Postoperative aspects of inguinal hernia surgery
Postoperative aspects of inguinal hernia surgery
Pain and recurrences
Abstract


Approximately one in four men will have surgery for inguinal hernia in their lifetime. In Sweden, 16 000 procedures are performed each year.

To investigate the possible link between handling of nerves and sensory disturbance, 97 groins in 92 patients were examined one year after inguinal hernia surgery. Sensory disturbances were found to be common after open surgery (29 %), but were not seen after the laparoscopic procedures. No significant relationship between sensory disturbance and handling of nerves or pain was seen.

The risk for recurrence has been significantly reduced due to the use of prosthetic meshes, but continued surveillance of this important outcome will always be necessary. In that context, the time frame in which recurrence develops in relation to possible risk factors can help our understanding of the underlying mechanisms. To explore such temporal relationships, 142,578 patients were included in a register study. A relative over-risk for early recurrence was seen after suture repair, laparoscopic repair, after postoperative complications, and after surgery for previous recurrence.

Corticosteroids are known to decrease pain and nausea after several surgical procedures. In a randomised trial on open hernia surgery, 398 patients were randomised to treatment with 12 mg of betamethasone or placebo. Decreased levels of pain were seen on the day of surgery, the next day and after one month. No difference was seen on days 2-7 and after one year. Nausea was not common and did not differ between the groups.

Reoperation is sometimes performed to correct a presumed structural defect thought to cause the long-term pain. In order to evaluate the result of such treatment, 111 cases were analysed based on register data, questionnaires and medical records. Sixty-two per-cent of the patients reported an improvement compared to before the reoperation, but a high level of pain remaining (42 %), and impaired quality of life was seen. There was no clear advantage for any surgical intervention over the other.

Keywords: Inguinal hernia, surgery, pain, reoperation, recurrence, betamethasone, sensory disturbance, nerve, groin.

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<td>Inguinal Pain Questionnaire</td>
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<tr>
<td>SF-36</td>
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<td>VAS</td>
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<td>IASP</td>
<td>International Association for the Study of Pain</td>
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<td>Totally ExtraPeritoneal repair</td>
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Introduction

In the “pre-mesh” era of hernia surgery, recurrence rate was regarded as the single most important endpoint. Since the introduction of synthetic meshes to routine hernia surgery in the 1980’s, the threshold for “acceptable” recurrence rate has decreased considerably. As a consequence, attention has shifted to other aspects of treatment, where there is potential for further improvement, in particular regarding chronic postoperative pain.

Since the 1990’s a number of studies have addressed this issue. Several risk factors have been found, such as young age, high preoperative- and postoperative pain level and surgery for recurrent hernia (1). Laparoscopic techniques are associated with a lower risk for chronic pain (2).

Pain, by definition, is an experience and as such subjective (3). In order to make statistical analysis possible, instruments such as dedicated questionnaires have been developed. The results of the following studies rely on such instruments and the effort that has been paid in their development and validation.

The management of chronic pain often involves several different kinds of medical expertise, such as pain specialists and general practitioners. However, the primary responsibility rests with the operating surgeon and it is he/she who must answer the complex question about reoperation to relieve pain. Unfortunately, the low reoperation rate and the heterogeneity of the problem make randomised trials difficult to perform and consequently, there is no hard evidence to guide decision-making. Management, therefore, relies heavily on the experience and judgement of the surgeon.

The aim of the studies presented in this thesis was to provide new information on chronic pain after inguinal hernia surgery, in order to facilitate our understanding of the problem and hopefully to prevent it. Furthermore the surgical treatment of the chronic pain is described. In a separate study, a way to illustrate the time profile of inguinal hernia recurrences is described.

History of hernia surgery

Inguinal hernia has probably existed since humans began to walk upright. The first known description goes back to 1552 BC, written on an Egyptian papyrus roll. In Alexandria’s heyday in the Third-Century BC, quite sophisticated surgery was performed, including the ligation of vessels under sedation using the medical herbs steeped in wine. This tradition spread to the ancient Greece and Rome. Hernia surgery, where the importance of preserving the testicle is described, indicates that quite advanced dissection
was performed. It is noteworthy that Hippocrates did not describe hernia surgery, although he otherwise described fairly advanced surgical procedures (4, 5).

During the Middle Ages, the surgical knowledge of the ancient world was lost in European traditions. In the scholastic tradition, surgery was not considered a part of medicine, and was left to bonesetters on the battlefields and barbers without formal education. The heritage from antiquity was, to some extent, preserved in Byzantine and Arabian traditions, but the practice seems to have shifted towards sacrificing the testicle. Blunt cauterisation through the skin after reducing the hernia was described.

Advanced studies of anatomy and further progression in the field of surgery saw light from the 15th Century onwards. The distinction between direct and indirect hernias was made, but the question as to whether to remove or preserve the testicle seems to have been controversial. Names such as Astley Paston Cooper of Norfolk (1741-1841) will forever be associated with the anatomy of the inguinal canal (4).

Prior to the 19th Century, opium, herbs, alcohol or the brute force of the surgeon’s assistants were the means of making surgery possible. Rapid technique was an important feature of a good surgeon. Nitrous oxide and ether were known chemical substances by the beginning of the 19th Century, but despite the terrible suffering that must have taken place in the contemporary operating theatres, they were first used for fun and entertainment. The first successful application of ether was made in dental surgery in the 1840’s. From that time on it became more widely used and, in combination with antiseptics, made the development of modern surgery possible. Cocaine was the first local anaesthetic agent to be used and Harvey Cushing described its implementation in hernia surgery in 1898 (4, 5).

Edoardo Bassini (1844-1924) described the technique that bears his name during the 1880’s. It involves ligation of the hernia sack and reconstruction of the floor of the inguinal canal using adjacent tissues in a triple layer.

A technique with more emphasis on high ligation of the sack and closure of the dilated internal ring was introduced in the United States by Marcy (1837-1924). Throughout the 20th century, various modifications and refinements of suture hernioplasty were made. One of the most important was that of E.E. Shouldice in the early 1950’s, and is described in the treatment section of this thesis. Even though more modern methods have proven to be superior in almost every aspect, the techniques of the late 1900th century are still practiced to some extent. In 2010, 153 Shouldice- and 43 Bassini procedures were registered in the Swedish Hernia Register (SHR). (4-6)
During the 1940’s and early 50’s tantrum gauze was used for the reinforcement of hernia repairs, but due to infection and other adverse effects, the results were disappointing. Silver filigrees had previously been used, but were abandoned, despite occasional promising results. Stainless steel meshes have also been tried, and may have been favourable in infected wounds. From the 1960’s onwards the synthetic meshes made of polypropylene were introduced in hernia surgery. A variety of materials beyond polypropylene, such as polyester, nylon, polytetrafluorethylene (PTFE) have been used since then. Numerous coatings have further contributed to the multitude of products. Porcine dermal grafts, as well as other biological materials, have also been evaluated, but have not been established in routine inguinal hernia surgery.

Another considerable advance was the use of the posterior approach to hernia surgery, described by Lloyd Nyhus (transverse incision) and Rene Stoppa (midline incision). The posterior placement of a mesh made tension-free repair possible, without dissection of the inguinal canal. Principles that were later adopted in laparoscopic hernia surgery.

Early attempts to perform laparoscopy were made in the beginning of the 20th Century, but the practical applications were limited. Some progress was made when the quartz light rod and fibre optic bundles were introduced in the 1950’s.

