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MINIMALLY INVASIVE HERNIA SURGERY

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Illustration on the rear side of the book cover

Warhol Andy
Where Is Your Rupture?, c. 1960
Water-based paint on linen
54 1/4 x 69 7/8 inches
Daros Collection, Switzerland

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To Lena, Hanna and Joel

ABSTRACT

Minimally invasive laparoscopic and open tension-free techniques have been evolved during the 1990's. Different laparoscopic techniques have been used, where the totally extraperitoneal hernioplasty (TEP) is a technically demanding but probably a better approach to minimally invasive hernia surgery than the transabdominal preperitoneal technique (TAPP), which may increase the risk of adhesions and postoperative intestinal obstruction. TEP has been criticized because of expensive disposable equipment. The standard polypropylene mesh used in tension-free operations induces a strong foreign tissue reaction with potentially harmful effects. A mesh with less polypropylene could possibly be beneficial.

The aim of this thesis was to evaluate and compare different minimally invasive techniques and meshes for inguinal hernia.

In three randomized controlled multi-center studies 1212 patients were randomized and included in follow-up: TEP with or without the use of a dissection balloon (322 patients); TEP using only reusable instruments, mesh-plug or Lichtenstein (299 patients); Lichtenstein with Prolene or VyproII (which contains less polypropylene) mesh (591 patients). In the last study all randomization and entering of data was performed online in a database through the Internet, which facilitated the completion of the trial. More than 80% of all patients in the studies were operated on in day-surgery.

There were more conversions to TAPP or an open technique if a balloon not was used. However the majority of the conversions occurred early in the learning curve, which indicates that the use of a dissection balloon can be helpful during the learning curve, but in experienced hands it just adds costs to the operation, without offering additional benefits
The operation time was shorter in the mesh-plug group compared to Lichtenstein and TEP. Postoperative pain was diminished after TEP compared to open repair. The time to return to work was shorter after TEP than Lichtenstein (5 vs. 7 days). The time of rehabilitation was shorter after TEP than mesh-plug or Lichtenstein (14 vs. 24.5 vs. 28.5 days). There was a tendency of more pain after Lichtenstein than after TEP or mesh-plug at follow-up. Laparoscopic hernioplasty (TEP) is superior to tension-free open herniorrhaphy with Mesh-plug and patch or Lichtenstein's operation in terms of postoperative pain and rehabilitation.
There was no significant difference between Lichtenstein with Prolene or VyproII concerning postoperative pain, complications, rehabilitation or quality of life.

All patients (n=33 275) with a unilateral primary inguinal or femoral hernia with only one operation recorded in the Swedish Hernia Register 1992-2000 were linked to the Swedish Inpatient Register and the Swedish Death Register for the period 1987-2000. The highest adjusted relative risk (RR) of postoperative intestinal obstruction was found in patients with previous multiple admissions for abdominal operations/inflammations, including intestinal obstruction, 58.99. The RR was 2.79 with TAPP and 0.57 with TEP compared to Lichtenstein operated patients.

Keywords: Inguinal hernia, minimally invasive, laparoscopic, TEP, TAPP, Lichtenstein, Mesh-plug, tension-free, mesh, rehabilitation, Swedish Hernia Register, learning curve, complications, intestinal obstruction, polypropylene, polyglactin

LIST OF PUBLICATIONS

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

I. Bringman S, Ek A, Haglind E, Heikkinen T, Kald A, Kylberg F, Ramel S, Wallon C, Anderberg B.
Is a dissection balloon beneficial in totally extraperitoneal endoscopic hernioplasty (TEP)? A randomized prospective multicenter study.
Surg Endosc 2001; 15(3):266-70.

II. Bringman S, Ramel S, Heikkinen TJ, Englund T, Westman B, Anderberg B.
Tension-free inguinal hernia repair: TEP versus Mesh-plug versus Lichtenstein: A prospective randomized controlled trial.
Ann Surg 2003;237(1):142-7.

III. Bringman S, Heikkinen T, Wollert S, Österberg J, Smedberg S, Granlund H, Ramel S, Felländer G, Anderberg B.
Early results of a single-blinded, randomized controlled, Internet-based multicenter trial comparing Prolene and VyproII mesh in Lichtenstein hernioplasty.
Submitted Ann Surg.

IV. Bringman S, Blomqvist P.
Intestinal obstruction after laparoscopic inguinal hernia repair.
Submitted Ann Surg.

CONTENTS

ABBREVIATIONS

ANOVA	Analysis of Variance
CI	Confidence Interval
EU	European Union
IPOM	Intraperitoneal onlay mesh
MRC	Medical Research Council
NICE	National Center of Clinical Excellence
OR	Odds Ratio
QR	Inter Quartile Range
RR	Relative Risk
SD	Standard Deviation
SF-36	Short Form 36
SHR	Swedish Hernia Register
SMR	Standardized Mortality Rate
TAPP	Transabdominal preperitoneal
TEP	Totally extraperitoneal
VAS	Visual Analogue Scale

INTRODUCTION

"The final word on hernia will probably never be written" (Sir John Bruce of Edinburgh) [1].

DEFINITION

A hernia is an abnormal protrusion of a peritoneal-lined sac through the musculoaponeurotic covering of the abdomen[2]. Operations for groin hernias are the most common in general surgery with an incidence of about 200 per 100 000 inhabitants in Sweden[3].

PATHOGENESIS

Why do humans develop groin hernias?[4]. There are congenital, metabolic, anatomic, and maybe physical factors influencing the incidence of hernias. A patent processus vaginalis is a well-known factor for indirect inguinal herniation[4, 5]. Epidemiological evidence have shown that 20% of men pass into adulthood with a patent processus vaginalis, of which less than 50% develop clinical herniation[6]. There is also a genetic influence with a familial tendency to groin herniation. A quarter of inguinal hernia patients give a history of similar hernias in their parents and grandparents [4].

Unlike inguinal hernia, femoral herniation is rare in infancy and childhood[4]. It is more common in women due to a larger and more oval femoral ring, weaker inguinal ligament and smaller iliopsoas muscle[4]. Previous Bassini-type sutured repairs also increases the risk of femoral hernia due to elevation of the inguinal ligament[4].

There is strong evidence for an association between abnormal metabolism of connective tissue and the development of groin hernia [5]. Biochemical, morphologic, and biomechanical differences have been found in the connective tissue in patients with hernia, compared to controls [5]. The prevalence of inguinal hernia rises with patient age[5]. The activity of collagen-degrading enzymes is higher in older patients, presumably due to a reduced inhibition of collagenase[7].
Smoking may be a contributor to the creation of groin hernia through inducing a systemic imbalance in levels of protease and antiprotease, which affects the connective tissue of the groin[4, 5]. Smokers have a higher risk of recurrence after hernia surgery [6].
In hernia recurrence, insufficient surgical technique may not be the only explanation for recurrence, but more likely it is a combination of an on-going defect in connective tissue metabolism and patophysiologic factors associated with the surgical technique applied [5].

Prolonged stretching and pressure of the fascia transversalis caused by raised intra-abdominal pressure is considered an additional facilitating factor for groin hernia formation[5, 8].
Heavy workload and lifting heavy objects repeatedly over long periods of time are also factors contributing to the development of hernias[9] but a single strenuous event preceded the appearance of inguinal herniation in only 7% of men questioned after presentation[10]. The physical habitus can also influence the development of a hernia. Patients with indirect hernias have been found to be both heavier and taller than controls[9].

HISTORY

Hernias have been described in the literature since ancient times. The earliest recorded reference to hernias appears in the Egyptian Papyrus of Ebers (circa 1550 B.C.) [11]. Tightly fitting bandages were used as treatment for inguinal hernia by physicians in Alexandria, and a 900 BC Phoenician statuette depicts a bilateral inguinal hernia so treated[12].

Aulus Cornelius Celsus (?–AD 50) introduced Greek and Alexandrian medicine to Rome. Trusses were widely employed; operation was advised for pain, especially in the young, but not with large protrusions or when the symptoms of strangulation supervened. An incision was made in the scrotum just below the pubis, and the sac was dissected from the cord and excised, the wound being left open to granulate. If large, it was cauterized to enhance scar formation[12].

However, during the Middle Ages the technical advances of Egyptian and Graeco-Roman surgery were largely lost. During the Renaissance, Paré (1510-1590) elevated surgery from an ill-reputed handicraft to a respected art[11].

The knowledge of the inguinal anatomy increased in the early nineteenth century. Many well-known surgeons such as Richter (1785), and Scarpa (1814), published in this field[12]. Primitive techniques of plugging the inguinal canal to prevent the emergence of herniated tissue were described during the mid-1830s. Pierre Nicholas Gerdy plugged the inguinal canal with an inverted fold of skin, scrotal or otherwise, maintained in position by both sutures and creation of a caustic-induced inflammatory response [12]. During the same era, C.W. Wutzer proposed temporary placement of a foreign body (i.e., a wooden hernia plug, pushing the scrotal skin and testicle in front of it) to help invaginate and hold tissue until the inguinal canal was closed by inflammatory adhesions[12].

