperative pain longer than three months after surgery where other causes of pain have been excluded (154, 271).

Furthermore, there is no uniform definition of pain intensity with clear cutoff-levels even though some studies give an approximate verbal description of the intensity of pain (4, 112).

According to HerniaSurge (93), an international collaboration for development and implementation of guidelines for treatment of groin hernia in adults, chronic

pain ought to be defined as moderate pain with impact on daily activities and lasting more than three months after operation.

#### *Incidence of chronic postherniorraphy pain (CPIP)*

Reported incidences of chronic postherniorraphy pain varies between studies. This is the result due to different definitions of pain, different tools for measuring pain and different lengths of follow up in studies. Incidences range from a few percent up to more than 60% one year after operation (1, 10, 16, 53, 170, 171, 188, 201). The incidence of severe chronic postherniorraphy pain is estimated to affect 1–3% of patients (92).

There are reports indicating differences in pain with lower incidences after laparo-endoscopic operations compared to open methods (29, 92, 158, 220). In a meta-analysis of TEP versus Lichtenstein chronic postoperative pain was reported in 12.5% and 16.8%, respectively (124). Köckerling et al reported worsening of pain on exertion at 1 year in 9.2% of the Lichtenstein group compared to 7.9% in the TEP group (122).

Fortunately, there are indications that pain may subside over time (1, 68, 155, 170). Six years postoperatively, Aasvang et al found less pain in 75.8%, the same pain in 16.7% and increased pain in 7.5% of a cohort of pain patients registered in the Danish Hernia Database (2). Moderate (clinically significant) pain affecting daily activities is 10–12% which decreases over time according international guidelines (10).

#### *Measuring chronic postherniorraphy pain*

There are various scales and questionnaires to measure pain. A simple tool for evaluation of chronic pain is the Visual Analogue Scale (VAS). Patients mark their pain level on a 10 cm line, starting with “no pain” on the left and ending with “maximum pain possible” to the right (42, 43, 49). VAS is commonly used for measuring several other clinical parameters and conditions, besides pain.

Other and similar methods are the Numerical Rating Scale (NRS) where patients describe their pain by choosing a numerical value between 0 (“no pain”) and 100 (“maximum pain possible”). The Verbal Rating Scale (VRS) introduced by Cunningham consist of defined descriptions of the consequences of pain (53). The VRS seem to be easier for the patients to use and possibly preferable to VAS according to an evaluation performed by Loos and co-workers (149), Figure 18.

The European Registry for Abdominal Wall Hernias QoL Score (EuraHS-QoL Score) has launched a questionnaire consisting of 9 questions covering three aspects: pain, restriction of activities and cosmetics discomforts (166), which has also been validated for laparoscopic inguinal hernia repair (167).

**Visual Analogue Scale (VAS)**  
 no pain worst imaginable pain

**Verbal Rating Scale (Cunningham)**  
 0=no pain    1=mild pain    2=moderate pain    3=severe pain

**Numeric Rating Scale**

**Figure 18.** Examples of validated tools for pain measurement

Kehlet et al proposed a uniform assessment of postherniorrhaphy pain in 2002 (110). Their work inspired a Swedish research group to develop the Inguinal Pain Questionnaire (IPQ), a validated instrument for measuring chronic post-herniorrhaphy pain (83). The alternatives for describing the consequences of pain was incorporated from the Duration Intensity Behavior Scale (DIBS) established by Budzynski et al (37). The DIBS consist of a 7-point scale: no pain; pain present, can easily be ignored; pain present, cannot easily be ignored, does not interfere with everyday activities; pain present, cannot be ignored, interferes with all activities; pain present, cannot be ignored, necessitates bed rest; pain present, cannot be ignored, prompt medical advice sought. Questionnaires that contains questions on functional impairment adds value compared to one-dimensional simple tests.

The disadvantage of simple instruments as VAS and NRS are that they only measure pain intensity and does not give a complete picture of the patient's pain as the quality, length and location of pain.

#### *Mechanisms and different types of chronic pain*

It is not fully understood why postoperative chronic pain occurs but several factors are likely to be involved (130). Among such factors are mesh properties, fixation of the mesh by tackers or staples, sutures, glue or self-gripping meshes, perioperative damage to nerves, nerve entrapment in fibrous tissue as well as individual patient factors.

There are two main types of chronic pain: nociceptive and neuropathic (111, 157, 173). Nociceptive or somatic pain occurs because of inflammation (4, 10, 15, 111), while neuropathic pain is a result of nerve damage. A nociceptive pain is often described as tender, pulling, drilling, dull, pounding or aching and neuropathic pain is described as stabbing, sharp, pricking, burning, radiating and shooting. In both types of pain, movements may trigger or impair the pain and tenderness at palpation could be found in both. Neuropathic pain radiates from the tender area and sometimes there is positive Tinel's sign with a neuroanatomic propagation of pain or disturbed sensitivity.

Nociceptive pain responds better to analgesics while neuropathic can be diagnosed by blocking the nerve involved with local anaesthetics (159).

In nociceptive pain sutures, staplers or screws attached to the symphysis and Cooper's ligament can cause inflammation and lead to osteitis pubica. This complaint may occur several months after surgery and then maybe due to pulling at the mesh attachment points due to shrinkage of the fibrous tissue surrounding the mesh.

Neuropathic pain is more difficult to treat and is related to the nerves present in the area: n iliohypogstricus (IHN), n ilioinguinalis (IIN), and n genitofemoralis (GF) with its femoral and its genital branch, n cutaneus femoris lateralis (CFL) and n femoralis. A lesion to one or several nerves is considered to be the cause of neuropathic pain and the IASP defined neuropathic pain as pain caused by a lesion or disease of the somatosensory nervous system (98). Nerve damage can occur during dissection or fixation of the mesh, the presence of the mesh itself may hypothetically cause a foreign body reaction with scarring encroaching on the nerves, but the pathophysiological mechanism of neuropathic pain is not known in detail (76, 89, 160, 170).

Laparoscopic operations may cause neuropathic pain if fixating staples/tackers are placed in or in close vicinity of the nerves or by a direct dissection injury. Later pain can be triggered by fibrosis in the area due to mesh placement that may involve nerves.

The nerves most exposed to laparoscopic operative injury are CFL and the genital branch of GFN and in open operation neuropathic pain may be due to involvement of IIN, IHN and the genital branch of GFN while the CFN seldom is engaged. A peroperative nerve laceration can result in a painful neuroma formation. Early neuropathic pain is caused by entrapment of nerves peroperatively under a tight mesh edge or in sutures. Late neuropathic pain can result from mesh shrinkage and formation of scar tissue.

Pain radiating to the scrotum and testicular pain can be due to damage of the genital branch of the genitofemoral nerve, narrowing of the internal ring, use of diathermia near sensitive spermatic cord structures and if large hernia sacks are dissected/extirpated far down the spermatic cord. This can lead to damage to the circulation in the spermatic cord and cause ischemic orchitis or injury to the sympathetic plexus spermaticus externus that runs in the spermatic cord.

Ejaculatory pain is seen as a result of damage to vas deferens or plexus spermaticus externus with a disturbed motion pattern in vas deferens.

#### *Risk factors for chronic postherniorraphy pain (CPIP)*

Bjurström et al described risk factors for CPIP as preoperative, peroperative and postoperative (31). Known risk factors for developing postoperative chronic pain are: operation of a recurrent hernia which increased the risk for chronic pain 4-fold. Age less than 40 years is another risk factor (40, 200); as well as preoperative pain; daycare surgery; full time employment (200); severe pain early after operation; extended sick-leave; absence of an inguinal bulge preoperatively (40); postoperative complications (82, 190); psychological factors such as depression (203); female gender (1); Raynaud's disease; fibromyalgia; back pain; migraine; irritable bowel syndrome; and, lower socio-economic status (52, 154, 258, 274). Genetic factors including variations in catechol-O-methyltransferase (COMT) gene can play a role in development of chronic pain (258).

Few of these, mostly preoperative, factors are possible to influence. A quantitative preoperative sensory testing with mechanical, thermal and electrical stimuli can predict 4% to 54% of the variance in postoperative pain (268) but there is no simple prognostic assessment method for the risk to develop postoperative pain.

Perioperative or intraoperative factors like surgical method, mesh weight and fixation method may have an impact on chronic postoperative pain occurrence, and are possible to influence. Less pain after laparoscopic surgery may be due to limited dissection and mesh placement on a distance from most of the nerves (6, 29, 65, 68, 131, 132, 231). The use of LWM results in less pain, without differences in recurrence rates, according to several studies (217, 233, 278), while other studies show similar result between LWM and HWM (172, 189). Reduced amount of foreign material in LWM might diminish foreign body reaction and inflammation with decreased fibrosis. A LWM with large pores shrink less resulting in reduced pulling on the neighbouring tissue and possibly thereby reduced chronic postoperative pain and foreign body sensation (34, 230)

A running non-absorbable suture is usually used in Lichtenstein operation for attachment of the mesh to the inguinal ligament. It has been hypothesized that use

of an absorbable suture may decrease long-term pain but a study comparing absorbable vs. non-absorbable sutures in mesh fixation did not show any difference in the occurrence of pain two years after surgery (187). Glue fixation has better results regarding pain compared to mechanical fixation (50, 81, 227) but there are also some studies showing no difference (57, 73, 207, 215). In a recent Cochrane review (242) less pain was found for glue fixation in a subgroup of patients operated with HWM.

During the last years, use of self-gripping mesh has decreased operative time, but not chronic pain compared with sutured mesh in open hernia surgery (73, 140, 191).

The use of local anaesthetics, instead of general or regional anaesthesia, have in some studies resulted in less postoperative pain (179, 234, 260).

Surgeon's skill and operation volume is reflected in low rates of chronic pain when specialised hernia centres were compared to teaching institutions (197). Unsupervised residents trained in the Lichtenstein operation according to a defined curriculum have been shown to perform as well as consultants (188) and laparoscopic inguinal hernia repairs performed by supervised surgical trainees has shown surprisingly low chronic pain rate of 1.5% (276), suggesting the great importance of standardised education and training.

#### *Management of chronic post herniorrhaphy pain*

Treating chronic post herniorrhaphy pain is a challenge and often very difficult (256). As for all complications, prophylactic measures are mandatory which include avoiding known risk factors, meticulous surgical technique and prompt appropriate action in case of direct severe postoperative pain. This is a known risk factor for developing chronic pain (270, 271) and, even though there are no studies on the subject, current guidelines recommend early re-operation to exclude nerve entrapment and to perform neurectomy in case of a nerve injury (10, 93).

Despite precautions, chronic pain will develop in some patients and the problem need to be handled. It is important to exclude recurrence, meshoma and non-hernia-related causes of pain hence examination with ultrasonography and/or magnetic resonance imaging is recommended.

Analgesics, non-steroid anti-inflammatory drugs, tricyclic anti-depressive drugs, selective serotonergic receptor inhibitors, gabapentin, pregabalin and other drugs may be tested but generally only give partial relief and do not address the cause of pain (76).

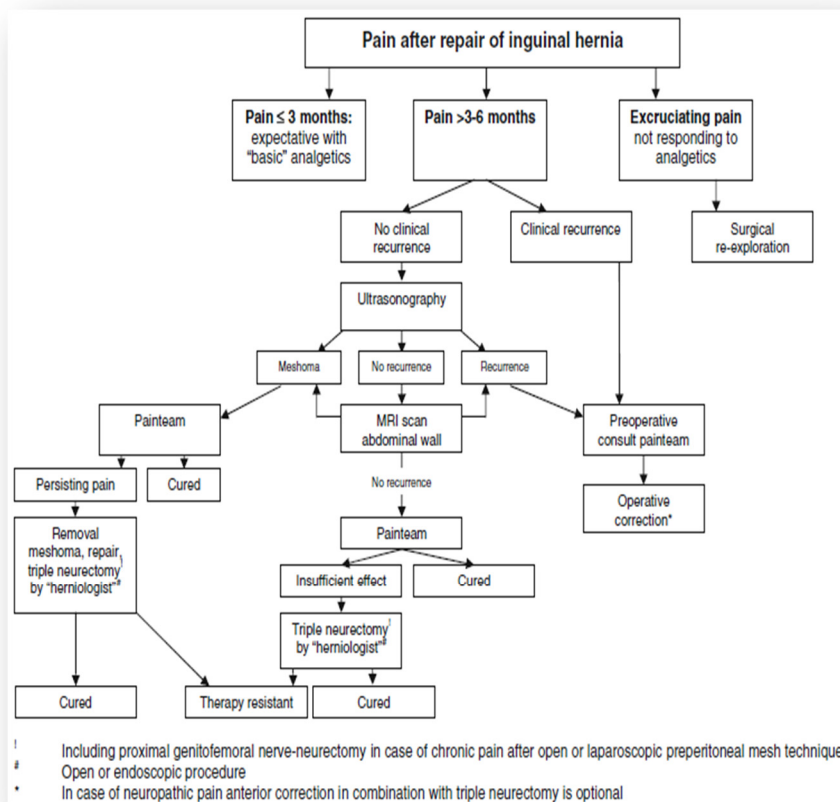
Nerve blocks and infiltration of local anaesthesia in tender areas may be helpful in differentiating between neuropathic and nociceptive causes of pain. Adding steroids to the injections may be successful both for a nociceptive inflammatory



cause of pain as well as for a neuropathic with 50% of patients experiencing pain relief after local anaesthesia and steroids in a study by Thomassen et al (251).

Nerves may also be destroyed or paralysed by the use of radiofrequency ablation (107, 108, 202, 269), cryoablation (41, 72), phenol or alcohol (112) injections.

Conservative treatment is recommended for at least six (76) to 12 months (10) before surgical treatment is considered. International guidelines for the prevention and treatment of CPIP from 2011 (10) and an international consensus algorithm for CPIP from 2014 (130) propose triple neurectomy and/or mesh removal by an expert hernia surgeon after excluding differential diagnosis and multidisciplinary pain team management has failed, Figure 18.



**Figure 19.** International consensus algorithm for management of chronic postoperative inguinal pain (130). With permission from Springer.

Both open neurectomy and endoscopic retroperitoneal neurectomy has acceptable results in selected patients (5, 31, 130, 150). Patients often present with pain that has features of both neuropathic and nociceptive character. This suggests that mesh and fixating sutures or staples also should be removed at re-operation of these patients. If a meshoma is diagnosed mesh removal is recommended (75). To be useful, guidelines and algorithms have a tendency to become simplified and generalized. Some patients might be cured with less extensive surgical approaches like selective neurectomy and/or partial mesh removal but scientific proof is lacking.

Pain relief may be obtained by neuromodulation (271) on different peripheral (137, 275) or central levels (dorsal root ganglion stimulation and spinal cord stimulation) and these techniques should not be forgotten in a multimodal treatment of these patients.