The development gained momentum during the 1980’s when techniques for laparoscopic cholecystectomies and appendectomies were developed. Laparoscopic hernia repair were introduced the same decade and the basic principles of the methods used today were known in the early 1990th. Initial setbacks due to insufficient mesh size and lack of understanding of the preperitoneal anatomy have been overcome gradually.

**Epidemiology**

Hernia surgery is common, particularly in men and the elderly. In Sweden 16 000 hernia repairs are performed each year, making it the most common surgical procedure in men.

The incidence of hospitalisation with inguinal hernia was 13.9 % for men and 2.1 % for women over a 20-year period in a US-population. The lifetime risk for inguinal hernia surgery was 27 % for men and 3 % for women in a British study.

Over the last 10 years, long-term pain has become a major outcome measurement besides recurrence. The prevalence observed varies, but the
existence of some degree pain ranges from approximately 10 % to 30 %(1, 12-14).

Anatomical considerations
A thorough knowledge of the anatomy of the groin is crucial for understanding hernia recurrence as well as chronic pain.

Nerves
In open anterior hernia surgery three major nerves cross the operating field and may come in conflict with the technique chosen.

- The iliohypogastric nerve emanates from the first lumbar root and enters the abdominal wall, supplying the skin over the lower anterior abdominal wall.
- The ilioinguinal nerve comes from the same root but runs more caudally though the inguinal canal and supplies the skin of the groin and scrotum.
- The genitofemoral nerve arises from the first and second lumbar roots and runs in front of the psoas muscle. It divides into the genital branch that joins the spermatic cord and supplies the cremasteric muscle, and the femoral branch (not seen in open anterior hernia surgery) that supplies a small area of skin over the proximal thigh.

In posterior hernia surgery, most often performed by laparoscopy, interference with these nerves is avoided. Instead the lateral cutaneous nerve of the thigh from the first and second lumbar roots and femoral branch of the genitofemoral nerve may be encountered as they transverse the iliac fossa (7, 15, 16).

In addition to the anatomy described above, nerve fibres along the lamina propria of the vas deferens have recently been proposed to carry sensory impulses from the testicle, and are thus involved in postherniorrhaphy orchialgia(17).

Muscle and connective tissue
The muscles and aponeurosis of the groin region constitutes a diagonally running connection between the abdominal cavity and the subcutaneous space. In males the vas deferens and the spermatic artery and vein pass
through this opening, covered by the cremaster muscle. In woman, the round ligament of the uterus represents the content of the inguinal canal.

**Treatment options**

Surgery is the only cure for inguinal hernia. During the past 130 years, a multitude of techniques have been developed. At least three fundamental distinctions can be made:

- Sutured vs. mesh reinforced techniques
- Open vs. laparoscopic techniques
- Anterior vs. posterior approaches

Sutured repairs have been shown inferior with respect to both recurrences and chronic pain (18), and are generally not recommended (19). The Shouldice repair is considered to be the best among sutured repairs. It is performed by opening the inguinal canal, dividing the transvers fascia, and then reconstructing the posterior wall using the transverse abdominal fascia and the internal oblique muscle. In the original description, four layers of running sutures using metal wire were used (7).

Whereas a multitude of operation techniques characterised the pre-mesh era, a comparable diversity of mesh products characterises hernia surgery today. The most important prosthetic material is polypropylene. It can be used alone or in combination with an absorbable component to make the repair softer and more flexible so as to reduce the risk for chronic pain and discomfort. Other materials, such as polyester are also available. In addition to the choice of material, structural properties will effect the overall characteristics. Such variables are density, the size of the pores and whether it is made from monofilament or multifilament. Meshes placed in direct contact with bowel may be coated with degradable materials such as methylcellulose to avoid adhesions.

The use of mesh facilitates tension-free repairs by bridging the gap of the hernia defect, rather than closing it by approximating the surrounding tissues. The most commonly used methods can be divided into three groups, using the distinctions above.

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<th>Posterior approach</th>
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<td>Plug repairs</td>
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</tr>
<tr>
<td>Laparoscopic techniques</td>
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**Anterior approach**

The Lichtenstein repair was described in 1989 by the man who gave the method its name (20). Some modifications have been made (21) but the principal stages remain the same:

1. The inguinal canal is opened and the hernia identified
2. The hernia sack is invaginated, or if continuing to the scrotum, transected
3. The femoral ring is explored
4. A mesh is placed on the inguinal floor with a slit at the lateral side, creating two tails around the spermatic cord.
5. The mesh is anchored with a non-absorbable running suture in the aponeurotic tissue around the pubic tubercle, avoiding sutures in the periosteum, and then continued along the inguinal ligament. A new internal ring is made by closing the slits of the mesh with a non-absorbable suture. The upper edge of the mesh is sutured to the internal oblique aponeurosis or muscle, using a few absorbable sutures.

The advantages of this method are the low recurrence rate, the short learning curve, safety and low cost. It can be performed under local anaesthesia with prompt return to normal activities.

The risk for postoperative pain seems to be significantly higher after the Lichtenstein repair, compared to laparoscopic approaches such as TAP or TEPP both in the short- (22) and in the long term perspective (2). Management of the nerves of the inguinal region during the Lichtenstein repair is a major issue, since the procedure necessitates dissection and positioning of a prosthetic mesh in close proximity to the nerves.

Plug repairs, using devices of different shapes and material have been developed as mean of facilitating hernia surgery. The general principle is to place a plug in the hernia defect. The method can be modified to fit all kinds of hernias, including femoral hernias and recurrences (7). Due to a relative lack of evidence compared to the Lichtenstein procedure, plugs are not recommended by the European Hernia Society (EHS) as a primary technique (19). Plug techniques constituted about 5 % of hernia operations in Sweden 2010 (6).

**Posterior approach**

In the methods described above, the mesh is placed outside the hernia defect, resulting in a situation were the pressure of the abdominal cavity pushes the mesh away from the repair. Following a posterior repair, on the other hand, the mesh is pressed towards the aponeurotic structure it is
intended to reinforce. Thus, a theoretically more favourable placement is achieved. Three different posterior methods are of importance today.

In the totally extraperitoneal repair, TEP, a space is created between the peritoneum and the abdominal wall, by means of an inflatable balloon or blunt dissection. Using a camera port below the umbilicus and two ports in the lower midline, the peritoneum can be dissected down from the groin region to give access to all three possible hernia defects. A mesh is positioned to cover all defects, and is most often fixated by tacks or fibrin glue.

The transabdominal preperitoneal repair, TAPP, makes use of the abdominal cavity, thus more similar to other laparoscopic procedures in abdominal surgery. The peritoneum is opened and dissected from the inside to give access to the preperitoneal space. A flat mesh is used to cover all three possible hernia sites and is then covered by peritoneum.

The same principle as in the TEP procedure can be utilised by a transverse incision above the inguinal canal to make use of the same mesh position as in the laparoscopic procedures, but without the increased complexity of laparoscopy. The method was advocated by Lloyd Nyhus, by whom it has been named. Compared to the conventional open procedure, e.g. Lichtenstein, the advantage is the theoretically favourable mesh position and decreased risk of interfering with the nerves of the groin.
**Aims of the thesis**

The overall objective of this thesis is to describe certain aspects of postoperative adverse outcomes following inguinal hernia surgery. The specific aims of each study were:

1. To measure sensory disturbances (SD) and pain one year after hernia surgery and analyse their association with perioperative nerve handling.
2. To analyse the time profile for inguinal hernia recurrence and identify risk factors for early and late recurrence.
3. To investigate the effect of a single dose of betamethasone on pain in the short- and long-term perspective, as well as postoperative nausea and vomiting after open inguinal hernia surgery.
4. To evaluate reoperations for chronic pain after hernia surgery and measure the outcome in terms of residual pain and quality of life.
Materials and Methods

Measuring pain and quality-of-life

What is pain?
Pain is defined by the International Association for the Study of Pain (IASP) as:

“An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”(3)

The subjective nature of pain makes it impossible to measure directly. However, through scales and questionnaires, categorical or ordinal data can be retrieved. Proxy measurements such as use of analgesics or the hindrance of activities can also be used. Other aspects to consider are differences between acute and long-term pain, and between pain at rest as opposed to at mobilisation.