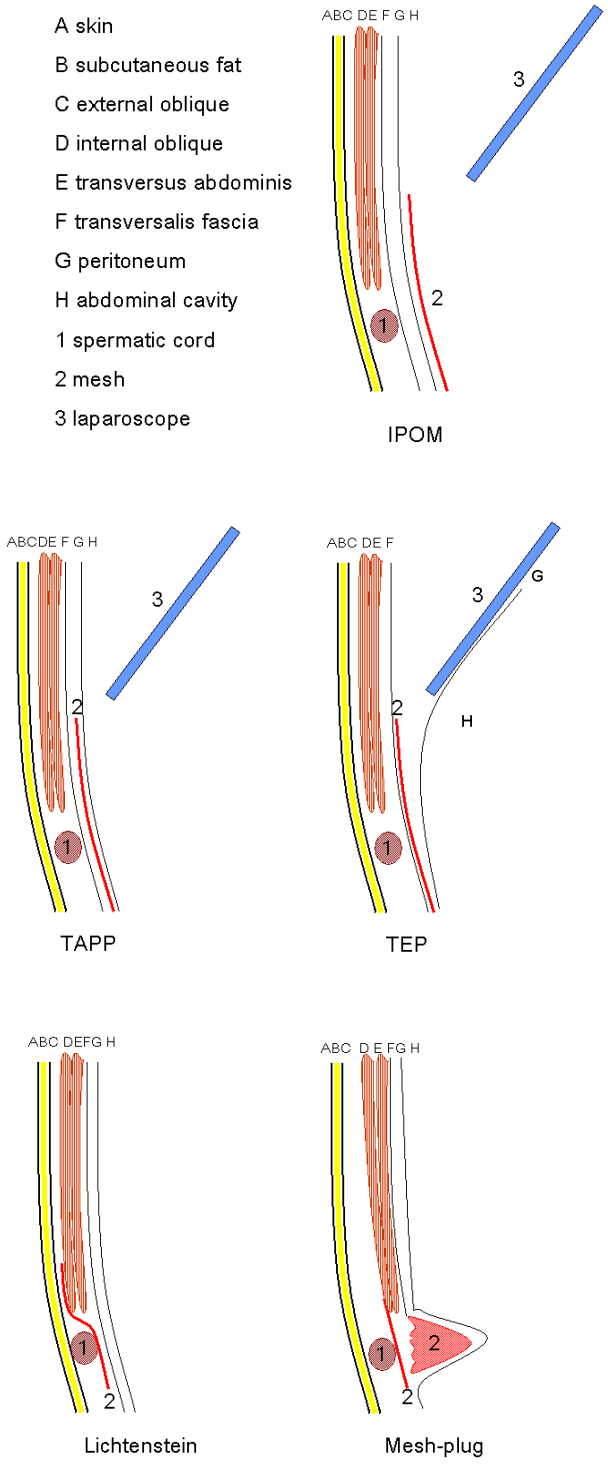
The creator of modern hernia surgery was the Italian surgeon Eduardo Bassini (1844-1924) [11]who published his monograph on hernia repair 1889[13]. He made a 3-layer reconstruction of the posterior wall of the inguinal canal where he used the transversalis fascia – an important step often corrupted in the operation carrying his name[14]. In his series of 262 patients he reported only seven recurrences with 90% follow-up at 4½ years[15]. The Shouldice repair, developed by E.E. Shouldice in the late 1930s in Canada[16], is based on the same principles as the Bassini repair – a pure tissue repair of the posterior wall, but with a continuous monofilament suture, traditionally steel wire[15].

TENSION-FREE HERNIOPLASTY

Mesh

Theodore Billroth (1829-1894) stated, “If we could artificially produce tissues of the density and toughness of fascia and tendon, the secret of the radical cure of hernia would be discovered” [17]. A lot of different foreign biologic and artificial materials have been tested. Marcy experimented with animal tendons in the end of the 19th century. Other authors recommended fascia lata strips and there were a large combative literature during the 1930’s and 1940’s, reporting the use of various natural organic prostheses[12]. As late as 1975 Sames described the use of vas deferens in hernioplasty[18]. There are hardly any controversies concerning this anymore: homologous and heterologous fascia has no value in hernioplasty. It is, after all, implanted foreign organic matter and undergoes complete phagocytic degeneration after a time[19]. Metallic materials such as silver mesh filigree were introduced

Figure 1. SAGITTAL VIEW OF THE ABDOMINAL WALL. LAPAROSCOPIC AND OPEN TENSION-FREE HERNIA REPAIRS



in the beginning of the 20th century [20] but initial high expectations were not met, with subsequent reports of metal fragmentation, sinus formation, tissue erosion, and hernia recurrence[12].

Mesh by polyester (Dacron, Mersilene) was introduced 1939 and it was the first mesh to stand the test of time. Its use has decreased, but it is still in clinical practice. Recently new polyester products has been manufactured and tried in large trials[21]. Polypropylene mesh (Marlex, Prolene) was introduced by Usher in the late 1950s[22, 23] and is now the most popular mesh for surgical implantation. It is macroporous with pores larger than 75 microns, which is the required pore size for admission of fibroblasts, blood vessels and collagen fibers in the pores which enhances the incorporation of the biomaterial[24]. The macroporousity of polypropylene makes it also possible for the macrophages and neutrofilic granulocytes to enter the pores in the event of a bacterial infection[24]. Polypropylene is however, associated with a strong foreign body reaction with potentially harmful side effects such as chronic inflammation[25].

Approaches of tension-free hernia repair

The mesh repair can be done in an anterior mode, posterior mode or by a combination of the two.

Anterior

Irving Lichtenstein introduced the anterior repair with a flat piece of polypropylene mesh among common surgeons in every-day practise[26]. The repair can be performed minimally invasive through a 5 cm incision[27](Fig 1 and 4).

Posterior

A posterior repair can either be performed preperitoneally with an open approach such as advocated by Stoppa[28] or minimally invasive with the use of a laparoscope.

The first report of a laparoscopic hernia repair was published by Ger in 1982, using a technique without a mesh[29]. During the 1980s there was a fast development of the video-endoscopic equipment facilitating laparoscopic surgery. The options of technical development in laparoscopic hernia surgery increased and different laparoscopic mesh techniques evolved. Schultz et al described a trans-

Figure 2. PREPERITONEAL ANATOMY (LEFT SIDE) AS SEEN IN TEP

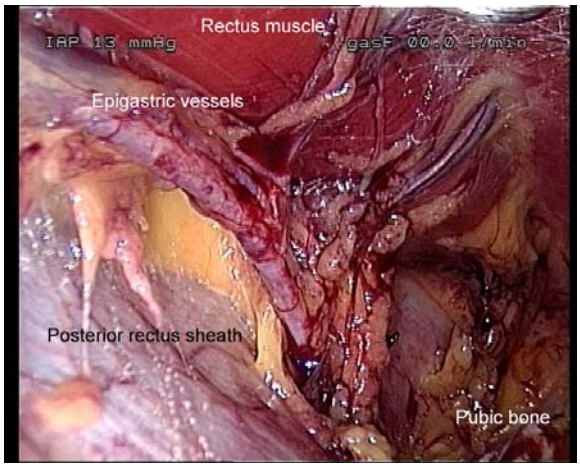
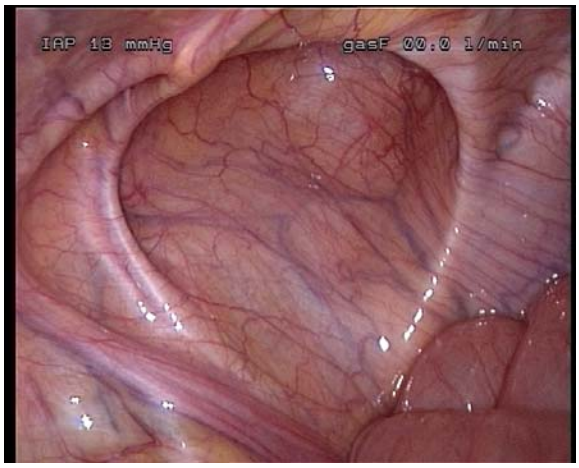


Figure 3. LARGE DIRECT INGUINAL HERNIA (LEFT SIDE) AS SEEN IN TAPP



abdominal laparoscopic technique 1990, where a preperitoneal polypropylene plug was put in the internal ring without stapling[30]. The 2-year recurrence rate was however 25% with this method and it was soon abandoned. Another technique that has been tried but with disappointing results is the intra-peritoneal onlay mesh technique (IPOM)(Fig 1), with recurrence rates of 43% with a mean follow-up of 43 months[31].