#### *Conclusions of CPIP Management*

If a neuropathic cause for the pain is suspected it is recommended to start with an IIN block at “spina iliac anterior superior”. If pain reduction is achieved, continue with repeated injections until the pain cycle is interrupted. Adding steroids might be beneficial. If an IIN block is unsuccessful, ask an anaesthesiologist to perform a paravertebral block of the GFN. If momentary pain reduction is achieved repeated blocks are recommended. If a block is unsuccessful a nociceptive cause is likely. It is suggested is to add non-pharmacological therapy i.e. behavioural therapy psychotherapy, hypnosis, acupuncture, biofeed-back.

Neurectomy and mesh removal seems rational after a minimum waiting period of 6–12 months without acceptable responses to other therapies. In case of a nociceptive cause, repeated local anaesthetic injections with steroids might diminish pain and might be reasonable to before decision on re-operation.

#### **Sexual dysfunction**

Pain-related sexual dysfunction associated with inguinal hernia is a relatively new issue that has gained interest the last ten years. Sexual function is often affected by disease, but may also be influenced by a hernia or its surgical treatments. The consequences of iatrogenic sexual dysfunction may be vast and are important to avoid.

Pain during intercourse/sexual activity can originate from tender scarring sensible to touching, from mechanical pressure or from the genital organs in terms of chronic testicular pain, ischemic orchitis and testicular atrophy. It may also present as pain at ejaculation. Infertility as a result of surgery is also a dysfunction although seldom accompanied by pain.

### *Pain at sexual activity and sexual dysfunction*

When trying to describe incidences for pain at sexual activity the problem with definitions is encountered and thereby a vast variation is found in the literature. The Danish Hernia Database have been the basis for several studies on pain-related sexual dysfunction after hernia surgery. Any groin or genital pain at sexual activity was reported to be 22% in a study by Aasvang et al in a study cohort mainly consisting of open repairs (3). The incidence of moderate to severe pain occurring at least every third time was 6.7% and 3% was concluded to cause significant clinical problems. Corresponding figures from a study on laparoscopic TAPP repairs was 11% and 2.4%, respectively (27). Eklund et al reported 1.3% pain during sexual activity five years after surgery in the Swedish RCT SMIL-II, comparing TEP and Lichtenstein repair without differences between methods (68).

In the recent guidelines from HerniaSurge the incidence of sexual dysfunction causing moderate-to-severe symptoms is reported to be 5–7% (93).

Most of the studies on pain during sexual activity and dysejaculation lack preoperative data. One study with prospective assessment of sexual activity impairment before and after TEP operations shows a prevalence of 32% preoperatively and 9% postoperatively and 2.3% without preoperative pain suffered new pain postoperatively impairing sexual activity (221).

### *Chronic testicular pain, ischemic orchitis and testicular atrophy*

Orchialgia and testicular problems seem to be present in 10% of patients with chronic groin pain after hernia surgery (29, 220). In a Danish study 18% testicular pain and 2.6–4.5% testicular atrophy was reported (1). Similar high proportions, one out of 4–5 patients, was found to suffer from urogenital complications such as chronic testicular pain or ischemic orchitis (207). On the other hand there are studies indicating much lower incidences, such as a meta-analysis comparing open preperitoneal versus Lichtenstein repair and reporting testicular problems in 1.3% and 1.9% respectively (138). Eklund et al reported 2.7% testicular pain five years after surgery in the SMIL II study comparing TEP and Lichtenstein repair without differences between methods (68).

Ischemic orchitis can be caused by injury to the arterial and/or venous vessels in the spermatic cord and can be associated with venous thrombosis caused by surgical trauma (261). In most cases ischemic orchitis causes testicular atrophy (248). Testicular atrophy appears in 0.8% without differences between LWM and HWM (139). Mesh repairs impair testicular perfusion and decrease testosterone levels and sperm motility in the early period after surgery (194, 248). However,

long-term follow-up does not report significant differences in testicular perfusion or testosterone compared to preoperative levels (20, 195).

Sexual dysfunction, as a result of inguinal hernia surgery, may be treated by neurectomy with or without mesh removal and funicular release. Ejaculatory pain is significantly reduced and sexual life stabilized in two-thirds of the patients (267).

#### *Dysejaculation*

Dysejaculation may be caused by spermatic duct trauma and/or a mesh-related inflammatory reaction around the duct. It was reported to be 7.6% in one study (26) and 3.1% in a questionnaire study conducted within the Danish Hernia Database collaboration (27).

#### *Sexual dysfunction not related to pain*

Sexual dysfunction due to low sexual desire has been reported to be less than 5% in men younger than 50–55 years, after which the prevalence gradually increases to 15–25 percent in 70–75 year old men (85, 134).

Risk factors for impaired sexual interest and function are disorders such as hypogonadism, prolactinoma, metabolic syndrome (51), diabetes mellitus Type 1 (70), Multiple Sclerosis (MS), Parkinson's disease, depression and stress (133, 134).

Sexual dysfunction due to insufficient erection is below 10% up to 50–55 years, then gradually increases to slightly over 50% in the 75–80 year old men (126).

Risk factors for erectile dysfunction are cardiovascular, neurological, endocrine, urologic, certain drugs, smoking and alcohol consumption (161, 250).

#### *Sexual questionnaires*

Sexual dysfunction is defined as “person's disability to participate in a sexual activity as he/she wishes”. There is no consensus on definitions, severity grade or duration time concerning sexual dysfunction. There are no validated and reliable questionnaires for neither clinical use nor research. The most widely used instrument for the assessment of erectile dysfunction is the International Index of Erectile Function, IIEF (210). The IIEF is a self-administered, multi-dimensional questionnaire that is useful in clinical praxis. It consists of 15 questions that examine 4 domains of male sexual function: erectile function, orgasmic function, sexual desire and intercourse satisfaction. A score of 0–5 are given to each of 15 questions.

Other questionnaires focuses on satisfaction, such as Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) (12), Treatment Satisfaction Scale (TSS) (61) and the validated self-administered patient questionnaire Male Sexual

Health Questionnaire (MSHQ) for assessment of ejaculatory dysfunction and ejaculation problems (211).

### **Health related Quality of Life (HRQoL)**

Quality of life (QoL) is a complex entity and has many definitions. To separate QoL related to socio-economic aspects from QoL related to disease the term health related QoL (HRQoL) was coined. There are two kinds of QoL instruments: generic and disease-specific. Generic instruments are used in large populations with all kinds of disorders and the disease-specific instruments are used in subgroups with a one dimensional problem, e.g. inguinal pain.

The most commonly used generic instruments are Short Form 36 (SF-36) and EQ-5D. The hernia disease-specific instruments are the Inguinal Pain Questionnaire (IPQ), Carolina Comfort Scale (CCS) and HerQLes questionnaire. The SF-36 and the IPQ questionnaires are used in all studies in the current thesis. At the time the studies were planned the IPQ was the only disease-specific questionnaire available and it was also developed and validated in Sweden.

#### *Short Form 36 (SF-36)*

The Short Form (SF-36) is a general health questionnaires and measures both physical and mental health (263). This health survey instrument was introduced in 1989 for patient reported evaluation of treatment effects (238). The survey was initially extensive and was shortened to 36 questions – the Short Form 36 (264). It has been translated and adapted for use in several countries, which make results comparable internationally. It is one of the most widely used validated instruments for quality of life measurement of today (265). However, the questionnaire is now copyrighted and researchers are required to buy the rights for use in trials.

In Sweden the translation and validation of SF-36 was done by the Health Related Quality of Life group (HRQL-group [www.hrql.se](http://www.hrql.se)) at Gothenburg University (198, 239-241).

The 36 questions contribute, in different constellations, to create eight subscales and two composite scores for physical and mental health (244). The four subscales for mainly physical health dimensions are: physical function (PF), bodily pain (BP), role limitations (physical) (RP) and general health (GH). The four subscales for mainly mental health dimensions are: vitality (VT), social functioning (SF), role limitations (emotional) (RE) and mental health (MH). The eight subscales are used in combination for calculation of the two overall domain scores: The PCS and the MCS calculation of the values of the SF-36 subscales was performed according to questionnaire manual.

The score is made comparable to the age- and gender-specific population means after additional calculations. Each subscale or composite score is presented as norm-based. The population mean, which is based on the results from a large population cohort, is set to 50 with a standard deviation of 10. A 5-point difference corresponds then to an effect size of 0.5 SD. It is by convention regarded as a medium-sized clinical difference (Cohen's *d*) (48).

#### *EQ-5D questionnaire*

The EQ-5D was developed by the EuroQol Group and is a generic instrument designed to assess and value health status. It consists of 5 questions that can be answered according to one of three levels (none, moderate and severe inconvenience) or in the latest version of five levels. The questions apply to five different dimensions: mobility, hygiene, usual activities, pain and discomfort, and anxiety or depression (33, 36).

The dimensions of the EQ-5D and SF-36 are not comparable, and it is difficult to assemble or compare the two instruments (182). A respondent satisfaction evaluation was performed comparing SF-36 and EQ-5D and both instruments were found comprehensive and easy to understand and fill out. SF-36 offered a possibility for the patients to report their health more extensively and was appreciated and preferred by some, despite the longer questionnaire (175).

#### *Inguinal Pain Questionnaire – IPQ*

The Inguinal Pain Questionnaire (IPQ) was developed according to a suggestion proposed by Kehlet et al (110). IPQ was the first tool specifically designed to assess pain after hernia surgery. The questionnaire shows good validity and reliability (83).

The IPQ questionnaire consists of 18 items and is divided in a pain intensity part using an ordinal 7-grade scale, and a second part describing interference with daily activities using a dichotomous scale. The 7-grade scale for intensity of pain range from “no pain at all” to “severe pain that necessitates seeking emergency care”.

The second part with questions relate to everyday activities and include questions aiming to describe difficulties in physical activities: getting up from a low chair; sitting for more than 30 minutes; standing up for more than 30 minutes; climbing stairs; driving a car and performing sports activities. Consumption of analgesics and need for sick-leave due to pain are also included. IPQ was designed to assess pain before and after surgery.

1. Estimate the severity of pain in the groin you felt before the operation	1. No pain	11. Does driving a car cause you pain?	
2. Estimate the pain you feel right now in the groin on the same side as the operation	2. Pain present but can easily be ignored	12. Has the pain limited your ability to exercise and perform sports?	
3. Estimate the worst pain you felt in the operated groin during this past week	3. Pain present, cannot be ignored, but does not interfere with everyday activities	13. Have you on any occasion taken pain-killers for pain in the operated groin?	No Yes
	4. Pain present, cannot be ignored, interferes with concentration on chores and daily activities		
	5. Pain present, cannot be ignored, necessitates bed rest	14. To what extent has pain in the groin limited your working capability in the last 2 months?	1. I have not needed to take sick leave 2. The pain made me take 1-7 days of sick leave during the last 2 months 3. The pain made me take 1-4 weeks of sick leave during the last 2 months 4. The pain made me take sick leave for the whole of the last 2 months 5. I have disability pension because of the pain in the groin 6. I am not working
4. If you answered "no pain" to question 3 try to remember when the pain in the operated groin disappeared after the operation	6. Pain present, cannot be ignored, prompt medical advice sought		
	1. The pain in the operated groin disappeared within 1 month after the operation	15. Estimate the severity of pain you feel right now in the groin opposite to the operated side	1. No pain
	2. The pain in the operated groin disappeared within 2-3 months after the operation	16. Estimate the worst pain you have felt in the groin opposite to the operated side during this past week	2. Pain present but can easily be ignored
	3. The pain in the operated groin disappeared within 4-6 months after the operation		3. Pain present, cannot be ignored, but does not interfere with everyday activities
	4. The pain in the operated groin disappeared within 7-12 months after the operation		4. Pain present, cannot be ignored, interferes with concentration on chores and daily activities
	5. The pain in the operated groin disappeared within 13-24 months after the operation		5. Pain present, cannot be ignored, interferes with most activities
	6. The pain in the operated groin disappeared recently		6. Pain present, cannot be ignored, necessitates bed rest
5. How often have you felt pain in the operated groin during the past week?			7. Pain present, cannot be ignored, prompt medical advice sought
	1. Once a week	17. To be answered by male patients: have you experienced testicular pain on the same side as the operated groin since the operation?	No Yes
	2. 2-5 times a week	18. Have you been operated on for hernia or had an abdominal operation since the hernia operation in 2000?	No Yes
	3. Every day		
	4. Every day and also during night time		
	5. I have had pain the whole week, both day and night		
6. How long have the episodes of pain lasted in the past week?			
	1. 1 minute to 1 hour		
	2. 1 to 5 hours		
	3. The whole day		
	4. Day and night		
	5. The pain lasted the whole week, day and night		
7. Do you find it difficult getting up from a low chair because of pain in the operated groin?			No Yes
8. Do you find it difficult sitting down for more than half an hour because of the pain?			I don't know
9. Do you find it difficult standing up for more than half an hour because of the pain?			Not applicable
10. Do you find it difficult going up or down stairs because of the pain?			

**Figure 20.** Inguinal Pain Questionnaire, IPQ.  
Kalliomaki et al, European Journal of Pain 2008, with permission.

The drawback of IPQ is that it is an extensive questionnaire which takes a long time to complete, while the strength is estimation of pain during the last week and not just pain right now.

### *Carolina Comfort Scale (CCS) and HerQLes*

The CCS is a hernia mesh repair-specific questionnaire developed in 2008 at the Carolinas Hernia Center, NC, USA. (90). It is a validated instrument that consists of 23 questions regarding difficulties in performing eight physical activities: laying down, bending over, sitting up, activities of daily living, coughing, deep breathing, walking stairs and exercise. Answers are graded from 0 (none) to 5 (worst) regarding mesh sensation, pain and movement limitation. A third part of the CSS is related to mesh sensation and therefore CSS cannot be used preoperatively. This problem has been overcome by the Modified Carolina Comfort Scale (MCCS™) where the third part concerning mesh sensation has been left out (120, 266). The same group have also developed an app CeQOL (Carolinas Equation for Quality of Life) for patients use to improve health and diminish related risk factors before operation.

HerQLes is a validated 12 question enquiry on different quality of life aspects related to a hernia that is yet not widely used (125).

### **Recurrence**

Unsatisfactory results of hernia surgery in terms of high recurrence rates has been a main issue for discussion and has driven the technique development during the history of hernia surgery. Since all recurrences are not reoperated the recurrence rate is higher than the cumulative incidence of reoperations and hard to determine in larger cohorts outside studies.

There are two types of recurrences: early and late (86). Early recurrences are technique related to surgeons experience and skills and/or postoperative complications, while late recurrences are often associated with patient-related factors and type of repair.

Recurrence rates between studies may vary because of a true difference in recurrence being used technique and surgical skills. Methodological differences such as length of follow up (236), method for follow-up (questionnaire/clinical examination/ultrasound or radiologic examinations) and definitions of recurrence (asymptomatic or symptomatic) are important to define and agree on if to compare results.

A postoperative infection and hematoma was found to be a major risk factor for development of recurrence. One third of the infected inguinal hernia repairs result in a recurrent hernia (86, 152).