Neuropathic Pain
Neuropathic pain is defined by IASP as:

“Pain caused by a lesion or disease of the somatosensory nervous system”(3)

In the case of hernia surgery, such a lesion can be either an accidental injury or a conscious transection of the nerve to facilitate the procedure or reduce the risk for nerve entrapment in open surgery. Entrapment of nerves, either by sutures in open surgery, or fixation devices in laparoscopic surgery, may cause similar iatrogenic damage. Postoperative scar formation in the presence of a prosthetic mesh is another cause of nerve injury and subsequent pain (23, 24).

Nociceptive pain (non-neuropathic pain)
Pain in the absence of nerve injury is generated by nociceptors, receptors sensitive to noxious stimulus, hence the term nociceptive pain or non-neuropathic pain. In the literature of hernia surgery, this is often used to describe pain caused by factors other than nerve injury, such as chronic inflammation, stretching of tissue, or pain from a lump of rolled-up mesh pressing on it’s surroundings.
The Inguinal Pain Questionnaire (IPQ)
As chronic pain became an important endpoint in hernia surgery, the need for a valid measuring instrument arose. In order to meet this need the Inguinal Pain Questionnaire (Appendix A) was developed. This instrument consists of seven step items to assess pain, with each question linked to pain behaviour. Interference with daily activities is measured in the second part of the questionnaire (25).
As a further development of the questionnaire, the IPQ-score can be calculated by adding the number of positive answers to the questions about activities that are limited by pain to the numerical answer to the question on worst pain last week.

The Visual Analogue Scale (VAS)
The VAS-scale is widely used for clinical and scientific pain measurement. The study subject is instructed to mark the experienced pain on a scale bounded by the descriptors “least possible pain” and “worst possible pain”. The continuous measurement is then transformed to a numeric value from 0-100 mm or 0-10 cm.
The smallest change in rating on the VAS-scale that has clinical significance has been found to be around 13 mm, at least for acute pain (26).
The VAS-scale is closely related to the Numeric Rating Scale (NRS), whereby pain is stated on a numeric scale from 0 to 10, bypassing the visual aspect of the VAS-scale. This makes it more practical to use, and the results have been found to be similar (27).

Short Form 36 (SF-36)
In order to assess quality-of-life The SF-36 health survey consists of 36 multiple choice questions that transform to eight scores.

- Vitality
- Bodily pain
- General health perceptions
- Physical role functioning
- Emotional role functioning
- Social role functioning
- Mental health

The transformation is made by means of an algorithm that weighs the questions included in the respective score. It has been validated (28) and broadly used in medical research and health economics.
The Swedish Hernia Register

The Swedish Hernia Register started in 1992 by eight hospitals. It has gradually grown to cover 95 operating units and more than 95% of all hernia operations in Sweden (age 15 and above). The County Council of Jämtland is the authority responsible for the register. The funding required to administer the register is provided by the National Board of Health and Welfare and the Swedish Association of Local Authorities and Regions. An annual external validation is performed at randomly selected units, to assure the accuracy of the data. Participation is voluntary for operating units, as well as for individual patients.

The register contains more than 200,000 operations. Among other items the register provides information on operation date, hernia anatomy, method of repair, prosthetic material used, operating unit, and surgeon and patient characteristics. Since 1999, reoperation because of chronic pain is included as a separate indication for surgery.

Paper I

All patients aged 18 and above operated on at Mora Hospital between January 30th and August 21st 2006 were included in the study. The Swedish Hernia Register was used to ensure complete coverage.

Data was collected in a standardised and prospective database at the time of surgery and one year postoperatively. A questionnaire to be answered by the surgeon included questions about whether the major nerves had been identified, and whether they were divided or preserved. Local anaesthetics were used at the discretion of the surgeon, and recorded in the questionnaire.

One year after surgery the patient was requested to answer the IPQ and invited to a follow-up visit. The IPQ was supplemented with a set of 18 verbal descriptors to describe pain quality, (Appendix B) previously proposed for describing pain after inguinal surgery.

Thirty-six groins in 25 patients were independently examined by two surgeons at the one-year follow-up visit, to evaluate inter-observer reliability. The examination was performed by an independent surgeon not involved in the operation. A method of examination to assess alteration of sensibility for touch, heat, cold and pinpricking was used. The method was designed to be fast, easy to learn and suitable for use in general surgical practice.

The preferred methods of repair were Lichtenstein hernioplasty for primary unilateral inguinal hernia in men, and TEP for bilateral hernia, recurrences and all groin hernias in females.
Statistical methods
Inter-observer agreement was tested using Cohen’s Kappa statistics. Pain ratings between groups were compared with the Mann-Whitney U-test. Ordinal data such as the pain descriptors were tested with Chi-square test.

Paper II

Study population
This study is based on SHR data from 1992 until 2006. During the study period 142 578 primary inguinal hernias were registered.

Statistical methods
Each year from surgery to five years after surgery was treated as a separate category, in a variable based on time after surgery. Death or no reoperation was treated as a censored event. All risk factor was tested for interaction with year after surgery, using Cox proportional hazard analysis. Risk factors that turned out to have a significant interaction to time after surgery were used in multivariate analysis.

Paper III

Study population
Patients aged 18-70 years scheduled for open inguinal hernia surgery March 2005 to December 2009 or Mora Hospital October 2006 to March 2009 were eligible for inclusion.
Exclusion criteria were: previous adverse reactions to drugs used in the study, heart-failure, diseases of kidneys or liver, current infection, diabetes, active ulcer or previous severe gastrointestinal bleeding, tuberculosis, diabetes, pregnancy, breastfeeding, psychosis, other severe general disease, treatment with diuretics or ACE-inhibitors.

Patients received written information two weeks prior to surgery, which was supplemented by verbal information on the day of surgery. Written informed consent was obtained.

Procedures
Patients were randomised to either betamethasone 4 mg/ml, 3 ml intravenously or placebo (saline). Randomization was by means of a computer-generated list, which was not available to the surgeon or to any of the staff involved in the care of the patient. The study substance was prepared by a nurse and labelled so that betamethasone and placebo syringes were indistinguishable, it was then handed over to the nurse responsible for the pa-
tient. Each syringe was identifiable so that the true nature of the study substance could be revealed in the case of a severe adverse event.

All patients were given paracetamol 30-90 minutes before surgery, 1.5 g if the bodyweight was less than 60 kg, or 2.0 g if above 60 kg. At the onset of anaesthesia the test-substance and a dose of parecoxib (Dynastat) 40 mg i.v. (if the bodyweight was less than 50 kg or the age was over 60 years, 20 mg) were given intravenously.

The anaesthetic technique varied depending on the patient at hand and the preferences of the anaesthesiologist and surgeon. General anaesthesia with laryngeal mask, spinal anaesthesia or local infiltration anaesthesia were used. In the case of general- or spinal anaesthesia, local infiltration was applied at the end of the procedure.

Paracetamol and diclofenac were prescribed for postoperative analgesia.