The two dominating laparoscopic techniques in the beginning of the 1990s were the trans-abdominal pre-peritoneal (TAPP) (Fig. 1 and 3) and the totally extra-peritoneal (TEP) (Fig. 1 and 2) hernioplasty. A common way to learn laparoscopic hernioplasty was to begin with TAPP, which is an easier operation, and once experience was gained, to continue with TEP[32]. Laparoscopic hernioplasty has been criticized because of its technical complexity, need for general anesthesia, risk for serious complications and increased costs [33]. However, most of these serious complications, such as major vessel or bowel injury, have been laparoscopy (TAPP) related, and avoidable when operating totally extraperitoneally (TEP) without entering the abdominal cavity[32, 34]. Since the peritoneal cavity is

Figure 4. VYPROII MESH IS SUTURED IN A LICHTENSTEIN REPAIR (RIGHT SIDE)

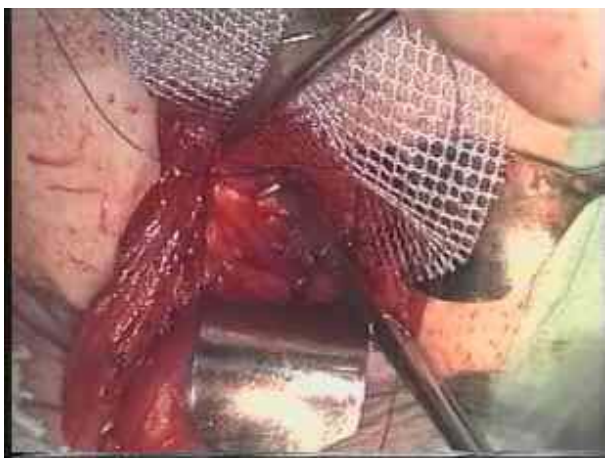


Figure 5. MESH-PLUG (PERFIX, POLYPROPYLENE)

entered during TAPP there is also a potential risk of postoperative intestinal obstruction due to adhesions or incarcerations in the trocar incisions[35]. In TEP, the peritoneal cavity is not entered and the risk of intra-abdominal intestinal obstruction is presumably the same as after open herniorrhaphy. However, there has been case reports describing intestinal obstruction after TEP where a peritoneal tear may be the cause of an incarceration[36, 37].

There is an undisputed learning curve associated with the TEP approach[38]. The operative costs of laparoscopic hernioplasties have been shown to be significantly higher when compared to the open anterior tension-free hernioplasties. This has been mostly due to longer operation time, instrument capital costs and the use of disposable instruments (trocars, hernia stapler, dissection balloon etc.)[39]. Although, there are significant potential indirect cost savings due to faster return to work[39, 40], the direct operation costs remain a key issue.
Disposable dissection balloons can be used in TEP hernioplasty to gain access to the initial preperitoneal working space. Despite their possible effectiveness, they also add a noticeable sum to the operation costs.

Anterior and posterior

A third approach to tension-free hernia repair is to plug the inguinal canal with a piece of mesh or mesh-plug in an open operation. Different plug repair techniques has been described by Lichtenstein, Gilbert, Robbins and Rutkow [41-43]. The mesh-plug and patch technique (Fig. 1 and 5) is a minimally invasive open procedure where the plug is placed pre-peritoneally in the hernial defect, i.e. posterior, and the patch is placed in an anterior approach. The operation with a mesh-plug and patch is easy to perform[44] while a TEP operation is technically more demanding [38].

HERNIA TRIALS

Evaluation of a new method or device in hernia surgery with enough power to detect relatively small differences in results and complications requires many observations. Consequently, multi-center studies are the best way to include a sufficient number of patients in a reasonable time. However, in multi-center studies the difficulties of randomization, monitoring and validation of data is larger than in a study in a single center. Communication between centers, keeping up the pace of inclusion in all centers and handling of data are problems to be addressed, and in most cases requires significant resources.

Follow-up

One of the problems in inguinal hernia research is that the patients must be followed during a significant period to evaluate the recurrence rate and the rate of late postoperative morbidity. Having all the patients returning to the hospital for a physical examination is time consuming and requires economic resources both for the patients and the health care system. Using a questionnaire for follow-up has been validated in two studies to be a convenient alternative to clinical visits[45, 46].

THE SWEDISH HERNIA REGISTER

The Swedish Hernia Register (SHR) was established in the year 1992[47]. Operations of groin hernias are prospectively documented by a protocol including patient characteristics, mode of admission, time on waiting list, type of hernia as defined during surgery, methods of repair, anesthesia, length of stay, complications within one month, reoperation for recurrence, and personal identification number. The personal identification number enables follow-up of the patients nationwide, even if they move. External reviews with site visits to hospitals to compare register data with SHR patient records are performed annually[47, 48]. Initially eight hospitals contributed, but now the majority of the Swedish surgical units have joined the SHR.

AIMS OF THE STUDY

To evaluate if a dissection balloon is beneficial in TEP. (Paper I)

To compare minimally invasive open and endoscopic hernioplasty. (Paper II)

To compare the postoperative course in tension-free hernioplasty with two different meshes. (Paper III)

To develop and establish an internet-based online method for clinical multi-center trials. (Paper III)

To evaluate the risk of postoperative intestinal obstruction after endoscopic hernioplasty. (Paper IV)

PATIENTS AND METHODS

PAPER I

A prospective randomized study performed in four Swedish hospitals. Men 30-75 years old with a unilateral primary or recurrent inguinal hernia were randomized for TEP with or without the use of a dissection balloon. A total of 322 patients were included in the study between 1994 and 1997. The patients were instructed to return to work and normal activities as soon as possible. Follow-up was done by questionnaires and an independent investigator saw the patients who presented with complaints, such as pain or a lump in the groin. The main outcome measures were operation time, technical difficulties and postoperative rehabilitation. The definition of recurrence was as described by Marsden[49].

PAPER II

A prospective randomized study performed in two Swedish hospitals. Men 30-75 years old with a unilateral primary or recurrent inguinal hernia were randomized to undergo TEP, Perfix mesh-plug and patch or Lichtenstein's operation. A total of 299 patients were included in the study between 1997 and 2000. The patients were instructed to return to work and normal activities as soon as possible. Follow-up was done by questionnaires and an independent investigator saw the patients who presented with complaints, such as pain or a lump in the groin. The main outcome measures were sick-leave, time to full recovery and operation time. The definition of recurrence was as described by Marsden[49].

PAPER III

A prospective single-blinded randomized study performed in five Swedish hospitals and one Finish hospital. Men >25 years old were randomized to undergo Lichtenstein's hernioplasty with Prolene-mesh or VyproII mesh. A total of 600 patients were randomized between December 2000 and April 2002. Three hundred one patients were randomized to Prolene and 299 to VyproII with the use of a computer algorithm in a database through the Internet. In the Prolene group 295 patients and in the VyproII group 296 patients were operated with the assigned method and were included in the analysis of the peri-operative and baseline data. The patients were instructed to return to work and normal activities as soon as possible. The patients recorded their rehabilitation in a diary with VAS scales and SF-36[50]. All data were directly entered, by each center, in the database through the Internet. The main outcome measures were postoperative pain and quality of life, time of rehabilitation and operation time.

PAPER IV

All patients with a unilateral primary inguinal or femoral hernia with only one operation recorded in the Swedish Hernia Register 1992-2000 were linked to the Swedish Inpatient Register and the Swedish Death Register for the period 1987-2000.
The main outcome measure was postoperative intestinal obstruction.

STATISTICS

The χ^2 test and Fisher's exact test was used to evaluate differences between categorical variables.
In the studies with two groups, Student's t-test was used to compare normally distributed continuous data and the Mann-Whitney U-test was used to test between continuous variables that where not normally distributed. (Paper I, III)
In the study with three groups (Paper II) The Kruskal-Wallis ANOVA was used to analyze the continuous variables and VAS, with multiple comparisons according to Siegel-Castellan to distinguish between the variables if a level of significance was found.
In Paper IV, uni- and multivariate Cox regression analyses were performed to estimate and compare unadjusted and adjusted relative risks.
A p-value <0.05 was considered statistically significant.

RESULTS

PROSPECTIVE RANDOMIZED HERNIA STUDIES (PAPER I-III)

Day-surgery

In all studies more than 80% of totally 1212 operations were performed in day-surgery. In Paper II all patients were operated on in day surgery or were admitted less than 24 hours. All TEP operations and the majority of the open procedures were performed under general anesthesia (Table 2).