#### *Suture versus mesh repairs and Lichtenstein versus TEP and TAPP*

Early sutured techniques such as the Bassini repair have been reported to have recurrence rates as high as 20–30% (86, 219). For the Shouldice repair recurrence rates of 1% for hernia expert surgeons (77) up to 10% recurrence rates at 10 years, even in herniologists' hands, have been described (104).

Over the last two decades the recurrence rates have dropped considerably and the use of mesh in hernia repair is the most important factor for this improvement. (158, 220, 225) A tension-free mesh repair ad modum Lichtenstein have been described to have recurrence rates lower than 1% even when performed by non-expert surgeons (114, 229). Other studies show somewhat higher recurrence rates. A Swedish study reported a cumulative 2-year reoperation rate for primary hernias of 1.7% and 4.6% for recurrent hernias (226) while the reoperation rate in a Danish study was 2.4% after primary Lichtenstein repair (38). Many of the recurrences after open mesh repair are found medially interpreted as inadequate overlap at the pubic tubercle (66).



Other studies report total recurrence rates around 3% in mesh repairs with similar recurrence rates in laparo-endoscopic and open mesh repairs (124, 158, 280). However, there are studies and meta-analyses that claim a greater risk of recurrence after laparo-endoscopic repair (186, 220). It has been proposed that inadequate mesh size is an important risk factor for developing a recurrence, particularly after laparo-endoscopic repairs (86, 136). In a meta-analysis by Schmedt et al, one study using small meshes for the laparo-endoscopic repairs (168) influenced the results strongly. Excluding that study caused the difference in recurrences to disappear (93). Schouten et al have pointed out that the higher recurrence rates for laparo-endoscopic repairs reported by some may be explained by a longer learning curve and that the results many times reflect part of the learning curve (222).

In the recently published HerniaSurge Guidelines one of the key questions was whether recurrence rates differed between laparo-endoscopic (TEP/TAPP) and Lichtenstein repairs. Studies comparing these techniques concluded that laparo-endoscopic techniques have a longer the learning-curve, less chronic pain, and similar recurrence rates (93). From the SHR Sevonius et al reported that Lichtenstein repairs of a primary hernias result in a somewhat lower reoperation rate for recurrences while a preperitoneal mesh technique is the best for repair of a recurrent hernia (226).

Inadequate or no mesh fixation has been proposed to be a risk for recurrence in laparo-endoscopic techniques (86, 136). However, there are conflicting findings from meta-analyses reporting no differences between fixed and non-fixed meshes (215, 245, 249). Furthermore, there seem to be no difference in recurrence rates between glue and staples/tacks fixation (109, 218) or between LWM and HWM (54, 217).

#### *Patient-related risk factors for recurrence*

The cumulative incidence of reoperations for recurrent hernias according to the SHR is 3% following repair of primary inguinal hernias and 7% following repair of recurrent inguinal hernias over a five year period (226). Operations for recurrent hernias have also been described as a risk factor in a systematic review and meta-analysis study from Denmark (39).

Other patient-related factors may also increase the risk of recurrence. Women are at higher risk than men since a femoral hernia may be missed if an open repair is performed without examining the femoral canal (91, 181, 257). Size of the hernia does not seem to relate to the risk of recurrence. However, a direct inguinal hernia has a higher risk of recurrence compared to other hernia locations (39). Obese patients have a higher risk for recurrence compared to non-obese patients

(39, 208). Furthermore, smoking increases the risk for suffering a recurrence (39, 104, 235) and so do collagen disease (118), malnutrition, diabetes, use of corticosteroids, chronic lung diseases, etc.

#### *Surgeon-related risk factors for recurrence*

The impact of the surgeon's experience and skills on recurrence rates are interesting to explore. Several authors have pointed out the learning curve differences between hernia repair techniques. The laparo-endoscopic repairs have a longer learning curve than Lichtenstein do and surgeons under training need 30–100 laparo-endoscopic repairs to become skilled enough to perform the operation on their own (8, 74, 142, 163, 273). Schouten et al reported that the surgical skills increases up to 400 laparo-endoscopic operations when measuring the frequency of recurrence and conversion (222). Inadequate dissection without sufficient exposure of all inguinal openings is probably an important cause of recurrence rather than an overlooked hernia after laparoscopic surgery (86).

Training residents in laparo-endoscopic hernia surgery is not a risk. A Finnish study has reported similar results for supervised resident-performed operations as for operations performed by consultants (188). When adequate laparo-endoscopic skill is reached, 30 operations per year is enough for maintaining good results (11). Few hernia operations per year (less than 5) have been shown to result in increased recurrence rates independently of hernia repair technique (169, 180).

Establishing specialised high-volume hernia centres have decreased recurrence rates significantly (14, 246) by standardisation of surgical techniques and educational curriculums.



To investigate:

- ❖ Chronic postoperative pain and QoL in Totally ExtraPeritoneal (TEP) repair in men comparing permanent fixation to no fixation
- ❖ If TEP without mesh fixation is safe concerning recurrence of hernia
- ❖ Pain and QoL before and one year after surgery comparing TEP to open mesh repair by Lichtenstein
- ❖ Long-term sexual dysfunction after TEP repair in sexually active men, introducing a new short form questionnaire for inguinal hernia related pain at sexual activity
- ❖ Long term sexual dysfunction comparing TEP to Lichtenstein in sexually active men



# METHODS

The thesis is based on two large patient cohorts, one from data of the Swedish Hernia Register and one RCT study. We have analysed chronic pain and sexual dysfunction in both patient cohorts.

## Swedish Hernia Register study

It is based on data from the SHR register. All men in Sweden, 30–75 years old, operated with a TEP for a primary hernia 2005–2009 registered in SHR were included. A questionnaire was sent in 2010 with one reminder.

The questionnaire consisted of four parts: questions on associated diseases, IPQ, SF-36, and a specific questionnaire on sexual dysfunction (the latter only sent to patients being 30–60 years old).

Data selected from the SHR were: age, ASA, BMI, hernia size according to the EHS classification (162), hernia type, type of mesh (HW and LW), type of fixation (no fixation, glue or staplers/tackers), intraoperative complications, operative time, inpatient or outpatient, and postoperative complications within 30 days.

## Randomized control trial

It is a single centre randomised study from Skåne University Hospital, Malmö. Outpatient operations were performed in Landskrona Hospital. All men between 30–75 years with a unilateral primary inguinal hernia were assessed for inclusion and randomised to either TEP or Lichtenstein treatment. Patients were included between 2008 and 2014.

A detailed protocol for history and clinical examination was registered before surgery, at one month and one and three years after surgery. Weight, length, ASA class, hernia side, occupation, and symptoms. Physical functions were registered like climbing stairs, squatting and rising from bed. Clinical examination of the

groin was performed according to a specific protocol in 5 anatomical points in groin. Examination was performed using a cotton swab and toothpick symmetrically on both sides.

IPQ, SF-36 and a specific questionnaire on sexual dysfunction (the latter only sent to patients being 30–60 years) were administered at all visits.

All surgeons agreed on the highly standardized surgical techniques and were board certified. Documented operative data was: operating surgeon, time for anaesthesia and operation, hernia type, handling of nerves in the open group, intraoperative complications, and the surgeon's grading of technical difficulties and the surgeon's satisfaction with the operation. Hospital stay, postoperative

NP = No pain										
T = Tenderness										
HT = Hypoesthesia, on touch										
HN = Hypoesthesia, with needle										
HE = Hyperesthesia										
RP = Radiated pain										

Right side:										
	NP	T	HT	HN	HE	RP				
1	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				
2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				
3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				
4	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				
5	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				

Testicular atrophy	Right	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
	Left	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
Varicocele	Right	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
	Left	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
Tenderness adductor tendon	Right	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
	Left	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
Pain on adduction of hip	Right	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
	Left	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
Pain on rotation of hip	Right	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No
	Left	<input type="checkbox"/>	Yes	<input type="checkbox"/>	No

**Figure 21.** Protocol for clinical examination of both sides of the groins

complications within one month, reoperations, sick leave and time to full recovery was recorded.

## Chronic pain studies

### **Register study - chronic pain (Paper I)**

The aim of this study was to examine whether the method of fixation of the mesh influences the occurrence of chronic postoperative pain/discomfort. We studied no fixation/non-permanent fixation (NF/NPF) to permanent fixation (PF) in men operated with TEP repair for a primary inguinal hernia.

Our hypothesis was that unfixated mesh resulted in less chronic pain or discomfort than fixated mesh without paying the price of a higher recurrence rate.

Our definition of a *clinically relevant* level of pain was *pain that could not be ignored* namely Grade 3 or worse in question 2 of the validated inguinal Pain Questionnaire (IPQ).

We used the Short Form-36 (SF-36) for assessing of health-related quality-of-life (HRQL). The IPQ questionnaire was used to measure hernia-induced pain and functional disabilities. Pain reaction over time was also studied.

The assumption regarding chronic pain was 8% in NF/NPF and 16% in PF group. 329 patients were required in each group to detect 8% difference ( $\alpha=0.05$ ) with a power of 80% and calculated attrition of 30%.

### **RCT – chronic pain and QoL (Paper II)**

The aim was to analyse chronic pain and quality of life comparing TEP to Lichtenstein before and one year after surgery in a standardized setting for operative techniques in primary unilateral inguinal hernia in men. Both techniques were performed by department certified hernia specialist.

The hypothesis was that unfixated preperitoneal mesh gives less chronic pain or discomfort compared to Lichtenstein and is comparable regarding recurrence.

Primary endpoint was pain/discomfort last week, IPQ 2, “Pain that could not be ignored” Grade 3 or worse comparing TEP to Lichtenstein one year after surgery. Secondary endpoints were complications, time to full recovery, quality of life, adverse events and recurrence at one year. SF-36 and the IPQ questionnaire was used. A risk factor analysis for chronic pain was performed.

The assumption concerning chronic pain was 8% in TEP and 20% in Lichtenstein. 174 patients were required in each group to detect a 12% difference ( $\alpha=0.05$ ) with a power of 90% and a calculated attrition of 13%.



# Sexual dysfunction due to groin pain

## **Register study – sexual discomfort/dysfunction (Paper III)**

The aim was to introduce a new questionnaire, easy to use in large cohorts of patients having pain/dysfunction at sexual activity related to the operation of the groin hernia.

A short form questionnaire for inguinal hernia-related pain-induced sexual dysfunction was developed based on the principles of professor Kehlets group and mailed to the patients 30–60 years of age (3).

IPQ, SF-36 and the specifically developed questionnaire on sexual dysfunction induced by groin pain were mailed to patients. Sexual dysfunction over time was analysed. A risk factor analysis for sexual dysfunction was performed.

## **RCT – sexual discomfort/dysfunction (Paper IV)**

The aim was to compare the effect of hernia surgery on groin pain induced sexual discomfort/dysfunction at one year comparing TEP to Lichtenstein in a randomised setting. Secondary aims were groin pain induces sexual discomfort/pain at three years, QoL in relation to pain at sexual activity over time and postoperative onset of pain at sexual activity, registered as harms.

The hypothesis was that unfixed preperitoneal mesh gives less sexual pain/discomfort compared to Lichtenstein but is comparable regarding recurrence rate.

A specific questionnaire for sexual dysfunction/pain, SF-36 and the IPQ questionnaires were used pre operatively, at one and three years in male patients aged 30-60 years. A risk factors analysis for pain at sexual activity was performed.

A total of 131 patients in each group were required to distinguish a difference of 12% ( $\alpha = 0.05$ ) with a power of 80%. Allocation ratio was 1:1.

## Statistical methods

IBM SPSS Statistics Software version 22 was used. Age and BMI are reported as mean and standard deviation (SD). Operation and follow-up time were reported as median and interquartile range (IQR) in the register based study and as mean and standard deviation in the RCT.

Continuous variables: age, BMI, operating time, follow-up time and SF-36 were calculated using Student's t-test. Categorical variables: IPQ, recurrence and

physical functional score (only paper 2) was calculated using Pearson's  $\chi^2$  test or Fisher's exact test when appropriate.

Pain over time was calculated using ANOVA. The risk factor analysis was calculated using binary logistic regression. Risk factors were chosen before analysis and entered simultaneously.

**Sexual Survey**  
after inguinal hernia surgery

**A: Are you sexually active?**

Yes  
 No

If you answered "Yes", continue to answer the next question.

---

**B: Do you have pain/discomfort in your groin during sexual activity?**

Yes  
 No

If you answered "Yes", continue to answer the questions below.

---

**If you have pain or discomfort during sexual activity please answer the questions below:**

**1. Does the pain or discomfort in the groin impair your sexual activity?**

Yes  
 No

**2. How often do you have pain or discomfort during sexual activity?**

Rarely (every 4th time or less)  
 Often (every 2nd or 3rd time)  
 Always (every time)

**3. Mark with an X on the line, which best suits your average pain experience during sexual activity**

no pain at all \_\_\_\_\_ worst pain imaginable

**4. Mark with an X on the line any impairment of erectile function?**

no impairment \_\_\_\_\_ total loss of erectile ability

**5. Mark with an X on the line any impairment of ejaculatory function?**

no impairment \_\_\_\_\_ total loss of ejaculatory ability

**6. Do you feel depressed because of your sexual dysfunction?**

Yes  
 No

Figure 22. Questionnaire on sexual dysfunction

## Ethical considerations

Both the register based and prospective randomised study were approved by the Regional Ethics Review Board.

### **Information about study and consent**

Careful, oral and written information was provided by the physician and the patient also received information on the benefits and risks of participating in the research study. Patients were aware that we did not yet know which operating method was better in preventing chronic postoperative inconvenience, but that both methods were used without difference regarding complications. Patients were informed that participation was voluntary and that they have the right to cancel participation without explanation and without consequences. For those who wished, consideration time were offered.

The patient received a stamped envelope to return the completed Signed Informed Consent within one week if they agreed to participate in the study. Telephone contact with the study coordinator at the secretariat (a specially trained research nurse) was offered for supplementary questions on the participation of the study.

### **Data collection and data management**

The study was controlled via an established secretariat in Malmö. Principle investigator was responsible for register data that was kept on a separate computer without general availability. In case of inclusion and randomisation, each individual was assigned a unique protocol number from the study secretariat. Study data was collected in standardised protocols, which was then transferred to a data register for statistical analysis. All data was anonymised after data registration prior to analysis. Therefore, researchers or unauthorized persons could not connect data with the patients. The register thus contained no person numbers, names or addresses.

A special register was kept for monitoring and follow-up during the study period, in which the person numbers could be linked to the protocol number. After the completion of the study, the control data file is to be destroyed. The coding is then only available in paper print during the archive period stored in the research archive at the secretariat.

In addition, all data is reported in statistical groupings, mainly after the randomization outcome, without identifying any individuals.

### **Evaluation of the risk-benefit ratio**

Participation in the study does not change the two established operating techniques or the risk profile associated with the method. Therefore, there is no more risk of patient injury than the one usually happens in today's established operations.