Follow up
Pain, nausea, vomiting, mobilisation, oral intake and need for analgesics were recorded every 30 minutes until discharge. The VAS scale was used to rate pain.

A form was filled in daily by the patient for the first seven days after surgery recording pain (maximal- and minimal VAS), nausea, use of medication, food intake, degree of mobilisation and adverse events. Patients were contacted by phone on the first postoperative day to answer the same questions and to ensure that the form was completed.

One month after surgery a second phone call was made to record pain, use of analgesics, return to normal activities and adverse events.

After one year the IPQ was sent for assessment of chronic pain.

Statistical methods
Multiple linear regression analysis adjusted for time after surgery was used to compare the level of pain at rest and on mobilisation. Nausea during the postoperative period was tested in the same manner.

Paper IV

Study population
Patients operated on for chronic pain after previous inguinal hernia surgery, were identified from the SHR. Patients operated 1999 to 2006 were included in the study. Data from patients where the previous operation was also registered were included. Patients were contacted by mail and asked about participation. Non-responders were sent one reminder and then contacted by telephone.
Data collection
Prospectively collected data were obtained from the SHR regarding operation date, gender, side operated, operating unit and method of repair.

Information on the reoperation, previous surgery and management in-between were abstracted from patent records, according to a standard protocol. Data on perioperative findings at reoperation, identification and management of nerves, extraction of mesh or plug and subsequent repair (when applicable), were extracted.

The effect variables were assessed using three questionnaire forms sent to the patient.

1. SF-36 to assess quality-of-life
2. IPQ to measure groin pain
3. Two additional questions to address the change in pain between
   1) prior to the latest operation and present time
   2) prior to the first operation until present time

Statistical methods
Data from the sources described above were assembled in a database and analysed using the chi-square test and t-tests to compare groups. Expected health-related quality-of-life was obtained from an age- and gender-matched database (28).

Ethics approval
Papers I, III and IV were approved by the Regional Ethics Review Board in Uppsala. Paper II was approved by the ethics review board in Lund. *

Results

Paper I
There were 128 hernia repairs in 116 patients (including 12 bilateral) initially registered in the study. The total amount of procedures performed during the study period was 157. Of these, 92 patients, including 5 operated bilaterally, attended the follow-up visit and were included in the analysis.

Thirty-six repairs (28 %) were performed using the TEP technique. The remaining were Lichtenstein procedures. Median age was 61 years (range 19-87 years). Three patients had signs of recurrence at clinical examination one year postoperatively. Two of those stated pain that could not be ignored, but did not affect daily activities, and one patient perceived no pain.

The prevalence of pain was fairly low. Seventy-seven (79 %) stated no pain on the “pain right now” item and 69 (71 %) on the “worst pain last week” item of the IPQ questionnaire. (Figure 1:1.)

The finding of sensory disturbance (SD) more than two cm away from the scar was considered a positive finding. SD in the immediate vicinity of the scar is more difficult to assess and can be caused by transection of very peripheral branches. SD extending more than two cm were found in 20 groins (21 %), all of whom had undergone a Lichtenstein procedures. No significant association between the intraoperative handling of nerves and

Figure 1:1. Patient reported pain “right now” and “worst pain last week”. Scale 1-7 according to IPQ.
SD was seen. The ilioinunal nerve was transected in 17 cases. No association between pain and sensory disturbance was seen. (Table 1)

**Table 1.**

<table>
<thead>
<tr>
<th>Sensory disturbance</th>
<th>Pain</th>
<th>No Pain</th>
<th>20</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>No sensory disturbance</td>
<td>16</td>
<td>61</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>77</td>
<td>97</td>
</tr>
</tbody>
</table>

**Paper II**

Mean age of the study population was 59 years (SD 15.9 years) and 7.7 % were women. The recurrence rate was 4.3 % in five years.

Results from the Cox proportional hazard analysis revealed a relative increase in hazard for early versus late recurrence for the following risk factors: Previous recurrence, postoperative complications, laparoscopic repair, suture repair, open preperitoneal repair without mesh and for operations registered as “other methods”. Open preperitoneal repair with mesh (i.e. Lichtenstein) was used as reference. Plug and open preperitoneal mesh techniques did not differ significantly from the Lichtenstein, as regards the temporal distribution of recurrences. (Table 2:1)
Table 2.1. Cox proportional hazard analysis, testing for interaction between the year of surgery and the risk factor. Hazard ratios above 1.0 correspond to a relative over-risk for earlier recurrence.

<table>
<thead>
<tr>
<th>Preceding hernia repair</th>
<th>Hazard ratio (univariate)</th>
<th>p</th>
<th>Hazard ratio (multivariate)</th>
<th>p</th>
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<tbody>
<tr>
<td>Primary hernia</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>125.930 (88.3%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td>1.18 (1.15-1.21)</td>
<td>&lt;0.001</td>
<td>1.52 (1.34-1.70)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>16.648 (11.7%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Postoperative complication</th>
<th>Hazard ratio (univariate)</th>
<th>p</th>
<th>Hazard ratio (multivariate)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No complication</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>130.452 (91.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative complication</td>
<td>1.05 (1.02-1.09)</td>
<td>0.005</td>
<td>1.27 (1.12-1.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12.126 (8.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Method of repair</th>
<th>Hazard ratio (univariate)</th>
<th>p</th>
<th>Hazard ratio (multivariate)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior mesh</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>79.188 (55%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plug</td>
<td>0.93 (0.90-0.97)</td>
<td>&lt;0.001</td>
<td>1.00 (0.87-1.16)</td>
<td>0.989</td>
</tr>
<tr>
<td>17.188 (12.1%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open preperitoneal mesh</td>
<td>1.073 (1.01-1.15)</td>
<td>0.035</td>
<td>1.13 (0.85-1.49)</td>
<td>0.405</td>
</tr>
<tr>
<td>2.745 (1.9%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laparoscopic repair</td>
<td>0.98 (0.94-1.01)</td>
<td>0.193</td>
<td>1.18 (1.03-1.35)</td>
<td>0.021</td>
</tr>
<tr>
<td>13.311 (9.3%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture repair</td>
<td>1.03 (1.01-1.06)</td>
<td>0.019</td>
<td>1.20 (1.02-1.41)</td>
<td>0.030</td>
</tr>
<tr>
<td>22.105 (15.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open preperitoneal without mesh</td>
<td>1.31 (1.21-1.41)</td>
<td>&lt;0.001</td>
<td>1.50 (1.04-2.17)</td>
<td>0.031</td>
</tr>
<tr>
<td>1.099 (0.8%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other method</td>
<td>1.14 (1.10-1.19)</td>
<td>&lt;0.001</td>
<td>1.33 (1.09-1.62)</td>
<td>0.006</td>
</tr>
<tr>
<td>6.451 (4.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 2:1. Time to reoperation for the most commonly used groups of techniques

The time to reoperation for recurrence for different techniques is plotted in figure 2:1.

In order to evaluate the effect of prosthetic mesh, all such, methods were merged and compared to all suture methods in a separate analysis. The relative incidence of early recurrences following mesh repairs turned out to be lower than for early recurrences following suture repairs.
Paper III
Three hundred and ninety-eight patients were included in the study, of whom 199 received active treatment and 199 received placebo. Mean age was 52 years (SD 12 years). During the study period, 937 patients were operated at the participating hospitals. 539 patients were excluded for reasons given in flowchart in figure 3:1.