Operation time

The operation time was shorter in the balloon group than in the group without the balloon (Paper I) in the Mesh-plug group compared with TEP and Lichtenstein (Paper II) and in the Prolene group compared to VyproII (Paper III) (Table 2).

Peroperative

In the balloon group 83 (52%) patients had a peritoneal lesion and in the group without balloon 93 (58%), p=0,26. There were three (2,5%) conversions to TAPP or open herniorrhaphy in the balloon group and 17 (10,6%) in the group without balloon (p=0,002) (Table 1). The majority of the conversions (3/3 or 100% in the balloon group and 12/17 or 70% in the group without balloon) occurred for each surgeon's first fifteen operations included in the trial. All operations converted to TAPP because of difficult access, also had a peritoneal lesion recorded (Paper I). There were no conversions or peroperative complications in the groups in Paper II.

Table 1. REASONS FOR CONVERSION

	Anatomy	Difficult access	Hemorr-hage	Fixed hernia sac	Total
With balloon					
Conversion to TAPP	1	1	0	0	2
Open	0	1	0	0	1
Total					3
Without balloon					
Conversion to TAPP	0	8	0	2	10
Open	1	1	4	1	7
Total					17

Postoperative pain and quality of life

VAS was lower in TEP than Lichtenstein after two hours and four hours and lower compared to Lichtenstein and Mesh-plug in the next morning (p<0,0001) (Table 2).
There was no difference between Lichtenstein with Prolene or VyproII concerning postoperative pain (VAS) (Fig 6, Table 2) or the quality of life measured by SF-36 (Fig 7).

Table 2. PERIOPERATIVE AND POSTOPERATIVE RESULTS PAPER I-III

	PAPER I			PAPER II				PAPER III		
	Balloon	**No balloon**	**p**	**TEP**	**Mesh-plug**	**Lichtenstein**	**p**	**Prolene**	**Vyproll**	**p**
n	161	161		92	104	103		295	296	
Day-surgery (%)	130 (81)	132 (82)		90 (97)	97 (93)	95 (92)		243 (82)	242(82)	
Hospital stay	1.2 (0.5)	1.4 (0.8)		1 (1-1)	1 (1-1)	1 (1-1)		1 (1-4)	1 (1-4)	
Anesthesia										
General (%)	161 (100)	161 (100)		92 (100)	98 (94)	100 (97)		204 (69)	172 (58)	
Spinal or epidural (%)	0	0		0	6 (6)	3 (3)		59 (20)	89 (30)	
Local (%)	0	0		0	0	0		32 (11)	35 (12)	
Operation time, (min)	55 (24)	63 (26)	0.004	50 (25-150)	36 (19-88)	45 (24-100)	<0.0001	50 (21-140)	53 (27-144)	<0.05
Return to work	4.5 (0-45)	5 (0-500)	0.12	5 (0-30)	7 (0-150)	7 (0-70)	0.02	16.5 (0-97)	16 (0-66)	ns
Rehabilitation	14 (0-150)	14 (3-180)	0.01	14 (0-80)	24.5 (0-122)	28.5 (1-365)	<0.0001	21 (1-135)	19 (0-106)	ns
VAS pain day 1 (at rest)	..	..		10 (0-80)	20 (0-70)	20 (0-70)	<0.0001	18 (0-75)	16 (0-68)	ns

Data are given as median and range except operation time in Paper III (mean) and hospital stay in Paper I (mean, SD).

Hospital stay (days) are concerning only admitted patients

Rehabilitation (days): Time to complete recovery in PAPER I, II; Time to normal daily activities in PAPER III

Rehabilitation

There was no significant difference between the groups in terms of return to work between the two TEP-operations in Paper I or between the Lichtenstein groups in Paper III. In Paper II the patients in the TEP group had a significantly shorter period of sick-leave compared to the Lichtenstein group (Table 2).

The time to full recovery in the balloon group was significantly shorter than in the group without the balloon. It was also shorter in TEP than Mesh-plug or Lichtenstein. There was no difference between the Lichtenstein groups in Paper III concerning time to normal daily activities (Table 2).

Early complications

There were no major complications in the studies and no significant difference between the groups in each study respectively (Table 3). One of the complications in the balloon group and four in the group without balloon occurred after a conversion to TAPP or open hernioplasty. One patient in the VyproII group with a postoperative hematoma needed reoperation with evacuation of the hematoma on the day of the operation. One seroma in the Mesh-plug group was re-operated acute with an open exploration because the surgeon who was on call suspected an acute recurrence. All infections healed without surgical intervention. The patients with prolonged pain in Paper II had recovered completely before follow-up. There were seven (2,4%) patients with prolonged postoperative pain or neuralgia in the Prolene group and two (0,7%) in the VyproII group (95%CI -0,4% to 4,2%). All the infections were superficial and no meshes had to be removed.

Follow-up and late complications

The patients in Paper I were followed (SD) 26(10) and 27(11) months and the patients in Paper II were followed (SD) 19.8 (8.6) months. In Paper III the follow-up was eight weeks.
There were no significant differences between the groups in respective study concerning long-term complications including recurrences (Table 3).
All patients in Paper I with neuralgia had the mesh stapled. None of the patients with pain or mesh-related problems is permanently disabled or needs a re-operation. No patient has chronic pain.

There were four recurrences after a primary hernia and one after a recurrent hernia (3,1%) in the balloon group and five recurrences after a primary hernia and one after a recurrent hernia (3,7%) in the group without balloon (Paper I).

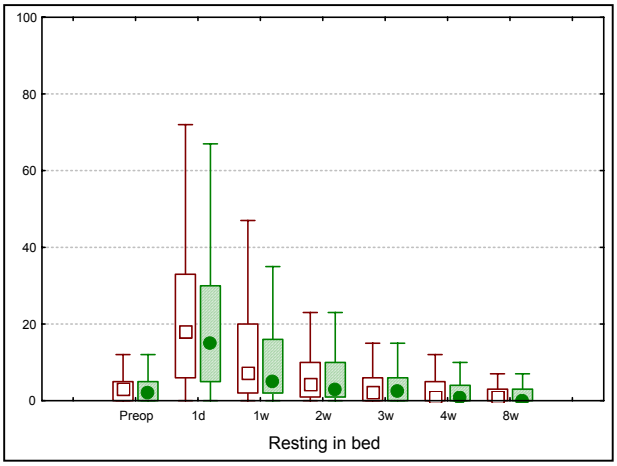
There was one early recurrence in the TEP group after five months after a repair of a primary direct hernia and one recurrence after follow-up, a repair of a primary combined hernia (2,2%). In the Mesh-plug group there were two recurrences both after repair of primary indirect hernias (1,9%). In the Lichtenstein group there were no recurrences (Paper II).

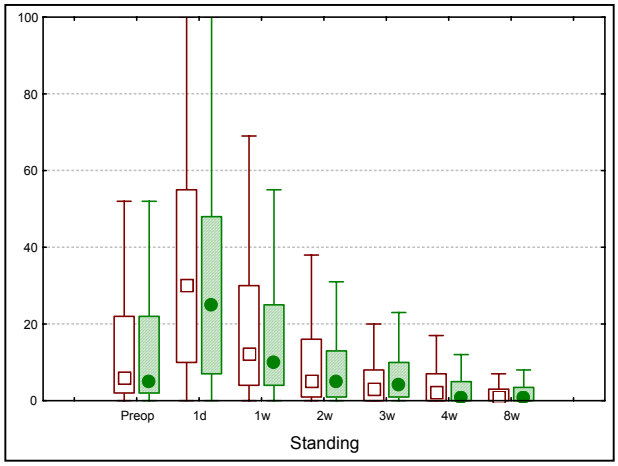
Table 3. POSTOPERATIVE COMPLICATIONS PAPER I-III (%)