It is advantageous for patients to be taken care of by surgeons who are specially working with hernia problems at our clinic and that they are offered more extensive personal contact and follow-up. In clinical practice, there are no return visits for patients who are operated for inguinal hernia except in case of inconvenience. Therefore, patients are extra controlled free of charge after one and three years and may then be offered extra discussion on remaining problems after surgery. The patient also receives a simple direct contact with the researcher.



# RESULTS

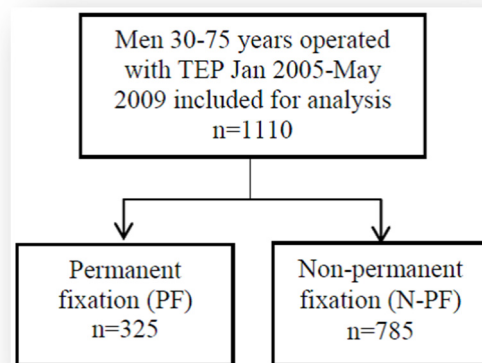
## Chronic pain

### Register study – chronic pain (Paper I)

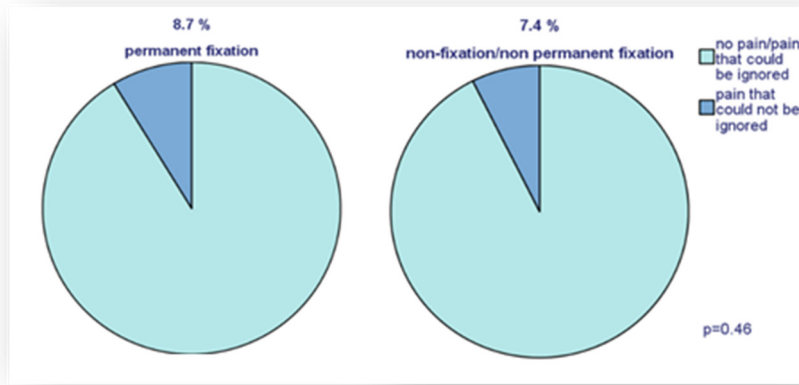
A total of 1892 patients were identified for possible inclusion and were mailed the questionnaire. A total of 1110 patients (68%) remained for analysis, Figure 23.

The mean age was 57 years, BMI 25 and 97% was ASA I or II. HWM were used in 66%, more frequently in the PF than in the NF/NPF group ( $p<0.015$ ). Postoperative complications were reported in 7.7% with no difference between groups. No reoperation within 30 days was reported. A recurrent operation was performed in 1.5% (5/325) in the PF and 1.3% (10/783) in the NF/NPF group after a median of 33 months follow up, ( $p<0.735$ ).

A total of 99% answered the IPQ questionnaire. For the primary endpoint “pain that could not be ignored” during the past week (IPQ Question 2), a total of 85 patients (7.7%) reported chronic pain with no difference between PF and NF/NPF, Figure 24. “Pain right now” (IPQ Question1) was reported by 59 patients (5.4%) with no difference between groups.



**Figure 23.** Flowchart - register study on chronic pain (Paper I)



**Figure 24.** Pain vs no pain using permanent or no/non-permanent fixation according IPQ Question 2.

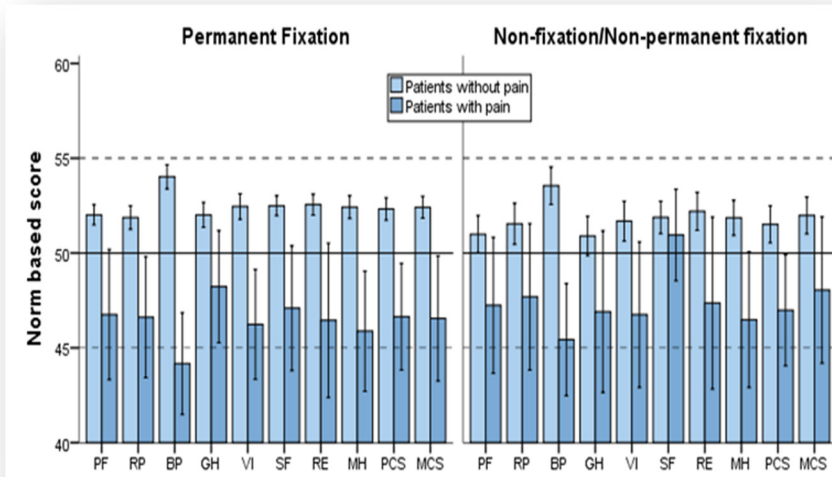
Six patients had severe pain immediately after their operation. Pain had disappeared in 81% of patients within one month (IPQ Question 3). Only one patient reported long term pain. Patients suffering pain “every day” or worse during the past week (IPQ Question 4) were reported by 42 (3.8%). Pain lasting “all day” or worse was reported by 2.0%. Persisting testicular pain (IPQ Question 16) was reported by 13.9%. Symptoms prior to surgery had disappeared at follow-up (IPQ Question 15) in 91% of patients. Other long term sequels are reported in Table 1. Risk factors for pain and SF-36 are reported in Table 2 and Figure 25.

	Permanent fixation (PF) n=325	No-permanent fixation (NF/NPF) n=785
Need of painkillers (IPQ 12)	0.9 %	1 %
Dissatisfied with operation (IPQ 14)	6 %	4 %
Testicular pain (IPQ 16)	12 %	15 %
Feeling mesh in groin (IPQ 17)	8 %	9 %
Developed new pain in groin (IPQ 18)	6 %	5 %
Regreting operation (IPQ 19)	2 %	1 %

**Table 1.** Inguinal Pain Questionnaire (IPQ), selected questions

Factors	Multivariable model (n=85)		
	OR	95% CI	P-value
Mesh Weight			
Light	1		
Heavy	0.99	0.55-1.78	0.975
Fixation			
PF	1		
NF/NPF	0.97	0.55-1.72	0.921
Postoperative complications			
No	1		
Yes	2.44	1.13-5.25	<b>0.023</b>

**Table 2.** Selected risk factors for pain. The only risk factor for long term pain was a postoperative complication. Neither fixation nor a HWM was a risk factor.



**Figure 25.** SF 36 comparing fixated to non-fixated mesh in TEP operated patients with and without pain. Quality of life is considerably reduced in both physical and mental domains in chronic pain patients including both physical and mental domains without difference between fixation or no fixation.



### Conclusion

There is no difference between permanent and no/non-permanent fixation concerning long term pain with a frequency of 7.7% over all. A post-operative complication was a risk factor for chronic pain. Reoperation rate for a recurrence was 1.3% after a median of 3 years follow up in a national wide study including surgeons at different educational levels performing a TEP operation.

### Randomized controlled trial – chronic pain (Paper II)

A total of 482 patients (240 TEP, 242 Lichtenstein) were randomised and 82% of patients remained for one-year analysis, Figure 26.

“Pain last week” was reported by 7.4% after TEP and 9.8% after Lichtenstein ( $p<0.398$ ) being the primary endpoint, Figure 27. Pain frequencies were less when reporting “pain right now” on 4.2% after TEP and 5.9% after Lichtenstein ( $p<0.450$ ) versus “pain last week”.

Surgeons considered TEP more difficult than Lichtenstein ( $p<0.001$ ) and considered also the operation to be technically more difficult in 14% of indirect and 1% in direct hernia ( $p<0.001$ ) irrespectively of operative technique used. The surgeon was satisfied with his/her performance in 100% of the Lichtenstein and in 96% in TEP ( $p<0.003$ ).

Pain modalities in different localisation are displayed pre and postoperative in Figure 28. Sensory changes preoperatively was found in 18.6% and postoperatively in 7.6% in TEP and 36.5% in Lichtenstein ( $p<0.001$ ). It decreased to low numbers in the TEP group, but increased substantially after Lichtenstein.

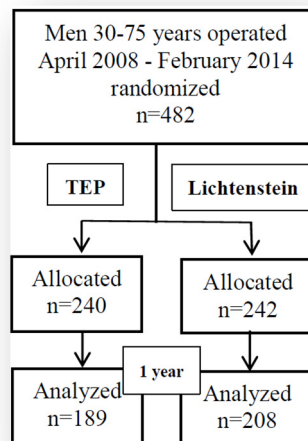
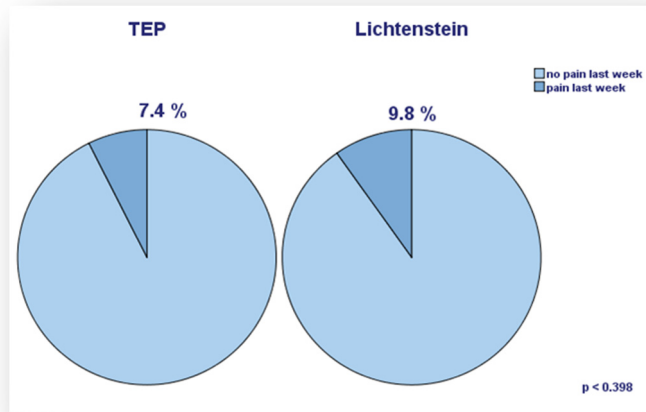
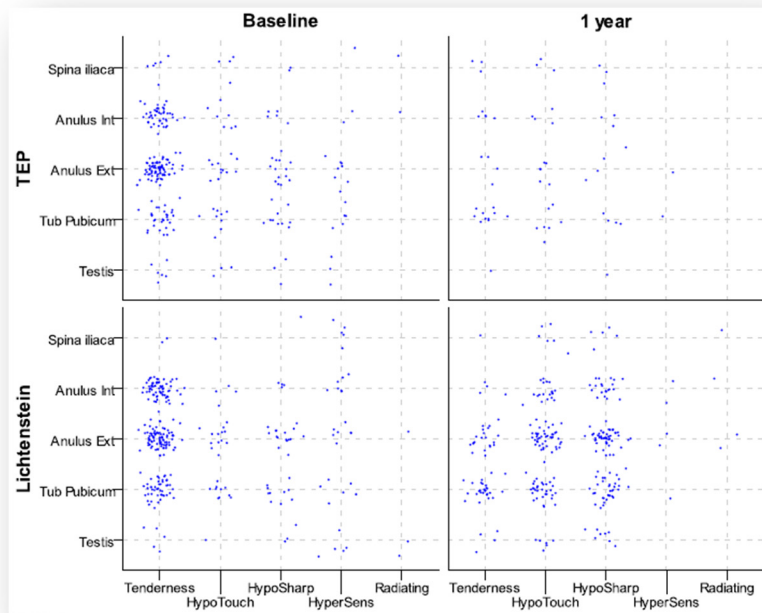


Figure 26. Flowchart RCT study - chronic pain (paper II)



**Figure 27.** Percentage of pain vs no pain according IPQ Question 2 for TEP and Lichtenstein operated patients.



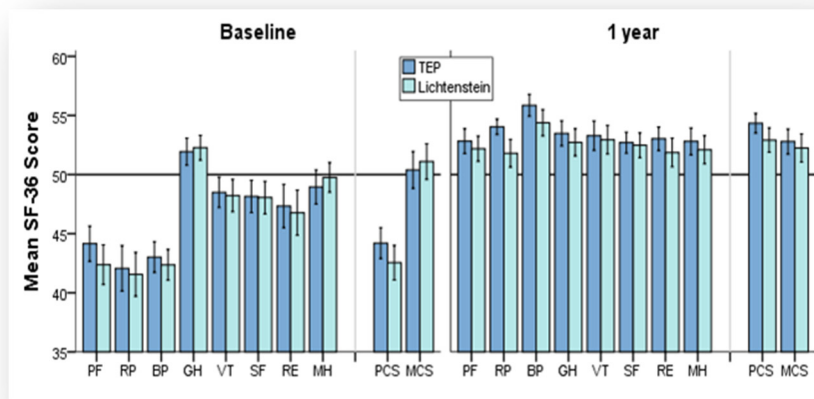
**Figure 28.** Clinical examination. Sensory changes for tenderness, reduced sensitivity for touch, reduced sensitivity of sharp picking, hyper-sensitivity for picking, radiating pain displaced. All displaced in five locations in the groin

SF-36 was reported comparing groups at baseline and one year, Figure 29. The preoperative registrations showed a remarked reduction especially in physical subscales resulting in a 7 point reduction of the PCS compared to the norm. There was no influence on the MCS compared to the norm preoperatively. All subscales and PCS increased to levels above the norm postoperatively in both groups.

At one year 1.6% recurrences were noted at clinical examination and 98% of patients were satisfied with the operation, with no difference between groups. Two patients in the Lichtenstein group regretted the operation but none in the TEP group.

*In conclusion*

The highly standardized setting, included consensus on operative strategy, education of surgeons performing the operations, extensive protocols for pre- and postoperative surveillance of surgical and patient reported outcomes resulted in satisfied patients, relatively low rates of chronic pain, good symptom relief, restored QoL and low recurrence rates with outcomes and less long-term sensory disturbances for TEP.



**Figure 29.** SF-36 The eight subscales and two composite scores of SF-36 at baseline and 1 year for the TEP and Lichtenstein group.

# Sexual discomfort

## Register study – sexual discomfort (Paper III)

A total of 538 patients were included and 44 (8.2%) reported pain during sexual activity (PS), Figure 30. Out of these reported 33 (75%, resulting in 6.1% of total number of patients) sexual dysfunction due to the pain in the groin in mean 33 months after surgery, Figure 31.

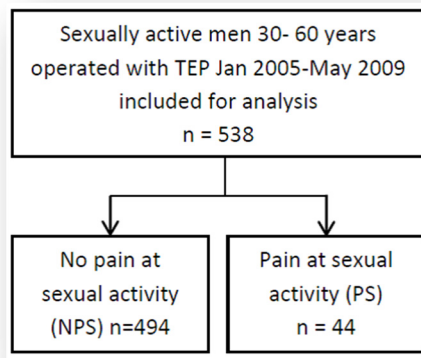


Figure 30. Flowchart – Swedish Hernia Register SHR study. Pain a sexual activity

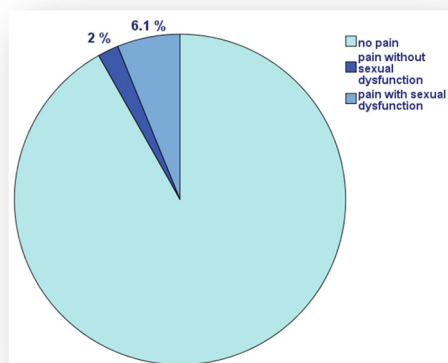


Figure 31. Pain during sexual activity and sexual dysfunction due to groin pain in TEP operated patients 3 years after operation

**Table 3.** SexIHQ results in the 44 patients having pain at sexual activity.

TABLE 3   SexIHQ results (n = 44).	
Questions	Patients n (%)
1. Impairment of sexual function	
No	11 (32)
Yes	33 (68)
2. Pain frequency	
Rarely	25 (57)
Often	11 (25)
Always	8 (18)
3. Pain (VAS, cm)	
<3	25 (58)
≥3-7	14 (33)
>7	4 (9)
4. Erectile dysfunction (VAS, cm)	
<3	29 (71)
≥3-7	8 (19)
>7	4 (10)
5. Ejaculatory dysfunction (VAS, cm)	
<3	26 (63)
≥3-7	7 (17)
>7	8 (20)
6. Depression	
No	21 (52)
Yes	19 (48)

**Table 4.** Inguinal pain questionnaire results for specific questions on postoperative issues.

	No pain at sexual activity (NPS) n=494	Pain at sexual activity (PS) n=44	p-value
Postoperative complications	6 %	18 %	< 0.005
IPQ 2 pain past week	5 %	44 %	< 0.001
IPQ 14 operation dissatisfaction	3 %	33 %	< 0.001
IPQ 16 testicular pain	13 %	49 %	< 0.001
IPQ 19 regretting operation	1 %	14 %	< 0.001

There were no differences between the NPS and PS groups regarding mesh-weight, fixation, uni- or bilateral operation, intraoperative complications, operation time, and hospital stay.