Assessed for eligibility
n=937

Excluded
n=539
laparoscopic procedure: n=112
Not wishing to participate / Other reason: n=427

Randomized
n=398

Allocated to betamethasone
n=199
Received allocated intervention
n=199

Allocated to placebo
n=199
Received allocated intervention
n=199

Lost to follow-up:
first week: n=20
one month: n=26
one year: n=10

Lost to follow-up:
first week: n=10
one month: n=40
one year: n=6

Analysed:
first week: n=179
one month: n=159
one year: n=189

Analysed:
first week: n=189
one month: n=173
one year: n=193

Figure 3:1. Flowchart of trial enrolment and group assignment
Pain
Pain estimate at rest prior to discharge was significantly lower in the betamethasone group (p<0.001). (Figure 3:2) The significant difference in pain remained the day after surgery (mean VAS score 3.75 vs. 2.98). Pain did not differ significantly between the groups from day 2 to 7. (Figure 3:3) Type of anaesthesia was included in the multivariate logistic regression analysis to evaluate its influence on pain. General anaesthesia was associated with significantly more pain on the day of surgery, but not thereafter.

Figure 3:2. VAS scores (95 % C.I.) on the day of surgery

Figure 3:3. Mean VAS score (95 % C.I.) day 1-7 after surgery
One month postoperatively, 33 of 159 (21 %) patients in the placebo arm reported pain compared to 21 of 173 (12 %) in the treatment arm (p=0.049).

At one year, 382 of 398 patients (96 %) returned the IPQ questionnaire. Pain of any degree was reported by 50/193 (26%) in the placebo arm, and by 62/189 (33 %) in the treatment arm. The number of patients stating interference with daily activities on the item on “worst pain last week” was 9/193 (5 %) in the placebo group and 8/189 (4 %) in the betamethasone group.

Secondary outcome variables
Time from end of surgery to oral intake, time to discharge or the need for analgesics did not differ significantly between the groups. The number of patients who reported nausea was small and no significant difference between the groups were seen. (Table 3:1)

<table>
<thead>
<tr>
<th>Episodes of nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of surgery</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Betamethasone</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
</tbody>
</table>

*Table 3:1. Nausea*
Postoperative aspects on inguinal hernia surgery

From the Swedish Hernia Register, 236 patients operated for chronic pain after previous hernia surgery up to 2007 were identified. Fifteen patients had died or could not be traced. Of 222 patients contacted, 45 declined participation, 4 were unable to answer due to medical reasons and 62 failed to respond. After the inclusion process, 111 patients remained for analyses, of whom 95 (86 %) were men and 16 women (14 %).

The clinical history of the participating study subjects was heterogeneous, but certain chains of events can be identified. The most common sequence was one primary repair and one reoperation for pain. (Table 4:1)

<table>
<thead>
<tr>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>One reoperation</td>
</tr>
<tr>
<td>More than one reoperation</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

*Table 4:1. Course of surgical procedures*

The Lichtenstein repair dominated the techniques used at the primary repairs, as expected, since it was the most frequently used technique during the years prior to the reoperations seen in this study.

**Measures at reoperation**

Measures at reoperation were grouped in order to provide a basis for statistical analyses. Three main strategies could be identified:

- Operations aimed at nerves
- Operations aimed at a mesh or plug
- Operations aimed at fixations such as sutures
Procedures aimed at nerves were performed in 42 (38%) cases. The mesh was removed completely in 31 (28%) cases, and partially in 14 (13%). In practice, different approaches are often combined and sometimes no clear strategy can be deduced from the records.

Surgical management of the nerves showed large variation, from not even being mentioned to being the primary focus of attention. Details are given in table 4:2.

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Identified</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ilioinguinal nerve</td>
<td>36</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>(32%)</td>
<td>(12%)</td>
</tr>
<tr>
<td>Iliohypogastric nerve</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>(13%)</td>
<td>(14%)</td>
</tr>
<tr>
<td>Genitofemoral nerve</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>(9%)</td>
<td>(11%)</td>
</tr>
</tbody>
</table>

*Table 4:2. Management of nerves at surgery for chronic pain*
Outcome
When requested to compare present pain to the level of pain prior to latest surgery, 69 (63 %) reported a decrease. (Table 4:3) Despite the improvement, 47 (42 %) of the patients reported pain that interfered with activities of daily living. (Table 4:4)

<table>
<thead>
<tr>
<th>Answer</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very much less</td>
<td>24 (22)</td>
</tr>
<tr>
<td>Considerably less</td>
<td>23 (21)</td>
</tr>
<tr>
<td>Somewhat less</td>
<td>22 (20)</td>
</tr>
<tr>
<td>Neither more or less</td>
<td>21 (19)</td>
</tr>
<tr>
<td>Somewhat more</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Considerably more</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Very much more</td>
<td>6 (5)</td>
</tr>
</tbody>
</table>

*Table 4:3. Current pain compared to pain prior to latest reoperation*

<table>
<thead>
<tr>
<th>Present pain</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td>16 (15)</td>
</tr>
<tr>
<td>Pain present but can easily be ignored</td>
<td>21 (19)</td>
</tr>
<tr>
<td>Pain present, cannot be ignored, but does not interfere with everyday activities</td>
<td>27 (24)</td>
</tr>
<tr>
<td>Pain present, cannot be ignored, interferes with concentration on chores and daily activities</td>
<td>31 (28)</td>
</tr>
<tr>
<td>Pain present, cannot be ignored, interferes with most activities</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Pain present, cannot be ignored, necessitates bed rest</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Pain present, cannot be ignored, prompt medical advice sought</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

*Table 4:4. Present pain reported on the seven-step IPQ scale*

In an attempt to identify a relationship between the measures at reoperation and the patient-reported outcome, similar interventions were grouped together and compared to the remaining cases. Operations aimed at nerves, whether resection, neurolysis or division, did not score better than those who had their nerves left intact. In a similar analysis, operations where the mesh was removed, totally or in part, did not score significantly differently than the remaining study subjects.
Patients who were subject to local anaesthetic treatment as a part of the preoperative management, regardless of whether the purpose was diagnostic or therapeutic, reported significantly higher IPQ-scores than those who did not receive such intervention.

Quality-of-life, measured by SF-36 was significantly reduced, compared to the general population, matched by age and gender. In particular, the categories “role-physical” and bodily pain” was affected.
Discussion

Handling of nerves and postoperative pain in open inguinal hernia surgery

Sensory disturbances are as shown in Paper I common after inguinal hernia surgery. Chronic pain is also known to be a major concern for a considerable proportion of the patients (1). In theory, a correlation between altered nerve function and neuropathic pain could provide an instrument for the primary investigation of chronic postoperative groin pain. Furthermore, the use of verbal descriptors of pain characteristics has been proposed as a means of characterising nociceptive and neuropathic pain. The results of Paper I, however, do not give support to such possible use of neurologic examination and verbal descriptors in clinical routine.

The role of sensory disturbances and a possible link with pain was also addressed by Mikkelsen et al (30) who did not find any correlation between pain and hypoaesthesia. Another Danish study, using an advanced sensory mapping protocol, found no direct relationship between sensory loss and pain, but did find signs suggesting intraoperative nerve injury (31). A Swedish case-control study using a similar examination procedure identified a significant correlation between pain and hypoaesthesia as well as allodynia (32). The striking difference in sensory disturbances following Lichtenstein and TEP procedures in Paper I indicate that open groin exploration has a causal relationship to altered postoperative sensibility.

The second clinically important question to be addressed in this context is whether an expedient handling of the nerves can prevent chronic pain?

The ilioinguinal nerve, the iliohypogastric nerve and the genital branch of the genitofemoral nerve are all at risk to be injured during the procedure or to come in conflict with the repair. A nerve left in close proximity of the mesh may be affected by inflammation or entrapment and thus cause pain (33). If resected, a neuroma or sensitisation process might cause pain in the long term perspective (34).