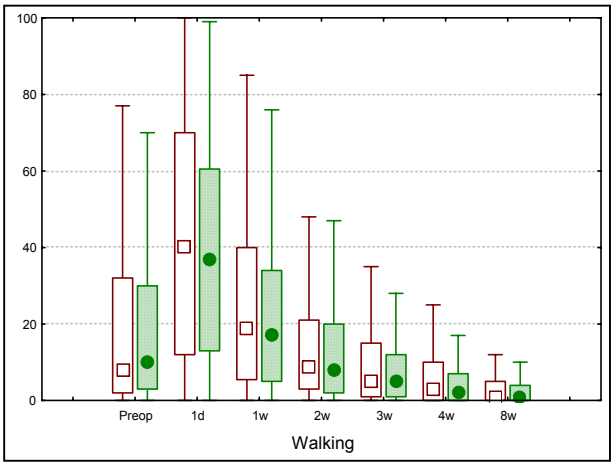
	PAPER I			PAPER II				PAPER III		
	Balloon	**No balloon**	**p**	**TEP**	**Mesh-plug**	**Lichten-stein**	**p**	**Prolene**	**Vyproll**	**p**
n	161	161		92	104	103		295	296	
Early complications										
Seroma	1 (1)	1 (1)		1 (1)	1 (1)	0		2 (1)	3 (1)	
Hematoma	2 (1)	5 (3)		3 (3)	7 (7)	8 (8)		11 (4)	14 (5)	
Testicular swelling/epididymitis	0	1 (1)		0	0	2 (2)		0	0	
Urinary retention	1 (1)	1 (1)		2 (2)	0	0		0	1 (0)	
Infection	0	1 (1)		1 (1)	3 (3)	4 (4)		6 (2)	5 (2)	
Pain	0	0		0	1 (1)	2 (2)		7 (2)	2 (1)	
Other	0	0		1 (1)	1 (1)	0		2 (1)	3 (1)	
Sensory loss	0	0		0	1 (1)	2 (2)		2 (1)	1(0)	
Wound secretion	0	0		1 (1)	2 (2)	3 (3)		0	0	
Total	4 (3)	9 (6)	0.26	9 (9)	16 (16)	21 (21)	0.34	30 (11)	29 (10)	0.9
Complications at follow-up										
Recurrences	4 (2)	5 (3)	0.8	2 (2)	2 (2)	0		..	..	
Pain/neuralgia	1 (1)	4 (2)	0.37	3 (3)	4 (4)	10 (10)		..	.	
Sensory loss	0	0		0	1 (1)	3 (3)		..	..	
Hyperesthesia	0	0		0	1 (1)	0		..	..	
Mesh-related problems	0	0		0	2 (2)	2 (2)		..	..	
	5 (3)	9 (5)		5 (5)	10 (10)	15 (15)	0.14	..	..	

Early complications < 30 days PAPER I, II, < 8 weeks PAPER III.

Figure 6. BOX PLOT VAS (PAIN) IN DIFFERENT POSITIONS/ACTIVITIES
□PROLENE ●VYPROII
Median; Box:25%, 75%; Whisker: Non.Outlier Min, Non-Outlier Max







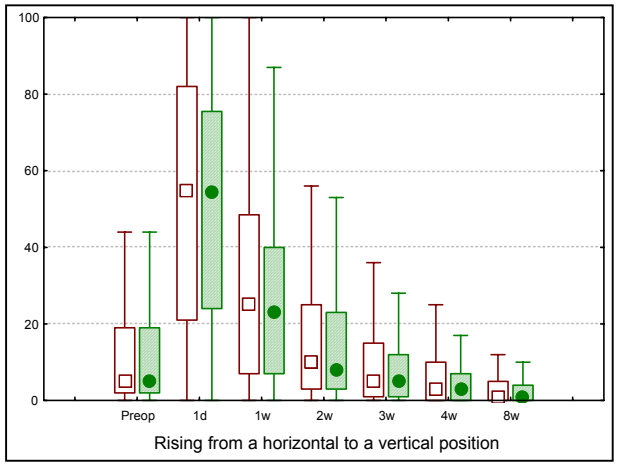
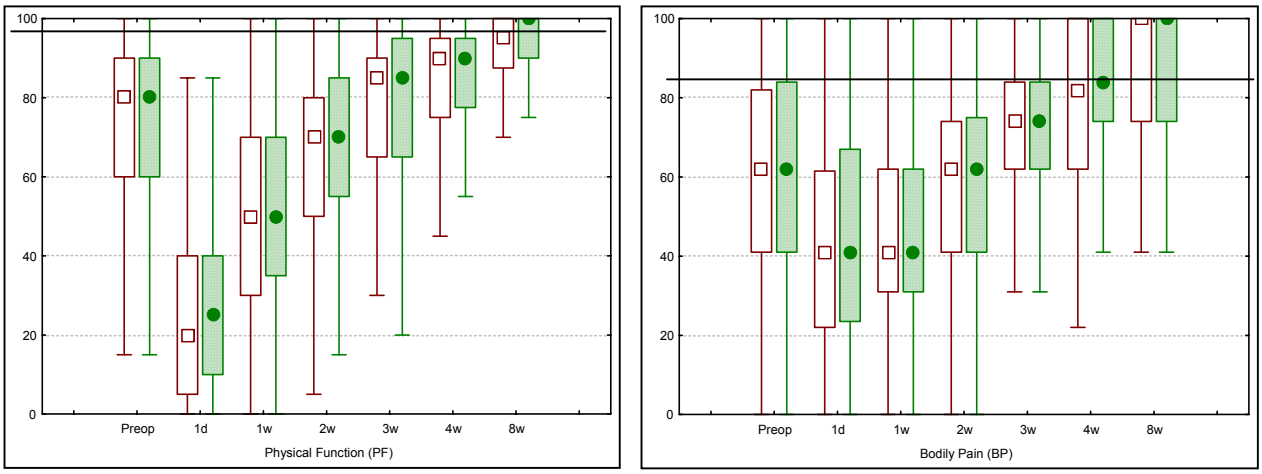
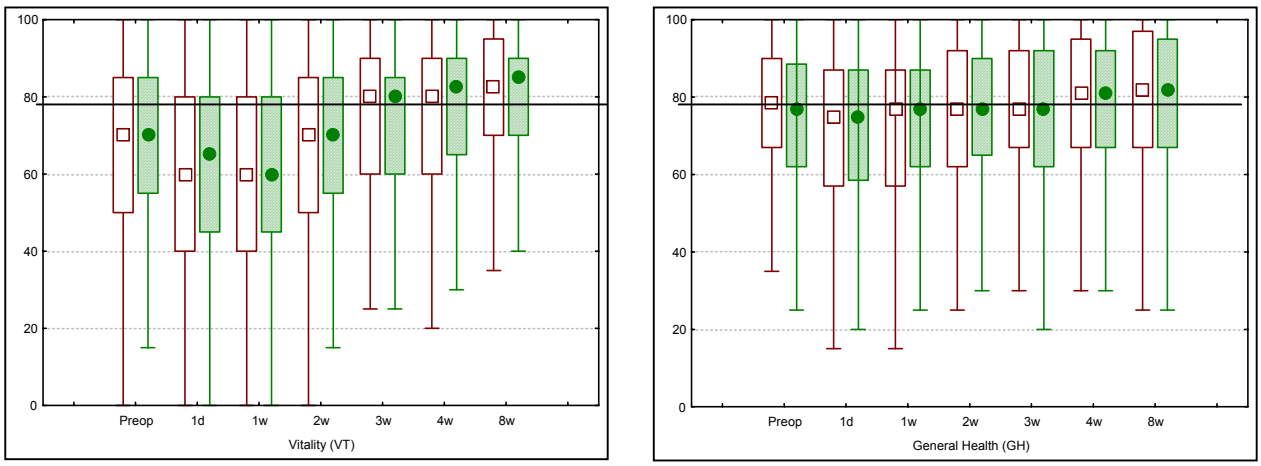


Figure 7. BOX PLOT SF-36
Median; Box:25%, 75%; Whisker: Non.Outlier Min, Non-Outlier Max
The black lines indicates the median ina a Swedish male population 40-70 years old, mean age 52.6 (SD9)
□PROLENE ●VYPROII

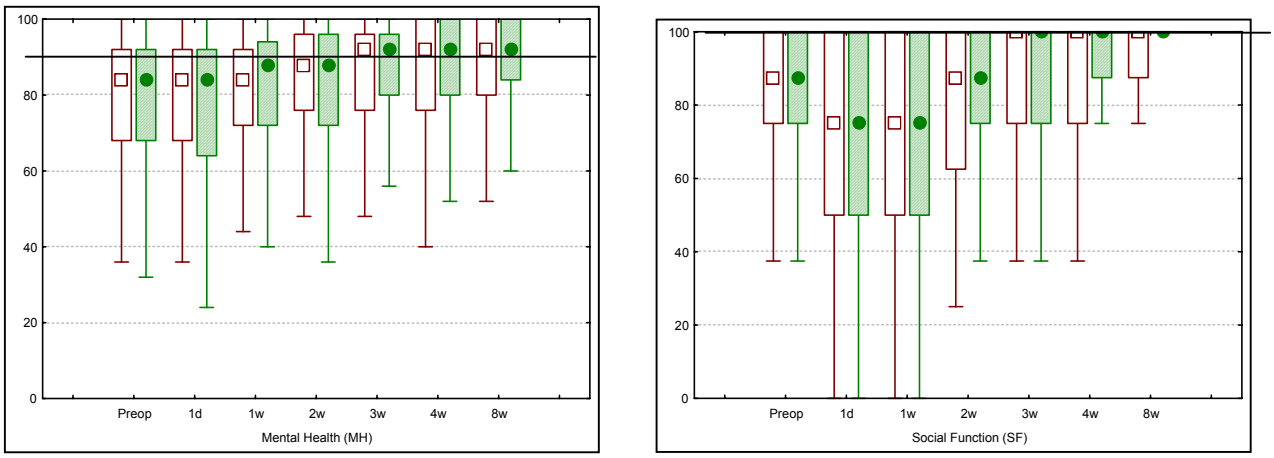
Physical



General



Psychological



INTESTINAL OBSTRUCTION AFTER HERNIA SURGERY (PAPER IV)

The SHR study cohort consisted of 33 275 patients. The median age was 60 years (QR48-71). The patients were followed 370 316 person years before the hernia operation, median 11.7 years (range 5-14) and 88 554 person years, median 2.1 years (range 0-9.1) after the hernia operation.