A postoperative complications was reported in a total of 6.5%, with 6% in the NPS and 18% in the PS group ( $p < 0.005$ ). A postoperative infection was reported in 0.6% (3 patients), all in the NPS group. No reoperation within 30 days was performed.

The option “Always having pain during sexual activity” was reported by 1.5% of the patients, “severe erectile dysfunction” (VAS  $\geq 7$ ) by 0.7%, “severe ejaculatory dysfunction” (VAS  $\geq 7$ ) by 1.5% and “depression due to sexual dysfunction” by 3.5%, Table 3. The proportion of patients having “Pain at sexual activity” (PS) did not change over time. Some of the IPQ results are reported in Table 4.

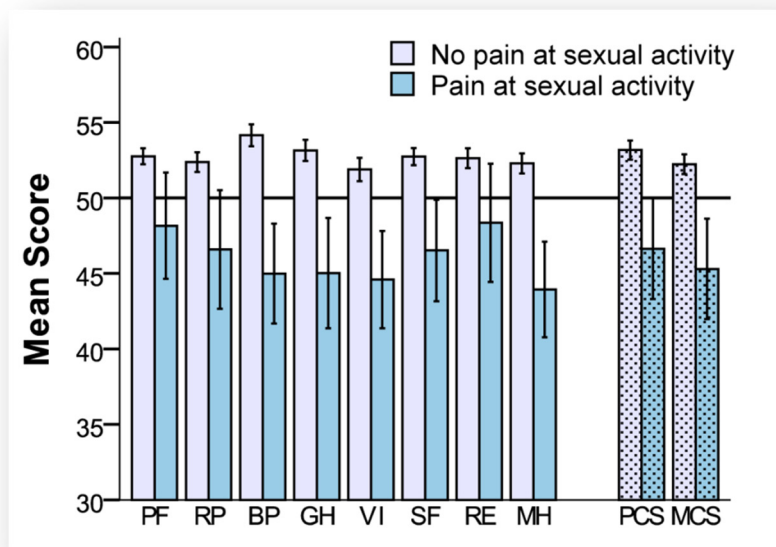


Figure 32. SF-36, pain vs no pain patients. Pain patients  $n=44$

SF-36 scales were lower compared to the norm in PS patients but slightly above the norm in NPS patients, Figure 32. Postoperative complications was a risk factor for during sexual activity, OR 4.89 (95% CI 1.92–12.43;  $p < 0.001$ ).

### Conclusion

SexIHQ was developed to assess sexual dysfunction due to pain after inguinal hernia repair in male patients. Sexual dysfunction due to groin pain after hernia surgery by TEP is surprisingly common. It is suggested to inform the patient preoperatively on the risk of having pain during sexual activity following hernia surgery. SexIHQ is an easy-to-use questionnaire that can be applied in large cohort of patients.

### RCT – sexual discomfort/dysfunction (Paper IV)

A total of 243 patients (111 TEP, 132 Lichtenstein) were finally operated, Figure 33. 97% remained for 1-year and 90% for 3-year analysis. 35% of patients experienced pain at sexual activity preoperatively. This was reduced to 6% in TEP and 12% in Lichtenstein ( $p<0.09$ ) after one year and to 7% in TEP and 9% in Lichtenstein ( $p<0.56$ ) after 3 years. Pain patients at sexual activity over time is described in Figure 34.

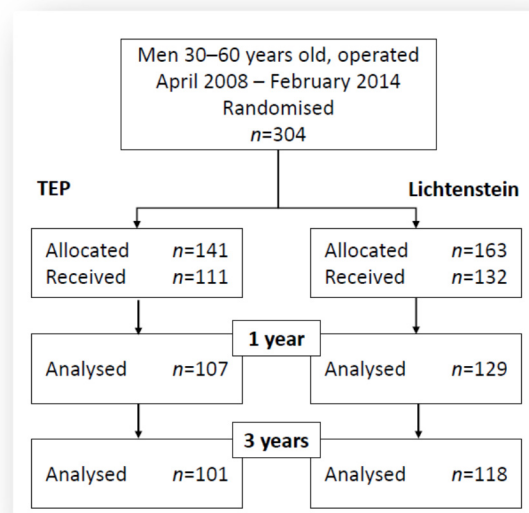
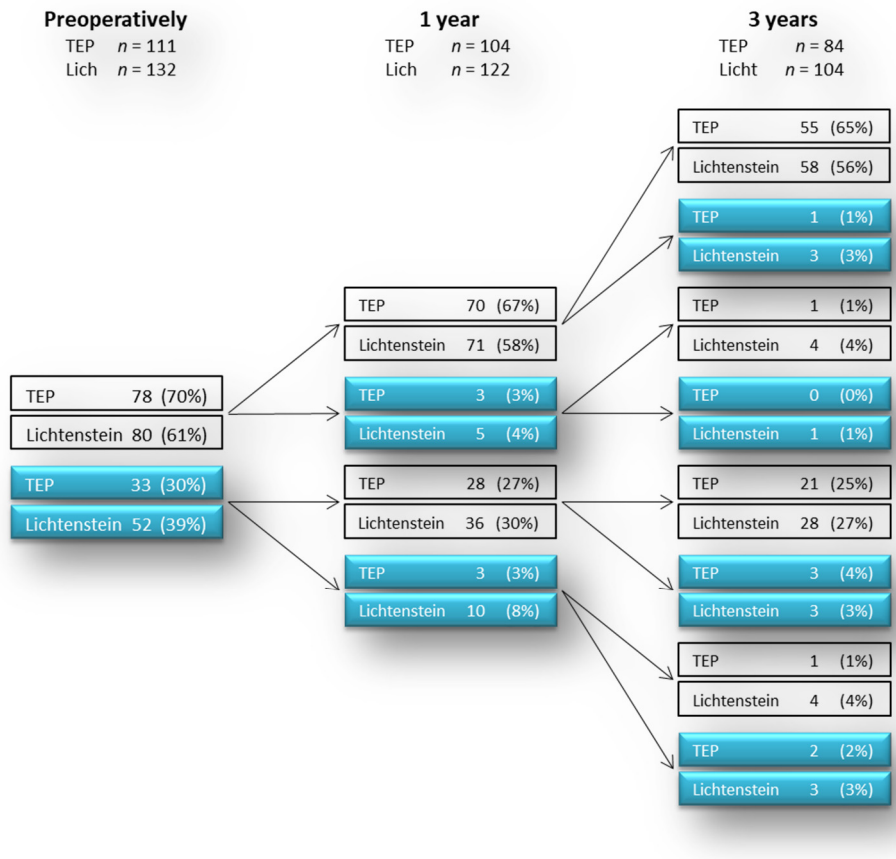


Figure 33. Flowchart RCT – sexual dysfunction

QoL measured by SF-36 was preoperatively reduced especially in physical domains and in patients with pain at sexual activity. It improved (especially in physical domains) over time in for both pain and no-pain patients with no difference between TEP and Lichtenstein groups, Figure 35. Risk factors for pain at sexual activity was the Lichtenstein technique and preoperative pain.



**Figure 34.** Patients with and without pain at sexual activity in TEP and Lichtenstein at different time points. The move over time in having pain or not pain are displaced. Blue are pain patients and white non-pain patients.

Patients should preoperatively be informed on the relation between pain at sexual activity and inguinal hernia/operation.

*Conclusions*

Pain at sexual activity in inguinal hernia patients is far more common than anticipated (35%) and reduces QoL. Patients will restore QoL but pain is still present at sexual activity after operation in 8% with no difference between techniques.



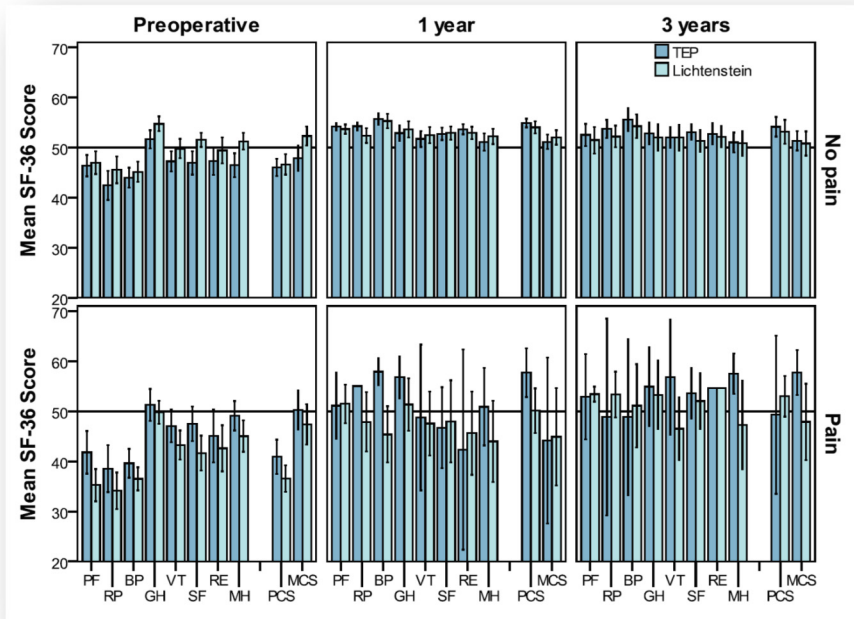


Figure 35. SF-36 in no-pain and pain patients comparing Lichtenstein to TEP over

# DISCUSSION

Both open mesh repair according to Lichtenstein and endoscopic techniques according to TEP are established methods for inguinal hernia repair. The aim of this thesis was to compare the techniques from different perspectives. We have concentrated to include only men with a primary inguinal hernia. Chronic pain is the most feared problem after inguinal hernia surgery.

We have performed a large study based on TEP operated patients in the SHR. Our aim was to compare permanent fixation to an un-fixed mesh concerning chronic pain without paying the price of a higher recurrence rate. Surgeons at different educational levels performed the operations. This would of course influence the quality of surgery and the outcome for the patients. A strength is that all operated patients are included and makes result more generalizable. The study is cross-sectional and results are gathered at a fixed time point making the follow up time different for patients. This might be a draw back for results, but it can be compensated by the large cohort of patients and the option to study results over time.

The other study is a randomised controlled trial (RCT) comparing TEP to gold standard Lichtenstein. The drawback of an RCT is that the inclusion criteria are more strict making results less generalisable since all patients will not meet the inclusion criteria. On the other hand the techniques could be highly standardised among performing surgeons. The complexity of a technique when used in different clinical situations are also important. One or the other technique could be mastered more easily in different clinical scenarios and the limits for this could be analysed in a setting were surgeons are all skilled and have seen several scenarios over time.

## Chronic pain – paper I and II

We compared permanent (PF) with no or non-permanent (NF/NPF) mesh fixation in TEP in a register based study. Our hypothesis that permanent mesh fixation was associated with more pain was not confirmed in this study.

The strength is the comprehensive coverage and long-term follow-up of a large unselected cohort of consecutive patients. These are also recruited on a nationwide basis from the SHR that covers 95% of all groin hernia operations performed in Sweden. We can follow the results of every day TEP-performing surgeons, as opposed to hernia experts that participate in RCTs. A drawback is that preoperative data on the patients' symptoms and quality of life are lacking due to the retrospective follow up.

A validated questionnaire, IPQ, with detailed questions on pain and other postoperative complaints was used (82). IPQ Question 2 "worst pain perceived last week" was shown to be a better predictor for pain than the measure "pain felt right now". Our cut-off level of pain was chosen to select patients with *pain that could not easily be ignored*, regarded as clinically relevant (IPQ Q2 level 3–7).

Pain was reported by 7.7%. This is a relatively low incidence compared to other reports (224, 247, 252). We found no difference in pain between the PF and NF/NPF groups, in contrast to the results of the RCT, which reported a difference between PF (22%) and NF (15%) patients (247). This might be explained by the definition of pain. Some degree of pain was seen in 15% of PF and in 13% of NF/NPF patients in our study, i.e. no difference, and remained so between groups, even with the more strict definition. In another large RCT performed by our group, comparing TEP to Lichtenstein, the five-year pain level was 9.4% in the TEP (PF) and 18.8% in the Lichtenstein (68). Pain remained at the same level once it had levelled off, like in the Eklund study. This indicates that chronic pain may be a lifelong problem.

A low frequency of a recurrent hernia operation on 1.5% was noted, with no difference between PF and NF/N-PF after a median of 7.5 years follow-up indicating that permanent mesh fixation is not necessary to prevent recurrence.

SF-36 was used for QoL evaluation. Both groups performed above the norm in all sub-scales at long-term follow-up, indicating excellent results as a whole, also shown in an RCT (21).

In our RCT we applied an extensive protocol using several outcome instruments in order to analyse sequelae from different perspectives for both the individual patient as well as for the techniques of TEP and Lichtenstein. TEP had short term advantages but also demonstrated less sensory disorders at one year. Still patients had some pain after one year but it seemed low grade since 98% of patients were satisfied.

"Pain last week" was 7.4% after TEP and 9.8% after Lichtenstein ( $p<0.398$ ) and "pain right now" was 4.2% after TEP and 5.9% after Lichtenstein ( $p<0.450$ ) at one year respectively. Analysing pain over time ("pain last week") will include

every day activities and not only “pain right now”. In our study this increased the reported pain by more than 65% compared to the numbers reported at rest.

It was concluded in a fairly recent meta-analysis (32) that there was insufficient evidence to determine a greater effectiveness for either technique, although differences in favour of TEP were seen for short-term outcomes and chronic pain. In our study we did also show short-term advantages of TEP but no statistical difference between techniques concerning chronic pain. Our hypothesis was not met which could be explained by better result for Lichtenstein patients than presumed. An explanation for this might be the high educational status, consensus on surgical details and training operative techniques caring for details.

A limitation is that the inclusions continued for 6 years due to strict criteria and incapability to include around 50% meeting the inclusion criteria. It is difficult run a randomised study the more people that are – and need to be – involved.