A definitive answer on when resections of nerves are indicated and how it is best performed is still lacking, but there is some knowledge to make a well-founded decision. Study I argue against a relationship between pain and sensory disturbances but was not intended to explore a direct relationship between pain and handling of nerves.

A prospective study by Tsakayannis in 2004 (35) concluded that division of the ilioinguinal and iliohypogastric nerves is safe and is not associated with chronic pain after one year. However, that study did not include controls. The prevalence of numbness was below 10% and deemed as not
disabling. A retrospective trial by Dittrick (36) the same year, including a control group, came to the same conclusion, but in a randomised study on prophylactic division of the ilioinguinal nerve, Picchio (37) did not find any significant association with postoperative pain, but a higher incidence of sensory disturbance in the intervention arm of the study. In 2006 an Italian multicentre study by Alfieri at al. concluded that identification of the nerves was associated with a decreased risk for chronic pain, and that division of all three nerves increased the risk for pain. Bartlett et al. followed up the somewhat contradictory picture with a prospective study (38), proposing a pragmatic approach based on the risk for nerve injury in the individual case. A recent meta-analyses by Hsu (39) of randomised trials looking at ilioinguinal nerve division, including the one by Picchio and five smaller studies, did not reveal a significant association with chronic pain. The question of whether identification alone of the nerves affects the risk for postoperative long term pain was recently addressed in a study by Bischoff et al. (40) where no significant difference was seen. The pragmatic approach suggested by Bartlett seems to be adequate.

Sensory loss caused by the division of nerves can be approached as a possible symptom of its own, or as a proxy indication of nerve injury. The possibility of sensory loss due to division of a nerve is mentioned in the studies discussed above, but no analysis of its clinical relevance is given.

As concluded, Paper I of this thesis shows that sensory disturbances are common after open inguinal hernia repair. The clinical significance thereof remains to be more specifically determined. The impact on health-related quality of life from altered or loss of sensation in this region is probably small and of limited clinical significance. The possible association to chronic pain, on the other hand, makes it worthwhile investigating. However, advanced neurological examination equipment is needed and the results are difficult to interpret. This possibly limits the use to a much smaller circle than the majority of general surgeons engaged in hernia surgery.

**Inguinal hernia recurrence – When and Why?**

The technique related variability in incidence of hernia recurrence in relation to time after the index operation described in Paper II, indicate heterogeneous reasons for these failures. Recurrence may appear early or late, depending on different mechanisms. Recurrence as a result of fatigue of prosthetic material or of weak collagen phenotype, where long-term strain on the tissue finally overrides the strength of the repair, would be expected develop over several years. On the contrary, a situation where the repair is inferior in terms of surgical quality would most likely develop soon after surgery.
Such situations can be expected after a previous recurrence, where the anatomy might be altered, and after postoperative complications, where the healing process is impaired.

The benefit of mesh was well established ten years ago (18). It has since then been occasionally questioned (41, 42), but the long-term results of randomised trials (43), as well as register-based studies (44) consistently show the advantage of mesh repair. Suture repair, a group of techniques that have proven inferior in terms of absolute recurrence rate, was also shown to have a large proportion of early recurrences in Paper II. This is consistent with the theory of a high proportion of early recurrence as a consequence of the choice of an inferior surgical method.

The mechanism of recurrence after open repair, especially Lichtenstein, has been found to be direct in more than 50 % (45, 46). The mechanism for recurrence after laparoscopic repair is more difficult to define, since the technique has evolved and has altered regarding mesh size, fixation and surgical approach. Data in Paper II was to a large extent gathered during a period when laparoscopic hernia repairs were under their early developmental phase. Thus, the high proportion of early recurrences may be explained by immaturity of the method. A more technically demanding procedure, requiring a longer learning curve, is another plausible explanation. The learning curve for TEP has been estimated to 50-100 procedures, (19) even though dedicated training programs can shorten the learning period required (47).

Even though Paper II shows that different time profiles for recurrence exists, interpretation must be made with caution. Reoperation was used as a proxy measurement for recurrence. A number of recurrences of uncertain clinical significance are thus not taken into account, possibly as high proportion as 40 % (48).

Reports from national hernia registers in Sweden and Denmark have reported one year reoperation rates to be around 1 % (6, 49). Given the recent reports of a considerably higher incidence of chronic pain, it is reasonable that the focus of hernia research has shifted towards pain and quality-of-life.

However, it is always of importance to evaluate recurrence, to ensure that the high standards remain, and that further improvements can be made.

**Minimising short term pain**

The proportion of patients being operated as day-case surgery for inguinal hernia has increased from 33.6 % in 1992, to 78.5 % in 2011, according to data from the Swedish Hernia Register (6). This change is probably
related to several anaesthesiology and surgery factors, as well as a general emphasis on improved efficiency and shortened length of hospital stay after surgery.

Paper III provides evidence supporting the use of glucocorticoids, as a means of optimising postoperative recovery, after open inguinal hernia surgery. The effect was detectable during the day of surgery, and the day after, which is congruent to the time frame of the pharmacological effect of the drug (50). Time to discharge is influenced by several organisational factors that possibly obscure the effect of betamethasone.

Interestingly, the difference in pain was not obvious during postoperative day 2-7. However, after one month a significant difference in pain perception was again apparent. This time related effect on pain perception is difficult to explain. The telephone call used a simple yes or no question that might yield different results than the VAS scale used during the first week. Furthermore, the need for analgesics at one month did not differ between the groups.

Short-term pain is of interest as an endpoint \textit{per se}, but has also been associated with risk for chronic pain after inguinal hernia surgery (1, 51). Whether a causal relationship between acute and chronic pain exists is difficult to determine. In Paper III, the incidence of chronic pain one year after surgery was not found to be affected by perioperative treatment with betamethasone. The hypothesis that chronic groin pain can be prevented by aggressively treating acute pain is thus not supported by the results of this study.

Tolver et al. studied the effect of 8 mg of dexamethasone after TAPP procedures in a randomised trial. No significant difference was seen regarding pain, but a decreased need for antiemetics was recorded in the dexamethasone group (52).

In a recent review of the literature by Joshi et al. (53), local anaesthetics, NSAID or COX-2 inhibitors and paracetamol are recommended after inguinal hernia surgery. Weak or strong opioids are recommended as supplement when necessary. The use of glucocorticoids was given recommendation grade B (according to the PROSPECT grades of recommendation), based on transferred evidence. The result of study III further supports the use of corticosteroids in inguinal hernia surgery. Since an increased risk for postoperative bleeding may occur, at least according to one study on tonsillectomy (54), further studies on complication rates may be needed.
**Management of chronic pain**

As shown in Paper IV, surgical management of chronic pain after inguinal hernia surgery in Sweden is heterogeneous with respect to patient characteristics and outcome. More than half of the patients reported a beneficial effect compared to before surgery. However, impairment, as well as no effect was also observed. The absence of a reliable surgical technique for reoperation emphasizes the importance to consider how to avoid the development of chronic pain at the index operation.

By performing surgery, the risk of inflicting more damage than benefit, must be taken into account. By refraining from surgery in the asymptomatic or minimally symptomatic patient, the risk of causing chronic pain can sometimes be avoided. This has been the subject of two randomised trials (55, 56), as well as several observational and register-based studies. The results have recently been compiled in two review articles (57, 58). The drawback is a possible risk for future surgery due to progress of symptoms. In one study, the cumulative operation rate, was as high as 72 % at 7.5 years (59). The annual risk for incarceration is 0.4 % (58). In summary, to abstain from surgery is a safe alternative that should be considered.