In all, 90 patients developed intestinal obstruction. The risk following a Lichtenstein operation was 1.05 per 1000 person years, 1.14 after a TAPP and 0.28 after TEP, respectively.

During the index admission two patients died of intestinal obstruction and were subsequently excluded. During follow-up of the 90 patients with intestinal obstruction, another two patients died from intestinal obstruction. The total mortality within 30 days after the hernia operation was 99 patients per 33 275 (0.3%).

Significant risk categories of the risk factors for postoperative intestinal obstruction in the univariate Cox analyses were female sex, previous admissions, age above 60 years, acute operation, index operation combined with other surgery at the index admission, femoral hernia or other hernia. There were no statistically significant differences between the different types of hernia operations in the univariate analysis.

Considering all risk factors combined in a multivariate Cox analysis (Table 4), most risk factors were still significant, but the risk decreased slightly compared to the corresponding univariate analysis. The risk almost doubled by each age group. For women, the risk was still higher than for men, although not significantly. An acute operation more than doubled the risk. Earlier admissions markedly increased risks, particularly in patients with several admissions and a history of intestinal obstruction. The relative risk of intestinal obstruction was significantly higher with TAPP (2.79 CI95: 1.0; 7.42) than with any other type of hernia operation, while TEP did not bring an increased risk (Fig 8).

FIGURE 8 CUMULATED RISK OF INTESTINAL OBSTRUCTION AFTER AN OPERATION OF A PRIMARY UNILATERAL INGUINAL OR FEMORAL HERNIA. MODIFIED FOR OTHER RISK FACTORS

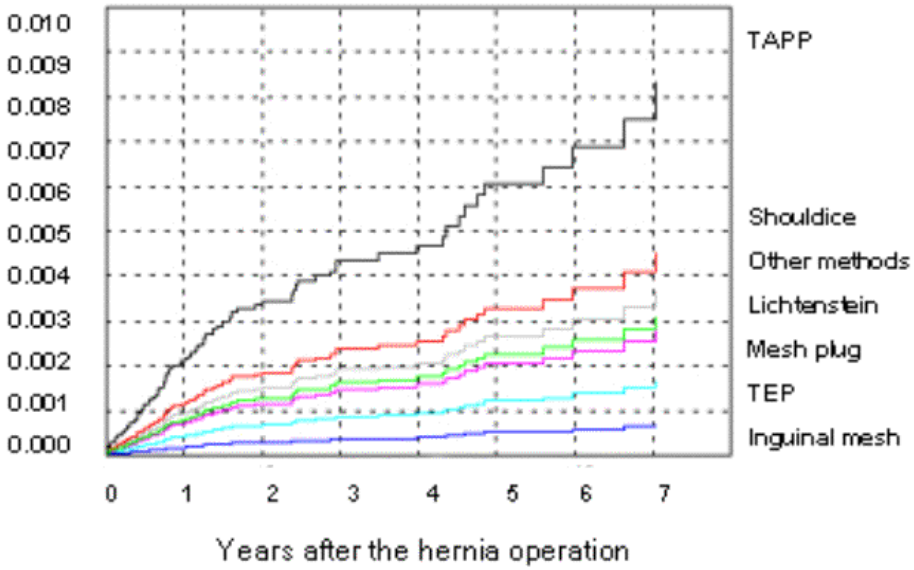


Table 4. INTESTINAL OBSTRUCTION AFTER HERNIA SURGERY MULTIVARIATE COX ANALYSIS (N=33 275)

	Hernia operations	Intestinal obstruction		Relative risk	95% CI	
	n	n	%		Low	High
Gender						
Male	30385	70	0.23	1.00	ref	ref
Female	2980	20	0.69	1.42	0.76	2.65
Age						
15-47	8141	6	0.07	1.00	ref	ref
48-59	8311	12	0.14	2.40	0.90	6.41
60-71	8079	21	0.26	4.40	1.62	10.08
71-	8743	51	0.58	7.38	3.12	17.48
Type of hernia						
Direct	9729	18	0.19	1.00	ref	ref
Femoral	882	11	1.25	2.21	0.85	5.72
Other	2966	13	0.44	1.90	0.93	3.9
Indirect	19698	48	0.24	1.27	0.74	2.19
Acute or planned operation						
Planned	31263	70	0.22	1.00	ref	ref
Acute	2012	20	0.99	2.16	1.16	4.03
Operation method						
Lichtenstein	9826	16	0.16	1.00	ref	ref
Shouldice	7778	27	0.35	1.46	0.77	2.75
Inguinal mesh	1867	1	0.05	0.23	0.03	1.73
Mesh-plug	4570	7	0.15	0.91	0.37	2.22
TEP	1357	1	0.07	0.57	0.07	4.33
TAPP	1157	6	0.52	2.79	1.01	7.42
Other	6720	32	0.48	1.13	0.58	2.18
Index operation						
Hernia only	32670	77	0.23	1.00	ref	ref
Hernia + intestinal obstruction	63	1	1.59	0.51	0.06	4.17
Hernia + other diagnosis	542	12	2.21	3.70	1.81	7.55
Previous admission						
No previous admissions	30981	62	0.2	1.00	ref	ref
One admission without intestinal obstruction	1861	13	0.7	3.60	1.97	6.56
One admission with intestinal obstruction	88	1	1.14	4.27	0.59	31.18
>1 admission no intestinal obstruction	259	5	1.93	11.01	4.37	27.72
>1 admission + intestinal obstruction	86	9	10.47	58.99	28.34	122.79

DISCUSSION

The present thesis was based on three prospective randomized controlled trials and one study based on the Swedish Hernia Register.

The randomized controlled trial is a powerful method of providing internally valid evidence that is externally valid for clinical practice [51]. Some aspects of care, cannot be answered with a randomized controlled trial, where audits e.g. through national registries can be beneficial [51]. Surgeons have been castigated for their failure to produce research on which to found their practice. Horton wrote "Surgical research or comic opera: questions but few answers" in the Lancet 1996[52]. Surgical practice is in some respects less suited than medical to the randomized controlled trial [53]. Inguinal hernia surgery is an exception [54]. The variation in the design in hernia trials is however a problem.

There are 20 randomized trials where at least one arm is TEP. Thirteen have open mesh-repair [55-64]or another TEP technique [65] (Paper I) in the other arm. The rest were compared to a sutured repair [66-72]. Mean or median follow-up is more than 18 months in seven studies [60, 63, 65, 69, 73](Paper I, II) and the number of included patients are more than 250 in six studies [55, 63, 64, 68](Paper I, II). Four studies have included more than 250 patients and have a follow-up of more than 18 months [63, 73](Paper I, II).

The mesh-plug technique has been published in several non-randomized series [41, 42, 44, 74-82]. There are only six randomized studies on the mesh-plug technique [64, 83-86](Paper II). The follow-up is less than 18 months in all studies but Paper II, which also includes more than 250 patients. Only one additional study has included more than 250 patients, but with a shorter follow-up than 18 months [64]. These two studies, (Paper II) [64]are the only trials on mesh-plug vs. TEP.

Repair with anterior mesh methods, dominated by the Lichtenstein repair, are now the most frequently used method of hernia repair in Sweden and Denmark[48, 87]. In a recent meta-analysis of 58 randomized mesh-repairs, Lichtenstein was the most frequent open repair [88]. Hence, the scientific knowledge of Lichtenstein is probably on a higher level than of mesh-plug. After this meta-analysis was completed, another 22 studies on various mesh-repair have been published [61-63, 65, 67, 83, 85, 89-101]. Many of the published randomized trials on inguinal hernia surgery with mesh have included a low number of patients. Out of these totally 80 trials published on mesh-repair (58 in the meta-analysis + 22 trials published after), just 21 have included more than 250 patients. In Paper III, 600 patients were randomized for Lichtenstein with different meshes. Only five published trials on tension-free repair are larger [55, 68, 91, 102, 103].