In conclusion, analysing chronic pain after inguinal hernia surgery, both from a national perspective in a register based study and from a highly specialised centre, in a randomised setting will show how techniques perform over all. Only TEP can be compared and the long-term levels of pain and QoL seem to be equal using the same instrument for evaluation. An explanation for this might be that TEP surgeons in Sweden consists of a fairly small group of dedicated surgeon and a majority of the operations are performed by these surgeons.

## Sexual discomfort – paper III and IV

The most important outcome regarding inguinal hernia surgery except chronic postoperative pain is postoperative sexual dysfunction due to pain in the groin. A relatively short questionnaire, specifically investigating genital pain and sexual dysfunction in hernia patients was developed based on the Danish questionnaire principles developed by professor Kehlet. We enhanced these ideas with the purpose of making a more user-friendly and specific questionnaire that only assessed impairment of sexual function caused by pain from the hernia or the surgical repair. The goal was to only approach the patients having sexual impairment, as a function of pain from a hernia or after hernia repair.

A limitation of a register based study is the lack of preoperative data. Including patients from a national register has also its advantages. All levels of experience and varying techniques used by operating surgeons are included, resulting in high external validity.

We have in our RCT study used the newly developed sexual questionnaires to investigate more in detail sequelae due to the surgery per se. In this RCT we also had the possibility to compare postoperative outcomes in relation to preoperative sexual impairments and to see how the operation affected the problems. Another strength of this randomized study is the existence of both preoperative and postoperative data and long term follow up of 3 years.

QoL is preoperatively often reduced in hernia patients, but will usually be restored after operation. SF-36 is a validated and commonly used instrument for QoL measurements. It is advisable to use a validated instrument so that data from different studies can be compared.

Harms (new chronic pain or other sequelae surgical that did not exist before operation) is an important outcome since it is irreducible and can cause lifelong suffering.

Our studies will hopefully bring some wider understanding on the importance of using validated instruments to report on outcome of hernia surgery with the aim to enhance quality and reduce chronic pain and sexual dysfunction.

# CONCLUSIONS

The TEP procedure for inguinal hernia repair in men is associated with a low frequency of chronic pain, with no difference between permanent and non-permanent fixation of mesh in a national population based study. A postoperative complication is a risk factor for chronic pain.

Both TEP and Lichtenstein repair result in low rates of chronic pain, good symptom relief, satisfied patients, restored QoL, and low recurrence rates when performed in a highly standardized setting. TEP is beneficial concerning short term outcomes and sensory disturbances.

A short form questionnaire, suitable for large cohorts, was developed to assess sexual dysfunction due to groin pain after inguinal hernia repair in male patients. Sexual dysfunction due to groin pain after hernia surgery by TEP is surprisingly common. Patients should preoperatively be informed of the risk of having pain during sexual activity following groin hernia surgery.

Pain at sexual activity (SEX-P) in inguinal hernia patients is more common than suspected and reduces QoL. Lichtenstein repair was one of two independent risk factors for one year postoperative SEX-P. Hernia repair will markedly reduce SEX-P and restore QoL in the majority of patients. The patient should be informed on the relation between SEX-P and an inguinal hernia as well as on possible consequences of hernia repair.



# FUTURE PERSPECTIVES

Inguinal hernia is still the most common surgical operation performed in males throughout life and sequelae from an operation is still too high. There is a need to tackle these problems much further and to find better solutions, to both prevent and cure this disease. Basal metabolic solutions to enhance quality of native collagen and fascia to “self-heal” is of course wishful thinking: that no surgeon will have the skills or capacity to solve. Qualifications for basic research is warranted. This is of course priorities to be made from the society and there are political decisions to be taken if resources can be raised.

From a more surgical perspective there is still a lot to be done to raise quality of inguinal hernia surgery. With the knowledge we already have on surgical performance and outcomes there are many actions that can be taken to enhance quality. Important issues and thoughts are:

- Set standard for quality – identify quality markers
- Set standards for indication including prePROM
- Set standard for techniques and agree on operative details – and follow them
- Team patient appointment in difficult hernia-related tasks
- Professional educational curriculums
- Record all operations – discuss – feedback
- Create hernia volume centres for education and technical developments
- Online registration in good quality registers with relevant outcomes
- Physiotherapists for objective evaluations pre and post op
- Easy hernia specific quality of life instruments to be used in registers pre/post Patient Reported Outcome Measure (PROM)
- Patient induced feed back
- Network and discussion forum for questions on easy and difficult patients
- Founded research units in association to the centres
- Rotation program for refreshment in operative techniques
- Collaboration on large multicentre studies

This is a wish menu of a hernia surgeon...





# POPULÄRVETENSKAPLIG SAMMANFATTNING

## Ljumsnbråckskirurgi på män – kronisk smärta och sexuella besvär

Operation för ljumsnbråck är den vanligaste allmänkirurgiska operationen. Årligen utförs ca 16 000 ljumsnbråcksoperationer i Sverige och 20 000 000 operationer världen över. Var fjärde man genomgår en eller flera ljumsnbråcksoperationer under sin livstid. De flesta patienter som opereras är män i arbetsför ålder. Bråck i ljumsken är 10 gånger vanligare hos män än hos kvinnor.

Risken för att drabbas av ett återfall av sitt bråck efter operation har tidigare varit hög. Fram till ca 1990 utfördes ljumsnbråcksoperationer med en teknik där man lagade bråcket med sydd förstärkning av svagheten eller defekten i bukväggen s.k. suturplastik. Denna typ av förstärkning resulterade vanligen i att 20–25% fick återfall av sitt bråck.

Under senaste två decennierna har man i allt större omfattning använt nät som förstärkning av bukväggen. Detta har minskat återfallsfrekvensen avsevärt. Samtidigt som man ökade användandet av nätet har smärta och obehag efter operation blivit ett mera uppmärksammat problem. Ett flertal studier har visat att 10–12% drabbas av vanligen måttlig smärta som kan påverka dagliga aktiviteter även flera år efter operation. I en stor svensk studie från 1990-talet jämförde man titthålsoperation med nät mot traditionell sydd förstärkning. Man såg inte någon skillnad avseende metoderna när det gäller smärta. Medelsvår till svår smärta kunde konstateras i 3% av opererade patienter som kvarstod efter 5 år. Svåra invalidiserande besvär som kvarstår kan ses i cirka 1–3% efter operation i andra studier.

Den enda effektiva behandling för ljumsnbråck är operation. De tekniker som i dag används mest är en öppen operation, Lichtensteins operation, eller en titthålsoperation, båda med nätförstärkning. Den öppna tekniken är den förhärskande tekniken och *gold standard* i de flesta länder. Enligt Svenskt

Bräckregister opererades 2016 ca 60% av svenska bräckpatienter med denna teknik och 28% med titthålsteknik.

Lichtensteins operation har utvecklats och har använts vid Lichtenstein Institutet i Kalifornien i sin nuvarande form sedan mitten av 1980-talet. Operationen innebär att man via ett ljumsksnitt lägger in ett nät som förstärkning på framsidan av bukväggens muskelskikt där svagheter har konstaterats. Största fördelarna med tekniken är att den är tekniskt relativt enkel och att inlärningskurvan är relativt kort.

Titthålstekniken innebär att man lägger ett nät på insidan av bukväggens muskelskikt (ljumskkanalens bakvägg) där sedan bukhinnan täcker nätet så att det inte exponeras mot bukhålan. Denna teknik kallas TEP (Totally Extraperitoneal Patch). Fördelen med titthålsbräckoperation är att patienten återhämtar sig snabbare och har kortare sjukskrivningstid i jämförelse med öppen teknik. Nackdelen med TEP operationen är att den är tekniskt svår och ger därmed en lång inlärningskurva. Detta har resulterat i att operationen framför allt görs på speciella centra med hög kompetens för titthålskirurgi. På specialiserade centra används tekniken mestadels vid återfallsbräck och samtidigt bräck i båda ljumskarna.

Sexuella besvär kan ha många medicinska orsaker som ger låg sexuell lust eller otillräckligt stånd (erektion). Sexuella besvär till följd av smärta på grund av ett existerande ljumskbräck eller som en effekt av en ljumskbräcksoperation är mycket sparsamt undersökt. Omfattningen av dessa besvär är kanske större än man anat. Besvären är säkert underrapporterade eftersom patienter ofta inte är så villiga att diskutera sina sexuella problem och läkaren kanske också avstår att fråga om inte patienten påtalar detta. I en studie från Danmark har man sett att 28% av patienterna rapporterade någon form av besvär vid samlag (vanligen lätta besvär) efter huvudsakligen öppna ljumskbräcksoperationer flera år efter bräckkirurgi där 2,8% rapporterade måttligt till allvarliga besvär med nedsatt sexuell aktivitet som konsekvens. Vid titthålsoperation är troligen påverkan på nerver, muskler och sädesledare mindre. I en dansk studie rapporterar 11% någon form av smärta. Totalt 2,4% hade måttlig till kraftig påverkan med nedsatt sexuell aktivitet som följd.

Det finns ingen samsyn på hur man definierar besvären, grad av påverkan eller varaktigheten av sexuella störningar. Det finns inga etablerade frågeformulär för att analysera sexuella besvär p.g.a. ljumskbräck eller eventuella besvär efter operation. De formulär som finns används av urologer och avser funktionella besvär som har annan orsak än ljumskbräck

En riskfaktor för långvarig smärta efter operation kan vara sättet på vilket man fäster nätet. Tanken är att man kan få en påverkan och inflammation i vävnaden

där man fäster nätet. När nätet läker in i vävnaden reagerar kroppen med en reaktion mot det främmande materialet och det blir en läkning med en ärrbildning. Denna ärrbildning kan göra att nätet dras ihop i början av läkningen och kan därmed leda till drag och smärta i områdena där nätet är förankrat. Denna mekanism kan ses vid såväl öppen som titthålsoperation. Vid TEP operationen används vanligen små titanskruvar. Vissa studier har visat att det är lika säkert att utföra en titthålsoperation utan att fästa nätet avseende förekomsten av ett återfall av bråcket. Det kan således vara en fördel för att undvika drag i fästpunkterna och därmed kanske minska risken för kronisk smärta.

Sökandet efter det ultimata nätet pågår och introduktionen av nya nät sker i snabb takt. Industrin erbjuder idag cirka 200 olika nättyper. Utvecklingskostnaderna är stora och ett nät kostar idag mellan 400 och 2000 kronor för ett ljumskbråcks nät. Mest använda nät är tillverkade av nylonliknande material (polypropylen eller polyester). Näten har olika stora ”porer” där vanligen storleken på dessa gör att nätet blir mer ”sladdrigt” om hålen görs större. Tanken är dock att stora hål befrämjar inväxten av nätet i vävnaden och minskar därmed risken för ärrbildning och skrupning. En porstorlek över 1,0 mm definieras generellt som *stor* porstorlek och resulterar att mindre mängd nätmaterial behöver användas. Detta gör att dessa nät väger mindre och benämns därför *lättviktsnät*. Dessa nät kan ha fördelar som minskad smärta efter operation och därmed kortare konvalescens. Det har dock visat sig att kronisk smärta vid titthålsoperation inte påverkas av nätvikten.

Det ideala nätet bör:

- ge god förstärkning av bukväggen
- inte vara för robust för att orsaka kroniska smärtbesvär
- bibehålla bukväggens elasticitet (minimal inflammatorisk reaktion)
- inte läka med skrupning av vävnaden
- var lätt att hantera
- vara kostnadseffektivt

Det är mycket svårt att utvärdera resultaten avseende kronisk smärta då det inte finns något bra mätinstrument eller protokoll för detta. Det finns ett otal olika skalor och frågeformulär för att mäta smärta. Ett enkelt och vanligen använt verktyg för utvärdering av smärta är ”Visual Analog Scale” (VAS). Ett enkelt verktyg som alla kan förstå ”Verbal Rating Skala” (VRS) introducerad av Cunningham som delade in smärta i: ”Ingen smärta”, ”Mild smärta” (begränsar inte aktivitet), ”Måttlig smärta” (förhindrar återgång till normala aktiviteter) och ”Svår smärta” (varaktig svår smärta som slår ut patienten).

Professor Kehlet, professor i Köpenhamn, är en ”ikon” när det gäller smärta i samband med operation och har varit med och utvecklat ett flertal instrument som också innefattar att analysera sexuella besvär i samband med ljumskbråck. Deras arbete inspirerade en svensk forskargrupp som utvecklade ”Inguinal Pain Questionnaire” (IPQ) ett vetenskapligt utvärderat instrument för att mäta smärta och besvär före och efter operation. Nackdelen är att det tar lång tid att fylla. En styrka är att man infört att mäta smärta över en tidsperiod istället för att fråga patienten om den aktuella smärtan vid en tidpunkt. Detta ökar användbarheten och återspeglar bättre den patientupplevda smärtan. Vi använder IPQ i denna avhandling. Formulär innehåller också frågor om funktionsnedsättning, typ av smärta, längd och lokalisering. Detta ökar värdet jämfört med ett endimensionellt enkla test. Förutom IPQ har vi använt SF-36, ett allmänt och väl validerat instrument som mäter fysisk och mental hälsa och är brett använt i många studier.

En noggrann preoperativ anamnes och undersökning är av största vikt för att utesluta andra medicinska tillstånd än bråcket som orsak till patientens besvär. Påvisas sådan orsak bör kanske kompletterande utredning göras och patienten informeras om risk för kvarstående besvär efter operation om oklarheter kvarstår.

Att kartlägga om smärtan är orsakad av en påverkan på en nerv eller på grund av en inflammation är av vikt då det finns ett flertal nerver i ljumskområdet som kan vara påverkade av bråcket eller kan skada vid operation. En nervskada ger ofta en utstrålade och huggande smärta och den inflammatoriska dov molande värk. De nerver (med latinska namn) som finns i området och kan påverkas är iliohypogstricus, ilioinguinalis, genitofemoralis, cutaneus femoris lateralis och femoralis.

Det är välkänt att det finns ömtåliga strukturer i ljumskan och att anatomin är komplex. Det finns många bråcktillstånd som kan förvränga anatomin och det är ett delikat område att dissekera i för en kirurg som måste behärska både kartläggningen och renoveringen av ljumskan.

#### *Avhandlingens syfte*

Syftet med denna avhandling har varit att analysera långvarig smärta, dess påverkan på livskvaliteten och sexuell aktivitet före och efter operation både ur ett generellt perspektiv där många bråckkirurger är inblandade samt ur ett högspecialiserat perspektiv där specialtränade bråckspecialister utför de i Sverige för närvarande vanligaste förekommande bråckteknikerna. Målsättningen är också att försöka hitta riskfaktorer för utveckling av kroniska smärta och sexuella besvär efter ljumskbråckskirurgi och på så sätt ge råd om hur man kan minimera risken dylika konsekvenser.

### *Tillstånd och patientinformation*

Samtliga studier har etiskt tillstånd och är registrerade enligt gällande rutiner i register. Patienterna har fått skriftlig information om studien, har skrivit under ett bevis och har accepterat deltagandet i studien. Alla patienter är informerade om att man när som helst kan avsluta sitt deltagande i studien.