Most often it is not advisable to completely avoid surgery. However, there are still some measures to consider in order to minimise the risk for chronic pain. The means of fixation of the mesh in open and laparoscopic surgery may also affect the risk. Two studies on sutureless fixation in open mesh repair show promising short-term results, but the possible disadvantage in terms of higher long-term recurrence rates remains to be excluded (60, 61). The use of fibrin glue, as a way to reduce the risk of pain, is well established in laparoscopic inguinal hernia surgery (62).

Traditional meshes in hernia repair weigh approximately 80 g/m². Over time, less dense mesh structures of 25-55 g/m² have gained popularity. The accumulated evidence, compiled in three different meta-analyses, shows some advantage regarding chronic pain and symptoms related to foreign body sensation. (63-65). The properties of a hernia mesh are determined by a number of factors, density being one. Mesh composition, poor-size and coating, can also be of importance, making the over all characterisation more complex(66).

Laparoscopic procedures are associated with a lower risk for chronic pain (2, 67). Fixation by means of tacks or staples is associated with an increased risk for pain after TEP, at least three months after surgery (62).

In addition to the mesh related factors, the handling of the nerves should also be mentioned in this context, and has been discussed above.

Surgical treatment of chronic pain, once it has occurred, has not been supported by high-level scientific evidence. Even though the issue has
gained more attention in recent years, the problem have been well known for a long time, as shown by this statement from 1981:

"Our experience, as well as the literature on this condition, indicates that therapeutic successes are uncommon regardless of the treatment modality utilized" (68)

Fortunately, much progress has been made since then, although randomised trials are lacking.

Most cases of chronic pain are relatively mild, as was shown in Paper I (fig 1:1). The natural course of the condition gives some hope of improvement over time, as the proportion of patients with severe pain often decline during many years after surgery (2). On the other hand, pain may also develop or increase in some patients, (69) which makes the picture more complicated.

In most cases of mild pain, exclusion of a recurrence and other causes of pain, and the hope for improvement over time, might be sufficient. In more severe cases, invasive procedures may be considered. As nerve injury is a likely cause of pain, interventions to correct such injuries is the most frequently described procedure.

The most radical approach is to divide all three major nerves in case of pain after previous open surgery. The procedure, called “triple neurectomy”, has been presented by Amid, who has reported favourable results, but based on a very short follow-up time (17, 24). A series of three patients has been published where the same nerves were divided in the retroperitoneal space, thereby avoiding the sometimes difficult dissection in a previously operated groin (70). A significant pain relief was seen, but revision surgery was required in one case.

Aasvang et al. have proposed a more conservative approach. They reported a favourable outcome regarding pain-related impairment six months after selective neurectomy of 1-2 nerves in combination with mesh removal. In a study by Delikoukos et al., a similar procedure was performed in 4 of 6 patients. The remaining two had a staple at the pubic tubercle removed. No re-occurring pain was reported, but details of follow up are not given (71). Laparoscopic selective neurectomy of 1-2 nerves have been reported by Giger at al., resulting in decreased pain in 27 of 29 patients after one year (72).

An even less invasive method is to use pulsed radiofrequency to temporarily block the nerve conduction, but the evidence is so far limited (73).

Sutures at the tubic tubercle are sometimes assumed to cause pain and are consequently removed at reoperation. Results from such procedures in Paper IV showed mixed results, and were to few for general conclusions.
Even if no strategy has been unequivocally superior to the others, thorough preoperative investigation and medical treatment by a pain specialist is recommended for a favourable outcome in the management of chronic postoperative pain.

Paper IV of this thesis, differs from previous publications in the description of results from a population based material, rather then the experience of single centre. This design is intended to give a true assessment of outcome in routine surgical practice.

Quality of life was impaired, not only on the subscales related to pain, but for the entire spectrum of SF-36. This indicates that there might be other factors involved, not related to the groin. The high proportion of non-responders may decrease the possibility to draw generalised conclusions. However, it might also indicate, that this group of patient reject contact with health care facilities, to which the study was related.

The result, in terms of residual pain, was worse after repeated reoperations. This might indicate that chronic groin pain, once it has developed, is not a process limited to the region. Altered excitability, changes in gene expression and loss of inhibitory interneurons, on the level of the dorsal root ganglion and dorsal horn of the spinal cord are described in postsurgical neuropathic pain (13, 34). Such mechanisms are, of course, unlikely to be cured by groin surgery.

The possibility of an overlooked reason for pain, completely separated from previous hernia and hernia surgery, might explain some cases.

"After the groin procedures (4), I have had both my hip joints replaced. Quite difficult to know what's causing what (pain)"
The field of surgery due to chronic pain after inguinal hernia surgery is developing rapidly, with regards to the number of publications, and the cumulated experience. Randomised trials would be desirable, but would be a challenge due to the limited number of patients in each centre, and the need for long-term follow up.
Conclusions

I. Sensory disturbances are common after open inguinal hernia surgery. No clear correlation to handling of the nerves can be demonstrated by basic neurologic investigation.

II. The time-profile for recurrence after inguinal hernia surgery varies, indicating different reasons for recurrence, depending on patient- and surgery-related factors.

III. Acute postoperative pain after open inguinal hernia is reduced by a single dose of betamethasone. Pain one year postoperatively is not affected by the treatment.

IV. Reoperation for chronic pain after previous inguinal hernia surgery has an overall positive effect, but considerable variation is seen. Dividing nerves or removing mesh or mesh fixation are common strategies at reoperation, but no method shows better results than the other.
Sammanfattning på svenska
(Summary in Swedish)

I Sverige utförs cirka 16 000 ljumskbråckoperationer varje år. En av fyra män opereras för ljumskbräck under sin livstid, vilket gör det till ett av de vanligaste kirurgiska ingreppen. Cirka nio procent av de som opereras är kvinnor.

Under de senaste decennierna har konstgjorda nät som förstärkning gjort att risken för ett nytt bräck i samma ljumske (recidiv) minskat påtagligt. Risken att behöva opereras igen på grund av recidiv är cirka 1 % efter ett år och 4 % efter fem år.

Vid operation för ljumskbräck används oftast ”Lichtensteintekniken”, vilket innebär att ljumsken öppnas och ett nät sys fast som förstärkning i ljumskkanalen. Vid sidan av det används laparoskopiska tekniker (tirthållskirurgi) vilket har visat sig fördelaktigt framför allt vid femoralbräck (lårbräck), ljumskbräck hos kvinnor och efter recidiv. Det ger även mindre smärta, men till priset av en lite mer avancerad och resurskrävande operation. Andra tekniker som bygger på att bräcket lagas med hjälp av suturer (tråd) eller en plugg av nät används också.

Allt eftersom resultaten förbättrats med avseende på recidiv har focus kommit att flytta över till andra utfallsmått, framför allt kronisk smärta (smärta mer än tre månader). Risken för smärta som påverkar dagliga aktiviteter är kring 6 %, men någon grad av smärta drabbar cirka 30 %.

Svenskt Bräckregister startades 1992 av åtta sjukhus och har med tiden utvidgats till att omfatta nära 100 % av svensk ljumskbräckskirurgi. I registret återfinns information om patienters identitet, operationsdatum, vilken operationsteknik som använts, vilken typ av ljumskbräck som opereras, vilken typ av nät som använts, om komplikationer tillstött med mera. Delarbete II och IV i denna avhandling utgår från material från Svenskt Bräckregister. Även delarbete I och III har dragit nytta av registermaterialet.