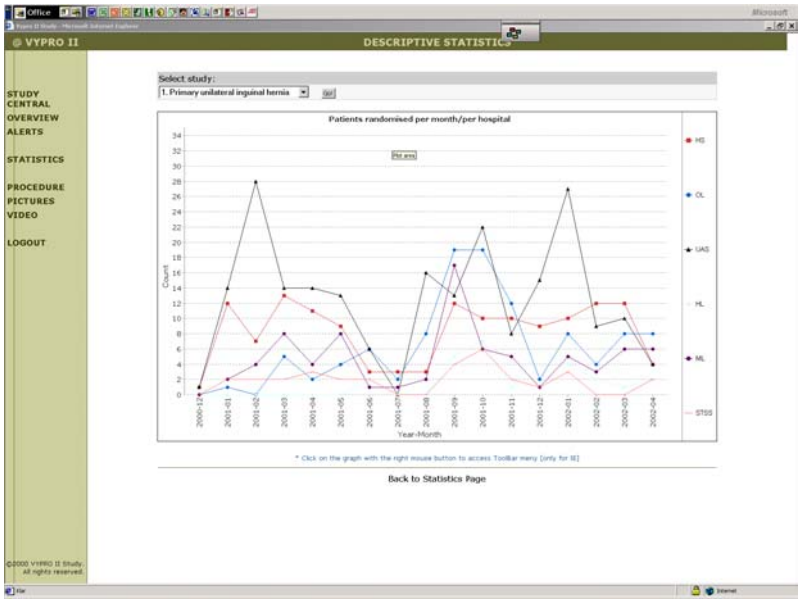
FACILITATING CLINICAL MULTI-CENTER TRIALS

Large multi-center trials would be the best and fastest way to include a sufficient number of patients in a study. The Internet has been used to some extent to establish quality registries [104]on certain clinical topics. The use of the Internet as a tool of solving the logistical problems in randomized multi-center studies has only been performed in a few studies, where the authors describe the design of the study, but no results [105-108].

To our knowledge the first time that a database through the Internet has been used in an international multi-center trial was in Paper III. The participating surgeons and staff appreciated the continuous feedback through the web site (Fig 9). We were able to include 600 patients in six centers in only 16 months, which we believe, was partly due to the informal competition between the centers as the pace of recruitment could be followed in real-time through the web. As a comparison we included 322

patients in four hospitals in 42 months in Paper I and 299 patients in two hospitals in 30 months in Paper II . In other Scandinavian hernia multi-center studies, the time of inclusion also has been much longer than in Paper III. In two Swedish studies the authors included 613 patients in 32 months in 10 centers [102] and 1042 patients in 37 months in 7 centers [91] respectively.

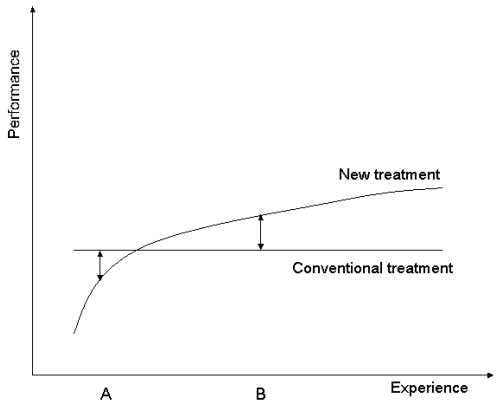
Figure 9. SCREEN PRINT FROM THE INTERNET DATABASE. DESCRIPTIVE STATISTICS SHOWING INCLUSION PER HOSPITAL PER MONTH



Another advantage of the Internet database was the simplicity of data handling and study monitoring. There were 308 values to be entered in the database for each patient, totally 184 200. The Internet also made it possible for each center to enter their own data directly in the database, which enhanced security, validity and data management. This decreased the workload by the study center personnel and after all data was entered in the database by the study hospitals, it was immediately ready for statistical analysis. Thus, there were no unnecessary delays due to mailing forms, validation of the patient data and entering it in the database by the study center personnel. In future national and international multi-center studies, the use of a database and randomization through the Internet may be the method of choice.

LEARNING CURVE

Figure 10. ILLUSTRATION OF A LEARNING CURVE



The performance of many repeated tasks changes with experience over time. Improvements tend to be most rapid at first and then tail off over time until a steady state is reached. The term "learning curve" is often used as short-hand to describe this phenomenon[109]. Changes in performance due to learning present particular difficulties in health technology assessment. Early assessment can give a distorted picture which is biased against the new technology[109]. This is illustrated in Fig 10. If the new treatment is assessed at time point A, the conventional treatment is preferred and if assessment is made at time point B, the new treatment is preferred. Hence, early assessment can give a distorted picture. On the other hand, when a new technology has clearly stabilized – sometimes on the basis of poor quality evidence – it can be argued that it is unethical to withhold the technique from potential patients[109]. This has been described

by Buxton: “It is always too early [for rigorous evaluation] until, unfortunately, it’s suddenly too late”[110].

The learning curve in TEP is suggested to be 30-50 operations[38, 57, 111, 112]. After this number of operations, the risk of complications including recurrence and conversions to another method is decreased[38, 57, 111, 112]. These findings are similar to our estimation of the learning curve (Paper I). However, if not only the trial cases, but all TEP cases in a surgeons’ practice the real learning curve might be even longer[109]. In the earlier mentioned meta-analysis[114] the conversion from a laparoscopic repair to an open repair was 2.7% and from an open to a laparoscopic repair 0.1%. The conversion rate from TEP to an open repair was 1/161 (0.6%) in the balloon group and 7/161 (4.3%) in the group without balloon, totally 8/322 (2.5%) in Paper I. In Paper II there were no conversions indicating a movement along the learning curve compared to Paper I.

One of the drawbacks of TEP is its technical complexity. Accordingly, it is important with experienced supervision during the learning curve in TEP[38, 57, 111, 112]. Surgeons in training should not make the same mistakes as their mentors made[111]. A surgeon in Paper I, who had easy access to supervision during his operations in the study, did not convert any operation during the study, which supports the importance of mentorship.

There are a number of important technical points having impact on the surgeons’ learning curve that can be suggested with the experience from Paper I and II which are in accordance with other authors[111, 113]:

1. A thorough understanding of the preperitoneal anatomy.
2. Correct tissue handling.
3. Full reduction of the hernia sac and a wide lateral dissection.
4. Leave the epigastric vessels tethered anteriorly.
5. Avoid dissection in the region of the iliac vessels.
6. Use a large piece of mesh (at least 10x15 cm).
7. Tether the lateral portion of the mesh laterally as the pneumopelvis deflates.

In the TEP operations in this thesis (Paper I, II) we used 10x15 cm mesh but in on-going studies and routinely we are using 12x15 cm to achieve a better coverage of the myopectineal area.

OPERATING TIME

The learning curve has impact on the operating time. In the study by Khoury the average operating time for TEP was 32 min, but for the last 75 cases in the study it was 20 min. This is illustrated when comparing Paper I and II. The operating time in TEP was 63 min without the balloon in Paper I. In Paper II when more experience was gained, the operating time was 50 min. Feliu-Pala et al reports a decrease in operating time from >60 min during the first 50 cases to 32 min for the last 200 cases in a series of 1227 hernia repairs [112]. In randomized studies on TEP the mean operating time is 32-82 min [114]. These studies probably represent different stages of the learning curve, which must be considered when interpreting the results.

Mesh-plug repair is generally believed to be an easy method with consequently short operating time[75, 78, 115].However , in randomized trials on mesh-plug and tension-free open or laparoscopic

repair, the operating time is longer compared to what Rutkow and Robbins stated (15-20 min) [115]: 30 min[64], 32 min[83] and 36 min. in Paper II respectively.

The mean operating time in the Lichtenstein groups in randomized studies on Lichtenstein is 38-57 min [114, 116]. Our results in Lichtenstein repair in Paper II, III are within this range.

The balloon group (Paper I), the mesh-plug repair (Paper II) and the Prolene group (Paper III) had slightly shorter operating time than respectively compared methods. These shorter operating times are not estimated to be of clinical relevance. The economic impact of a shorter operating time differs between health care systems and between countries. In our health care system relatively small differences in operation time between the groups doesn't have much economic impact.

COST AND CONVALESCENCE

Hospital stay

Inguinal hernia surgery can preferably be performed in day-surgery[91, 115]. In 2001 70% of all patient in the SHR were discharged from the hospital the same day as the operation [48]. The length of hospital stay can depend on the method of repair but hospital stay can reflect hospital policy more than a difference between methods [114]. A majority of the patients in this thesis were operated in a day-surgical setting, in Paper I and III 81-82% and in Paper II 92-98%.

Convalescence

The period of rehabilitation or sick leave needed after herniorrhaphy is not clear. Tension-free methods have been associated with shorter rehabilitation time than sutured repairs[116]. Some authors have proposed sick-leaves between 1-3 weeks after open mesh repairs[27, 115]. Laparoscopic repair has been shown to have even shorter rehabilitation[114].