Avhandlingens ingående delarbeten

Delarbete I och III i denna avhandling utgår från Svenskt Bräckregister och delarbete II och IV från en studie utgående från Malmö jämför två tekniker genom att lotta patienterna (randomisera) till endera tekniken.

### *Delarbete I*

Detta är en registerbaserad studie från Svensk Bräckregister (SBR), som jämför icke mekaniskt fäst nät mot klammer-fäst nät som förstärkning på bukväggens insida utfört med tithålsoperation.

Syftet med studien var att undersöka huruvida eventuell fixering av nätet påverkar förekomsten av kronisk smärta eller obehag.

Män 30–75 år registrerade i SBR mellan 2005 och 2009, som behandlades med TEP för ett förstagångsljumsbräck analyserad avseende kronisk smärta jämförande fixerat mot ofixerat nät. Patienter svarade på några frågor om tidigare operationer, SF-36 och IPQ (Inguinal Pain Questionnaire). Uppgifter om patientens generella sjukdomar och lokala uppgifter om bräcket hämtades från SBR och 1110 patienter analyserades. TEP har relativt sett låg (7,7%) förekomst av kronisk smärta utan skillnad mellan fixerat och ofixerat nät och verkar inte heller påverkas av uppföljningstidens längd. Patienter som har smärta "varje dag" under den senaste veckan (IPQ fråga 4) rapporterades med 3,8%. Smärtan som noterats före operation försvann i 81% av patienterna inom en månad. Operation för återfall av ett bräck var låg (1,4%) utan skillnad mellan fixerat och ofixerat nät efter en medelobservationstid på mer än 3 år.

Sammanfattningsvis kan man konstatera att förekomsten av kronisk smärta efter operation är relativt sett låg men ser inte ut att minska över tid. Andelen med svår smärta är dock högre än förväntat. Risken för återfall är mycket låg efter en mycket lång observationstid.

### *Delarbete II*

Detta är en prospektiv (framåtblickande) randomiserad (lottad) studie som jämför öppen nät operation enligt Lichtenstein med tithåls operation TEP.

Syftet var att analysera kronisk smärta och livskvalitet jämförande TEP med Lichtenstein före och ett år efter operationen i en standardiserad miljö för operativa tekniker vid ensidigt förstagångsljumsbräck hos friska män 30–75 år.

482 patienter randomiserades till TEP alternativt Lichtenstein. 418 patienter opererades inom ramen för studien. Data från klinisk undersökning, IPQ, SF-36 visade att "smärta sista veckan" rapporterades före operation i 73% av deltagarna och ett år efter operation med 7,4% efter TEP och 9,8% efter Lichtenstein utan statistiska skillnader mellan grupperna.

Både TEP och Lichtenstein operationen ger låg kvarstående kroniska smärtor. Operation ger mycket god symptomlindring med återställd livskvalitet hos flertalet, 98% var nöjda med operationen. QoL ökar till värden som ligger något över det normala. Återfall av bräck var mycket låg på 1.6% ett år efter operation utan skillnad mellan grupper. Kortsiktiga resultat som operationstid, 30-dagars komplikationer, tid till full återhämtning, känsla av främmande kropp i ljumske och sjukskrivning var generellt bättre i TEP-gruppen. Störningar av känseln i ljumskan var markant påverkad efter Lichtenstein men minskade efter TEP operation. Låg frekvens av både kronisk smärta och återkommande bräck kan förklaras av att operationer utförda i en högt standardiserad miljö av bräckspecialister.

### *Delarbete III*

Detta är registerbaserad kohortstudie som baserar sig på samma material som delarbete I och inkluderar sexuellt aktiva män, 30–60 år.

Syftet var att införa ett nytt frågeformulär, lätt att använda i stora kohorter av patienter som har smärta/dysfunktion vid sexuell aktivitet relaterat till ljumbräckoperation med TEP. Ett frågeformulär hade utvecklats (SexIHQ) baserat på principerna som professor Kehlets grupp utvecklat för att bedöma sexuell besvär/dysfunktion på grund av ljumsksmärta efter ljumskbräckskirurgi. Förekomsten av smärta vid sexuell aktivitet var förvånansvärt hög och rapporterades av 8,2% patienter och smärtrelaterad sexuell dysfunktion med 6,1% efter TEP-operation.

### *Delarbete IV*

Detta är en grupp av patienter från randomiserad studien från delarbete II som inkluderar sexuellt aktiva män, 30–60 år.

Syftet var att jämföra effekten av ljumskbräckskirurgi på smärtinducerade sexuella obehag/smärta vid ett och tre år efter operation för ljumskbräck jämförande TEP med Lichtenstein i en randomiserad studie. Ett frågeformulär utvecklades avseende smärtprevalens, frekvens, intensitet och försämring av sexuell funktion som orsakats av smärta vid sexuell aktivitet. Klinisk undersökning utfördes preoperativt och vid ett och tre år postoperativt.

Totalt 35% av patienterna rapporterade smärta vid sexuell aktivitet före operation. Efter ett år minskade besvären till 5,8% i TEP och 12,3% i Lichtenstein och efter tre år till 6,8% i TEP och 9,1% i Lichtenstein utan statistisk skillnad mellan grupperna.

#### *Slutsatser*

Både TEP och Lichtenstein operation resulterar i låga frekvenser av kronisk smärta och återkomst av ljumskbräck utan skillnader mellan grupper. Båda teknikerna minskar symtom och återställer QoL när det gäller smärta.

Smärta vid sexuell aktivitet samt sexuell dysfunktion på grund av ljumsksmärta i ljumskbräckspatienter är vanligare än man tror och minskar QoL. Ljumskbräckoperation med både TEP och Lichtenstein reducerar smärta vid sexuell aktivitet och återställer QoL hos de flesta patienter. Lichtenstein är en riskfaktor för smärta vid sexuell aktivitet.





## Hirurgija preponske kile kod muškaraca - hronični bol i seksualne tegobe

Operacija preponske kile je najčešća operacija u opstoj hirurgiji. Godisnje se izvede oko 16000 operacija preponske kile u Švedskoj i 20 miliona operacija sirom svijeta. Svaki četvrti muskarac prodje kroz jednu ili više hirurških intervencia zbog preponske kile tokom svog života. Većina pacijenata koji se operisu su muškarci u radnom dobu. Preponska kila je 10 puta češća kod muškaraca nego kod žena.

Rizik od ponovne pojave preponske kile, nakon prvobitne operacije, ranije je bio visok. Do 1990 godine operacije preponske kile su vrsene pomocu sivanja slabosti ili defekta u trbusnoj stijenci takozvanom suturplastikom. Ovakva vrsta pojaccanja obično je dovodila do 20–25% ponovnog pojavljivanja kile.

Tokom poslednje dve decenije, vjestacka mrežica se sve više koristi za jačanje trbusnog zida. Ovo je značajno smanjilo ucestalost ponovnog povratka kile. Istovremenno s povećanom upotrebom mreže, bol i nelagodnost nakon operacije postali su izrazeniji problem. Brojne studije su pokazale da 10–12% pacijenata pate od umerenog bola koji može uticati na dnevne aktivnosti čak i nekoliko godina nakon operacije. U jednoj velikoj švedskoj studiji iz devedesetih godina, laparoscopske operacije su uporedjivane sa tradicionalnim otvorenim operacijama tj sa sivanjem mreža. Nije bilo razlike u metodama sto se tice bola. Umeren/teški bol je pronađen kod 3% pacijenata koji je postojao i nakon 5 godina. Teške invalidizirajuće tegobe su se mogle vidjeti u približno 1–3% pacijenata nakon operacije u drugim studijama.

Jedini efikasan tretman preponske kile je operacija. Tehnike koje se trenutno koriste su otvorena Lichtensteinova operacija ili laparoscopska operacija, obadvije operacije su sa ugradjivanjem mreže. Otvorena operacija Lichtenstein je zlatni standard u većini zemalja. Prema švedskom hernia registru je operisano 2016-e godine oko 60% švedskih pacijenata sa ovom tehnikom i 28% sa laparoscopskim tehnikama.

Lichtenstein operacija se pocela koristiti u Lihtenštajn institutu u Kaliforniji u svom sadašnjem obliku od sredine 1980-ih. Operacija znaci da se kroz rez u preponi stavlja jedna mrežica kao pojačanje misica prednje trbusne stijenke gdje se slabost nalazi. Najveća prednost ove metode je da je tehnički relativno jednostavna i da je krivulja učenja relativno brza.

Laparoskopske metode uključuju stavljanje mrežice s unutrašnje strane trbušnog zida (preponski zadnji zid) i potrbusnica pokriva mrežicu tako da nije izložena u trbušnu šupljinu. Ova tehnika se zove TEP (Totally Extraperitoneal Patch). Prednost laparoskopske operacije kile je da se pacijent oporavlja brže i ima kraće bolovanje, u odnosu na otvorene metode. Nedostatak operacije TEP-a jeste to što je tehnički zahtjevnija i ima dugu krivulju učenja. To je dovelo do toga da se operacija prvenstveno vrši u specijalizovanim centrima koji imaju kompetenciju za laparoskopsku hirurgiju. U specijaliziranim centrima, metoda se uglavnom primjenjuje kod ponovnog pojavljivanja kile kao i obostranih preponskih kila.

Seksualna nelagodnost može imati mnogo medicinskih razloga koji uzrokuju smanjeni seksualni nagon ili nedovoljnu erekciju. Seksualne poteskoce kao rezultat bola zbog postojeće preponske kile ili kao efekat od operacije preponske kile su vrlo malo ispitani. Obim ovih poteskoca može biti veći nego što se mislilo. Ove poteskoce su svakako nedovoljno raportirane jer pacijenti često nisu toliko spremni da razgovaraju o svojim seksualnim problemima a i doktori ne zele pitati ako se pacijenti izricito ne zale na to. Jedna studija iz Danske je pokazala da 28% pacijenata ima neku formu tegoba prilikom seksualnog odnosa (obično blage simptome), uglavnom nakon otvorenih operacija preponske kile i vise godina nakon operacije od cega 2,8% ima umjerene do teške simptome sa smanjenom seksualnom aktivnoscu kao posljedicom. Laparoskopske operacije imaju vjerovatno manji nezeleni efekat na nerve, misice i sjemenovod. U danskoj studiji, 11% raportira neku vrstu bola. Ukupno 2,4% ima srednji do snazan negativan utjecaj sa smanjenom seksualnom aktivnoscu kao posljedicom.

Ne postoji dogovor o tome kako se definišu tegobe, stepen tegoba ili trajanje seksualnih poremećaja. Ne postoje etablirane ankete za analizu seksualnih problema uzrokovanih preponskom kilom ili operacijom preponske kile. Ankete koje postoje su uglavnom uroloske i odnose se na funkcionalne tegobe koje imaju drugi uzrok nego preponska kila.

Faktor rizika za dugotrajni bol nakon operacije može biti način na koji se mreža fiksira. Moze se dobiti negativan efekat i upala u tkivima na mjestima gdje se mrežica fiksira. Kada se mreža integrira u tkivo organizam reaguje na strani materijal i zarastanje se desava sa stvaranjem oziljka. Ovaj ožiljak može prouzrokovati da se mreža zateže na pojedinim mjestima na početku zarastanja i

tako može dovesti do bolova u područjima na kojima je mreža fiksirana. Ovaj mehanizam se može vidjeti i u otvorenoj i u laparoskopskoj operaciji. Kod TEP operacija obično se koriste mali titan sarafi. Određene studije su pokazale da je isto tako sigurno izvesti laparoskopsku operaciju bez fiksiranja mreže kad je u pitanju ponovo pojavljivanje kile. Laparaskopska operacija zato može imati prednost da se izbjegne zatezanje mrežice na tackama fiksiranja, čime se smanjuje rizik od hroničnog bola.

U potrazi za "idealnom" mrežom, uvođenje novih mreža se odvija u vrlo brzom taktu. Industrija trenutno nudi oko 200 različitih tipova mreža. Troškovi razvoja su visoki i mreža košta danas između 400 i 2000 švedskih kruna. Najčešće korišćene mreže su napravljene od materijala sličnog najlonu (polipropilen ili poliester). Velike pore podsticu urastanje mreže u tkivo, čime se smanjuje rizik od ožiljka i skupljanja. Veličina pora >1,0 mm je općenito definisana kao "velika veličina pora" i rezultira malom količinom mreže koja se koristi. To znači da ove mreže imaju manju tezinu i stoga se nazivaju "lake mreže". Ove mreže mogu imati prednost kao što su smanjeni bol nakon operacije i time kraći oporavak. Međutim, utvrđeno je da težina mreže ne utiče na nastanak kroničnog bola u laparoskopskoj hirurgiji.

Idealna mreža bi trebala:

- obezbediti dobro ojačanje trbusnog zida
- ne biti previše robusna da bi izazivala kronični bol
- održati elastičnost trbusnog zida (minimalna inflamatorna reakcija)
- ne zarastati sa stezanjem i smanjivanjem tkiva
- biti laka za rukovanje
- biti jeftina.

Veoma je teško procijeniti rezultate kroničnog bola jer nema dogovora oko mjernih instrumenata niti protokola za to. Postoje razne skale i ankete za merenje bolova. Jednostavan i najčešće korišćeni instrument za procjenu bolova je "Visual Analog Scale" (VAS). Jednostavan instrument koji svako može da shvati je "Verbal Rating Skala" (VRS) koju je uveo Cunningham i podelio bol u: "Nema boli", "Blaga bol" (ne sprečava normalne aktivnosti), "Umerena bol" (sprečava povratak u normalne aktivnosti) i "teška bol" (dugotrajni teški bol koji izbacuje pacijenta iz normalnih svakodnevnih aktivnosti).

Profesor Kehlet u Kopenhagenu, je "ikona", kada je u pitanju bol u vezi sa operacijama i razvio je niz instrumenata koji uključuje analiziranje seksualnih tegoba vezanih uz preponske kile. Njegov rad inspirisao je jednu švedsku istraživačku grupu koja je razvila Inguinal Pain Questionnaire (IPQ), naučno ocijenjeni instrument za merenje bolova i tegoba prije i posle operacije.

Nedostatak IPQ- ankete je da je potrebno puno vremena da se popuni. Prednost ankete je da anketa mjeri bol tokom određenog vremenskog perioda a ne samo da mjeri bol u jednom trenutku. Ovo povećava upotrebljivost ankete i bolje odražava bol bolesnika. IPQ se koristi u ovoj disertaciji. Anketa sadrži i pitanja o smanjenju funkcije, vrsti bola, dužini i lokaciji bola. Ovo povećava vrednost u poređenju sa jednodimenzionalnim jednostavnim testovima. Pored IPQ-a, u disertaciji se koristi i SF-36, široko validiran instrument koji mjeri fizičko i mentalno zdravlje i koji se široko koristi u mnogim studijama.