För att kunna mäta smärta behövs speciellt utarbetade formulär. I den här avhandlingen används framför allt ”Inguinal Pain Questionnaire”, ett formulär för bedömning av smärta i ljumsken, som tidigare validerats och använts i liknande studier. Utöver det används VAS-skalan för skattning av smärta och SF-36 för mätning av livskvalitet.

I delarbete I undersökt det möjliga sambandet mellan hantering av nerver vid bräckkirurgi och känselstörningar. 97 ljumskar hos 92 patienter undersöktes ett år efter operationen. Känselstörningar sågs hos en stor
Andel av de öppet opererade (29 %), men inte hos de laparoskopiskt opererade. Ingen relation mellan kronisk smärta och känselstörning sågs.

**Delarbete II** utgörs av en registerstudie av 142 578 ljumskbräckoperationer. Vid en jämförelse av de fem första åren efter operationerna undersöktes hur recidivrisken fördelades tidsmässigt. En högre andel av recidiven inträffade tidigt om den föregående operationen var en suturplastik, en laparoskopisk operation, en operation för recidiv eller om en postoperativ komplikation tillstött. Resultatet kan utgöra underlag för diskussion och teoribildning kring varför recidiv uppstår.

Kortisonpreparat har visat sig kunna minska smärta och illamående efter olika kirurgiska ingrepp. I **delarbete III** lottades 398 patienter till behandling med kortisonpreparatet betametason eller placebo. Lägre smärta för behandlingsgruppen sågs på operationsdagen och dagen efter, samt efter en månad. Ingen skillnad sågs dag 2-7 eller efter ett år. Illamående förkম i låg utsträckning i båda grupperna, och påverkades inte av behandlingen.

**Delarbete IV** utgår från patienter som reopererats på grund av kronisk smärta. Information om 111 patienter samlades in från Svenskt Bräckregister, journalanteckningar och enkäter. 62 % av patienterna rapporterade en förbättring av smärtan jämfört med före den reoperation de genomgått, men en hög andel hade fortsatt smärta (42 %) och vissa hade försämrats. Mätning av livskvalitet utföll lägre än för normalbefolkningen. Någon tydlig skillnad mellan olika kirurgiska åtgärder vid reoperationerna kunde inte ses.
Acknowledgements

This thesis project was made possible due to the guidance and help of a number of people, to which I would like to express my gratitude.

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# Appendix A

## The Inguinal Pain Questionnaire
for assessment of chronic pain after groin hernia repair

<table>
<thead>
<tr>
<th>1. Estimate the severity of pain in the groin you felt before the operation</th>
<th>(a) No pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>(b) Pain present but can easily be ignored</td>
<td></td>
</tr>
<tr>
<td>(c) Pain present, cannot be ignored, but does not interfere with everyday activities</td>
<td></td>
</tr>
<tr>
<td>(d) Pain present, cannot be ignored, interferes with concentration on chores and daily activities</td>
<td></td>
</tr>
<tr>
<td>(e) Pain present, cannot be ignored, interferes with most activities</td>
<td></td>
</tr>
<tr>
<td>(f) Pain present, cannot be ignored, necessitates bed rest</td>
<td></td>
</tr>
<tr>
<td>(g) Pain present, cannot be ignored, prompt medical advice sought</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Estimate the pain you feel right now in the groin on the same side as the operation</th>
<th>(c) Pain present, cannot be ignored, but does not interfere with everyday activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>(d) Pain present, cannot be ignored, interferes with concentration on chores and daily activities</td>
<td></td>
</tr>
<tr>
<td>(e) Pain present, cannot be ignored, interferes with most activities</td>
<td></td>
</tr>
<tr>
<td>(f) Pain present, cannot be ignored, necessitates bed rest</td>
<td></td>
</tr>
<tr>
<td>(g) Pain present, cannot be ignored, prompt medical advice sought</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Estimate the worst pain you felt in the operated groin during this past week</th>
<th>(e) Pain present, cannot be ignored, necessitates bed rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>(f) Pain present, cannot be ignored, prompt medical advice sought</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. If you answered “no pain” to question 3 try to remember when the pain in the operated groin disappeared after the operation</th>
<th>(a) The pain in the operated groin disappeared within 1 month after the operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(b) The pain in the operated groin disappeared 2–3 months after the operation</td>
<td></td>
</tr>
<tr>
<td>(c) The pain in the operated groin disappeared 4–6 months after the operation</td>
<td></td>
</tr>
<tr>
<td>(d) The pain in the operated groin disappeared 7–12 months after the operation</td>
<td></td>
</tr>
<tr>
<td>(e) The pain in the operated groin disappeared 13–24 months after the operation</td>
<td></td>
</tr>
<tr>
<td>(f) The pain in the operated groin disappeared recently</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. How often have you felt pain in the operated groin during the past week?</th>
<th>(a) Once a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>(b) 2–5 times a week</td>
<td></td>
</tr>
<tr>
<td>(c) Every day</td>
<td></td>
</tr>
<tr>
<td>(d) Every day and also during night time</td>
<td></td>
</tr>
<tr>
<td>(e) I have had pain the whole week, both day and night</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. How long have the episodes of pain lasted in the past week?</th>
<th>(a) 1 minute to 1 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>(b) 1–5 hours</td>
<td></td>
</tr>
<tr>
<td>(d) The whole day</td>
<td></td>
</tr>
<tr>
<td>(e) Day and night</td>
<td></td>
</tr>
<tr>
<td>(f) The pain has lasted the whole week, day and night</td>
<td></td>
</tr>
</tbody>
</table>
7. Do you find it difficult getting up from a low chair because of pain in the operated groin?  
   - No
   - Yes
   - I don’t know
   - Not applicable

8. Do you find it difficult sitting down for more than half an hour because of the pain?  

9. Do you find it difficult standing up for more than half an hour because of the pain?  

10. Do you find it difficult going up or down stairs because of the pain?  

11. Does driving a car cause you pain in the operated groin?  

12. Has the pain limited your ability to exercise and perform sports?  

13. Have you on any occasion taken pain-killers for pain in the operated groin?  
   - No
   - Yes

14. To what extent has pain in the groin limited your working capability in the last 2 months?  
   - (a) I have not needed to take sick leave
   - (b) The pain made me take 1–7 days’ sick leave during the last 2 months
   - (c) The pain made me take sick leave for 1–4 weeks during the last 2 months
   - (d) The pain has made me take sick leave for the whole of the last 2 months
   - (e) I have a disability pension because of pain in the groin
   - (f) I am not working

15. Estimate the severity of pain you feel right now in the groin opposite to the operated side  
   - (a) No pain
   - (b) Pain present but can easily be ignored
   - (c) Pain present, cannot be ignored, but does not interfere with everyday activities
   - (d) Pain present, cannot be ignored, interferes with concentration on chores and daily activities
   - (e) Pain present, cannot be ignored, interferes with most activities
   - (f) Pain present, cannot be ignored, necessitates bed rest
   - (g) Pain present, cannot be ignored, prompt medical advice sought

16. Estimate the worst pain you have felt in the groin opposite to the operated side during this past 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

18. Have you had a hernia or abdominal operation since the hernia operation?  
   - No
   - Yes
Appendix B

List of verbal descriptors used in paper I

Tender
Shooting
Constricting
Sharp
Pricking
Cleaving
Stabbing
Pulling
Drilling
Hot/burning
Dull/aching
Radiating
Pounding
Irritating
Tiring/exhausting
Sickening
Frightful
Punishing


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