Pažljiva preoperativna istorija bolesti i pretrage su od najveće važnosti da se isključe druge bolesti a ne preponska kila kao uzrok tegoba. Ako se nađe takav uzrok, možda je potrebno izvršiti dodatne pretrage i pacijent treba biti informisan o riziku od nastavljenog postoperativnog bola da ne dođe do nejasnoca.

Vazno je znati da li je bol uzrokovano promjenom/ostecenjem nerva ili zbog upale jer postoji jedan broj nerava u predelu prepone na koje može negativno uticati kila ili može biti oštećen tokom operacije. Oštećenje nerva često dovodi do radirajućeg bola u vidu uboda a upala do dubokok kontinuiranog konstantnog bola. Nervi (sa latinskim imenima) koji su prisutni na tom području i mogu biti pogođeni su iliohypogstricus, ilioinguinalis, genitofemoralis, cutaneus femoris lateralis i femoralis.

Razumljivo je da u preponi postoje osjetljive strukture koje imaju složenu anatomiju. Preponska kila može izmjeniti anatomiju i hirurrg mora da savlada anatomiju da bi reparirao preponu.

#### *Svrha disertacije*

Svrha ove disertacije je analiza dugotrajnog bola, njegovog uticaja na kvalitet života i seksualne aktivnosti prije i posle operacije, kako iz opste perspektive u kojoj su uključeni mnogi opsti hirurzi, tako i iz visoko specijalizovane perspektive u kojoj obučeni specijalisti obavljaju operacije. Cilj je bio i pokušati pronaći faktore rizika za razvoj hroničnih bolova i seksualnih problema nakon operacije preponske kile i na taj način savjetovati kako se može minimizirati rizik od takvih posljedica.

#### *Dozvola i informacije pacijentu*

Sve studije imaju etičku dozvolu i registrovane su prema postojećim rutinskim registrima. Pacijenti su dobili pisane informacije o studiji, potpisali i prihvatili učešće u studiji. Svi pacijenti su obavješteni da u bilo kom trenutku mogu završiti svoje učešće u studiji.

### *Dijelovi disertacije*

Dio I i III u ovoj disertaciji bazirani su na švedskom registru preponskih kila (SHR) a dio II i IV na studiju iz Malmö koja upoređuje dvije tehnike slučajnim odabirom (randomiziranjem) pacijenata u jednu od grupa tj TEP ili Lichtenstein.

#### *Rad I*

Ovo je istraživanje zasnovano na Švedskom registru kila (SHR), koje poredi nemehaničko fiksiranje mreže sa fiksiranjem mreže pomoću malih vijaka da bi se pojačala unutrašnja strana trbusnog zida, izvedenog laparoskopskom operacijom.

Svrha studije bila je da se istraži da li fiksiranje mreže utiče na pojavu hroničnog bola ili tegoba.

Muškarci od 30 do 75 godina registrovani u SHR između 2005. i 2009. godine, operirani TEP-om zbog primarne preponske kile analizirani su sto se tice hronicnog bola poređeci fiksiranu sa nefiksiranom mrežicom. Pacijenti su u anketi odgovarali na pitanja o eventualnim prethodnim operacijama, SF-36 i IPQ (Inguinal Pain Questionnaire). Informacije o opstim bolestima pacijenta i lokalnim informacijama o kili dobijene su od SHR-a i analizirano je 1110 pacijenata. TEP ima relativno nisku (7.7%) ucestalost hroničnog bola bez razlike između fiksiranih i nefiksiranih mreža, i ta ucestalost se ne mjenja duzinom pracenja pacijenata. Pacijenti koji imaju "svakodnevni" bol zadnje sedmice (IPQ pitanje 4) zastupljeni su sa 3,8%. Bol koji je postojao prije operacije nestao je kod 81% pacijenata u roku od mjesec dana. Operacija zbog ponovljene kile je niska (1,4%) bez razlike između fiksiranih i nefiksiranih mreža nakon prosječnog vremena pracenja više od 3 godina.

U zaključku se može videti da je ucestalost kronicnog bola posle operacije relativno niska ali da se ne smanjuje sa vremenom. Međutim, procenat jakih bolova je veći od očekivanog. Rizik za ponovno pojavljivanje kile je veoma nizak i nakon veoma dugog vremena pracenja.

#### *Rad II*

Ovo je prospektivna randomizirana studija koja upoređuje otvorenu Lihtestajn operaciju sa laparoskopskom TEP-operacijom.

Svrha je bila analiza hroničnog bola i kvalitete života poređeci TEP-a sa Lihtenštajnom prije operacije i godinu dana nakon operacije. Koristena je standardizovana operaciona tehnika jednostrane primarne kile kod zdravih muskaraca 30-75 godina.

482 pacijenata su slučajno odabrani (randomizirani) u TEP ili Lichtenstein. U okviru studije operirano je 418 pacijenata. Podaci iz kliničkog pregleda, IPQ, SF-36 su pokazali da je "bol zadnje sedmice" prije operacije bio kod 73% pacijenata i

godinu dana nakon operacije 7,4% nakon TEP i 9,8% nakon Lihtenštajna bez statističke razlike između grupa.

I TEP i Lihtenštajn operacija pružaju nisku učestalost hroničnog bola. Operacija pruža veoma dobro smanjenje simptoma sa vraćenom kvalitetom života u većini, 98% je zadovoljno operacijom. 1,6% je pogođeno ponovnom pojavom kile poslije jedne godine bez razlike između grupa. Kvaliteta života poslije operacije se povećava na vrijednosti koje su nešto iznad normalne. Kratkoročni rezultati kao što su vrijeme operacije, komplikacije do 30 dana, vreme do potpunog oporavka, osećaj stranog tela u preponi i bolovanje bolesnika uglavnom su bolji u TEP grupi. Poremećaji osjećaja u preponi su bili značajno izraženi nakon Lihtenštajna, ali su se smanjili nakon operacije TEP-a. Niska frekvencija kroničnog bola i ponovne pojave kile može se objasniti operacijama koje su u izvodjene sa strogo standardizovanim metodama od strane hirurških specijalista za kile.

### *Rad III*

Ova studija je dio (kohorta) od rada I, zasnovana na registru i na istom materijalu i uključuje seksualno aktivne muškarce, 30-60 godina.

Svrha je bila uvođenje nove ankete, jednostavne za korištenje u velikim kohortama pacijenata koji imaju bol/disfunkciju u seksualnim aktivnostima vezanim za TEP-operaciju preponske kile. Izradili smo jednu anketu (SexIHQ), zasnovanu na principima koje je razvila grupa profesora Kehleta, da bi procenili seksualne tegobe/disfunkciju zbog preponske kile i zbog operacije preponske kile. Incidencija bolova u seksualnoj aktivnosti bila je iznenađujuće visoka u 8,2% pacijenata a seksualna disfunkcija kao posljedica bola u 6,1% nakon operacije TEP-a.

### *Rad IV*

Ovo je grupa pacijenata iz randomizirane studije iz rada II koja uključuje seksualno aktivne muškarce, 30-60 godina.

Cilj je bio analiza efekata operacije preponske kile na bolom inducirane seksualne tegobe jednu i tri godine nakon operacije upoređujući TEP sa Lihtenštajnom u randomizovanoj studiji. Izrađena je anketa o učestalosti bolova, učestalosti, intenzitetu i pogorsanju seksualne funkcije uzrokovanih bolom u toku seksualne aktivnosti. Klinički pregled je obavljen preoperativno, jednu i tri godine nakon operacije.

Ukupno 35% pacijenata je raportiralo bol u toku seksualne aktivnosti prije operacije. Nakon godinu dana, incidenca je smanjena na 5,8% u TEP i 12,3% u Lihtenštajnu, a nakon tri godine na 6,8% u TEP i 9,1% u Lihtenštajnu bez statističkih razlika između grupa.

### *Zaključak disertacije*

I TEP i Lichtenstein operacija rezultiraju u niskim frekvencijama hroničnog bola i ponovnog povrata preponske kile bez razlika između grupa. Obe tehnike smanjuju simptome i vraćaju kvalitet života kad je u pitanju bol.

Bol u toku seksualne aktivnosti, kao i seksualna disfunkcija usljed bolova kod pacijenata sa preponskom kilom, češći je nego što se veruje i smanjuje kvalitetu života. Operacija preponske kile sa TEP i Lihtenštajnom smanjuje bol u toku seksualne aktivnosti i vraća kvalitetu života kod većine pacijenata. Lichtenstein operacija je faktor rizika za pojavu bola u toku seksualne aktivnosti.





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# PAPERS I–IV



# Medicinae doctores in chirurgia

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1951 Arne Malm	1976 Sverker Hellsten	1985 Kent Jonsson
1953 Erik Åkerlund	1977 Pål Svedman	1985 Hans Hedlund
1953 Nils P Berg	1977 Anders Henriesson	1985 Mans Bohe
1953 Nils Carstam	1977 Sune Wetterlin	1986 Henry Svensson
1955 Anders Wenckert	1977 Sven Genell	1987 Heitti Teder
1955 Las G Hallen	1977 Bo Lindell	1987 Hans Högstrom
1957 Lawe Svanberg	1978 Olof Lannerstad	1988 Per Uden
1958 Torsten Widén	1978 Magnus Åberg	1988 Erik Svartholm
1959 Ivar Borg	1978 Allan Eddeland	1988 Per-Anders Abrahamsson
1959 Arne Weiber	1978 Hasse Jiborn	1989 Toste Länne
1959 Knut Hæger	1979 Anders Borgström	1990 Bengt Hjelmqvist
1960 Stig Borgström	1980 Ingrid Tengrup	1990 Nils H Persson
1961 Karl-Fredrik Aronsen	1980 Göran Balldin	1990 Henrik Åkesson
1961 Oddvar Eiken	1981 Stephan Brandstedt	1990 Thomas Mätzsch
1961 Carl-Fredrik Liedberg	1982 Tomas Lindhagen	1990 Magnus Delshammar
1962 Bertil Olow	1982 Harald Ljungner	1990 Anders Törnqvist
1963 Claes-Göran Backström	1982 Carlos Esquivel	1990 Magnus Erlansson
1963 Thorsten Stenberg	1982 Igor Niechajev	1990 Jan Brunkwall
1967 Sten Jacobsson	1982 Einar Vernersson	1991 Johan Ottosson
1970 Bengt Lindskog	1983 Svend Borup Christensen	1991 Ragnar Källén
1971 Bertil Robertsson	1983 Afzal Vazeery	1991 Lars Salemark
1971 Björn F Ericsson	1983 Jan-Bertil Wieslander	1991 Claes Forssell
1971 Erik G Ohlsson	1983 Bill Marks	1991 Agneta Montgomery
1971 Sune Isacson	1983 Bengt Lindblad	1991 Jan Berglund
1972 Jörgen Gundersen	1984 Anders Larsson	1991 Hans Olof Håkansson
1973 Bo Phil	1984 Peter Blomquist	1992 Henrik Bengtsson
1973 Bo Husberg	1984 Åke Lasson	1992 Thomas Troëng
1974 Lars Janzon	1984 Claes-Göran Björck	1992 Anita Ringberg
1974 Sigvard Olsson	1984 Staffan Kallero	1992 Peter Björk
1974 Jerzy Senyk	1984 Per Almquist	1992 Michael Hartmann
1974 Göran Ekelund	1984 Anne-Greth Bondeson	1992 Henrik Weibull
1975 Bengt Pallin	1984 Peter Konrad	1992 Erney Mattsson
1975 Sven Kristersson	1984 Magnus Grabe	1992 Thorvaldur Jonsson
1976 Rabbe Takolander	1985 Anders Lindhagen	1992 Magnus Bergenfeldt
1976 Nils T Johansson	1985 Stefan Arvidsson	1993 Anders Lundell

1993 Baimeng Zhang	2002 Rene Schramm	2010 Björn Schönmeyr
1994 Staffan Weiber	2002 Ervin Tóth	2010 Fredrik Jörgren
1994 Stefan Matthiasson	2002 Daniel Klintman	2010 Patrik Velander
1994 Björn Sonesson	2002 Åke Mellstrom	2010 Andrada Mihaescu
1995 Jan Stewenius	2002 Amjid Riaz	2011 Salma Butt
1995 Björn Arnljots	2002 Matthias Corbascio	2011 Emma Hansson
1995 Jan Holst	2003 Nina Kvorning	2011 Aree Abdulla
1995 Leif Israelsson	2003 Gudmundur Danielsson	2011 Darbaz Awla
1995 Per Jönsson	2003 Fritz Berndsen	2012 Martin Rehn
1996 Norman Jensen	2003 Salathiel Mzezewa	2012 Milladur Rahman
1996 Jens Peter Game	2004 Marianne Starck	2012 Su Zhang
1996 Hans Bohe	2004 Li Xiang	2012 Jan Slotta
1997 Wayne Hawthorne	2004 Karl Malm	2012 Åsa Olsson
1997 Öyvind Östraat	2004 Claes Jansen	2012 Martin Öberg
1997 Yilei Mao	2004 Peter Danielsson	2012 Songen Zhang
1998 Diya Adawi	2004 Lisa Rydén	2013 Zirak Hasan
1998 Liselotte Frost-Arner	2005 Ann-Cathrin Moberg	2013 Karzan Hamad Palani
1998 Martin Malina	2005 Anders Holmström	2014 Thordur Bjarnason
1998 Thomas Björk	2005 Helene Malm	2014 Clara Pählman
1998 Mats Hedberg	2005 Carolin Freccero	2014 Ada Tosovic
1998 Håkan Brorson	2005 Cecilia Österholm	2015 Hannes Hartman
1998 Magnus Becker	Corbascio	2015 Mohammed Merza
1999 Zhonquan Qi	2005 Elzanaty Saad	2015 Rundk Hwaiz
1999 Stefan Appelros	2005 Björn Lindkvist	2015 Lingtao Luo
1999 Göran Ahlgren	2006 Louis Banka Johnson	2015 Yongzhi Wang
1999 Håkan Weiber	2006 Henrik Dyhre	2016 Fredrik Olofsson
2000 Ingvar Syk	2006 Erik Almqvist	2016 Jonas Roller
2001 Xiao Wei Zhang	2006 Yusheng Wang	2016 Stina Klasson
2001 Christer Svedman	2008 Peter Mangell	2016 Andrea Polistena
2001 Ulf Petersson	2008 Martin Persson	2017 Ali Bagher
2001 Mats Bläckberg	2008 Sara Regnér	2017 Jenny Rystedt
2001 Peter Månsson	2008 Stefan Santén	2017 Peder Rogmark
2001 Tor Svensjö	2008 Asaduzzaman Muhammad	2017 Hanna Sternby
2001 Ursula Mirastschijski	2008 Matthias Laschkse	2018 Jasmine Brandt Bratlie
2001 Torbjörn Söderstrom	2009 Martin Almquist	2018 Mattias Hoffner
2002 Thomas Sandgren	2009 Farokh Collander Farzaneh	
2002 Max Nyström	2010 Dorthe Johansen	