In the MRC trial the cost of the laparoscopic operations were more expensive than the open, mainly due to longer operation time and cost of equipment. They concluded that the use of a laparoscopic repair may be a viable alternative when reusable instruments are used [117].

The convalescence after hernia surgery has an important economic impact since hernioplasty is such a frequent operation. In two studies the total cost was lower in laparoscopic hernioplasty compared to open if the indirect cost of the sick-leave period was included [39, 58]. However if only the hospital cost was included the laparoscopic repair was more expensive. In these studies a fair amount of disposable instruments were used and the operation time was longer in the laparoscopic repair.

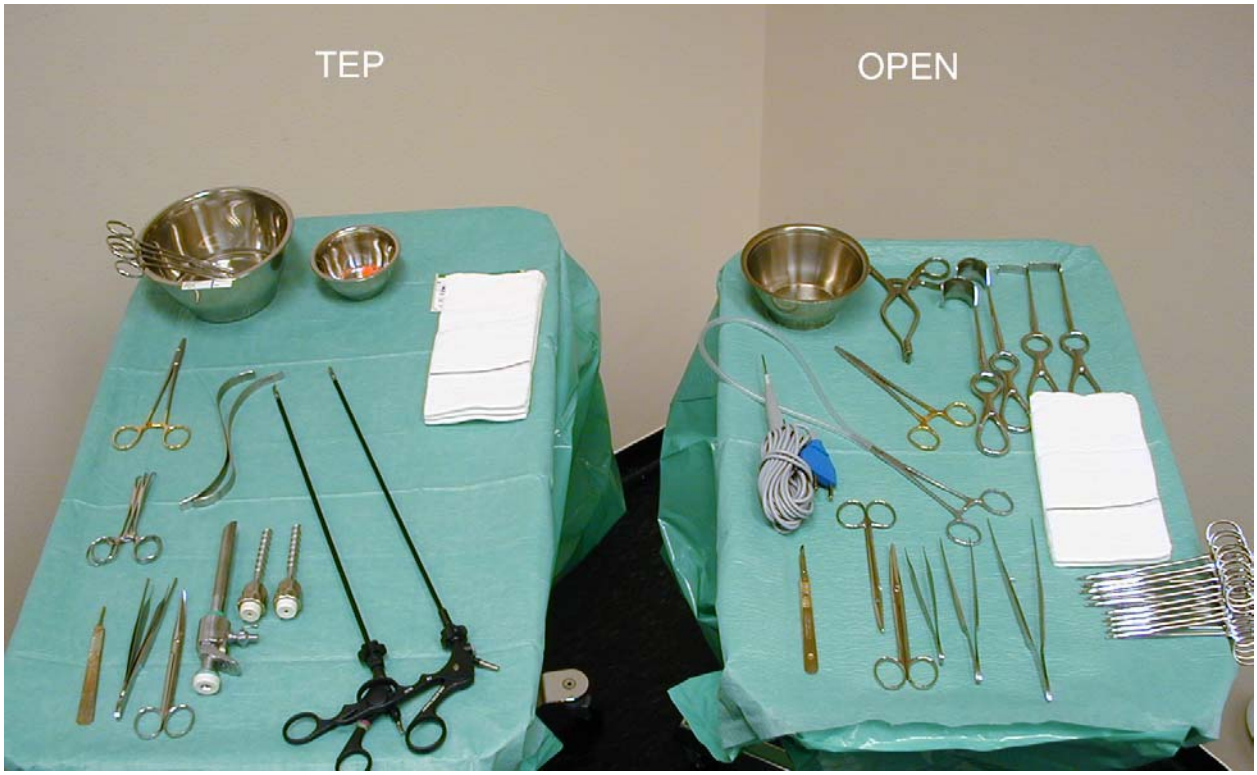
In laparoscopic hernioplasty it has been common to use disposable instruments, which may increase the direct cost (the cost for the hospital). We showed that it is possible to perform TEP without a dissection balloon (Paper I). In Paper II we used only reusable instruments, including the trocars. Thus the only cost for disposable material differing between the methods is the cost for the mesh. During the study period this was USD 30 in the TEP-group, USD 90 in the Mesh-plug group and USD 42 in the Lichtenstein group. Fig 11 illustrates the instruments used in TEP and open tension-free repair.

In a Dutch study the authors concluded that laparoscopic repair was more expensive but since it had a lower recurrence rate it was an economic alternative to the open repair. The study was performed with a kit of disposable instruments. Replacing them partially with reusable instruments would make the laparoscopic repair less expensive and more effective from a societal perspective [40]. Spitz et al used only reusable instruments in TEP, approximating the cost of open repair [118].

One argument in favor of open hernioplasty is that it can be performed in local anesthesia. But one must keep in mind that local anesthesia is not without problems. There is a significant risk of experiencing peroperative pain during surgery performed in local anesthesia. Callesen et al reported that 7.8% of the patients in a consecutive series of 1000 patients were dissatisfied due to intraoperative pain [119]. Local anesthesia has also been shown to be a risk factor for recurrence, OR 2.44 [6].

Workers compensation can significantly influence the outcome of the convalescence. In a Canadian study randomizing between laparoscopic and open herniorrhaphy, workers compensation was a true confounding variable with a stronger predictive value than the type of surgery[120]. Patients expectations or depression are also factors associated with the time to return to work [121]. In a Danish study the patients were encouraged to return to work the day after surgery if they did not have an occupation with heavy physical work. In that case they were recommended three weeks convalescence. The result was that the first group had six days and the second 25 days off work. Pain or information about prolonged time off work by General Practioners was the main reasons for the extended convalescence [122].

Figure 11. INSTRUMENTS USED IN TEP AND OPEN (LICHTENSTEIN OR MESH-PLUG) TENSION-FREE REPAIR



The patients in the randomized studies (Paper I-III) were all informed that they could return to work whenever they wanted to and that they could go back to their activities as soon as they felt ready for it. In the balloon study (Paper I) we did not find any difference concerning the return to work between the groups. This is consistent with the period of five days in the TEP group in Paper II. In this study TEP had a shorter convalescence than the open repairs and a shorter time off work than Lichtenstein. This is consistent with a recent meta-analysis where it was shown that laparoscopic repair had a shorter rehabilitation than open repair [123].

Prior to surgery, the study population in Paper III had lower SF-36 scores in all variables [124], except in General Health (GH) and Role Emotional (RE), compared to the median values in men of the approximately same age in a normal population (Fig3) [50]. This could mean that only relatively symptomatic patients were operated on. It could also indicate that inguinal hernias have a wider impact on quality of life than generally believed. The scores were worse the first couple of weeks postoperatively but they were back to the preoperative level within three weeks and improved to even higher values at eight weeks. This indicates that operating symptomatic hernias is beneficial for the patients, increasing their physical functioning. The SF-36 physical scores were higher than the preoperative levels after three weeks in both groups. This correlates well to the return to work, which was 16 days in both groups. It also corresponds to the return to normal daily activities of about three weeks in both groups. Thus, a sick leave of 2-3 weeks after Lichtenstein hernioplasty seems to be appropriate in most cases. However, in Paper II the sick leave was 7 days after both Lichtenstein and Mesh-plug repairs. The information about rehabilitation given to the patients were the same in both studies but there were a greater number of hospitals and surgeons participating in Paper III, which might influence the outcome.

COMPLICATIONS

Early complications

Serious complications are uncommon in hernia surgery. In a meta-analysis of laparoscopic vs. conventional repair of 7161 patients[114], there were 15 potentially serious complications (vascular or visceral) in the laparoscopic groups (all in TAPP) compared with five in the open groups. There were fewer postoperative hematomas (8.7% vs. 10.5%) and infections in the laparoscopic groups and a higher risk of seromas compared to the open groups. From the Swedish Hernia Register 2001[48] there were 3.8% hematomas and 1.5% infections reported in 11 742 patients. These figures are comparable to the results in Paper I-III. There also appeared to be a tendency of more frequent hematomas and infections in the open groups in Paper I-III.

Recurrence

The recurrence rate in hernia surgery has been high. In non-specialized centers recurrence rates have been reported to be 10-20% 1-4 years after surgery, with the highest figures after sutured repair[46, 125]. An estimation of the recurrence rate is the reoperation rate, which exceeds the reoperation rate with 40%[126]. The reoperation rate in the SHR 2001 was 11.4% (range 4.6-23.1%) [48] and the Danish Hernia Database reported a reoperation rate of 17% 1998-2000 [127]. Hence, an estimation of the true recurrence rate would be 40% higher.

Use of mesh reduces the risk of hernia recurrence irrespective of placement method [88]. Overall 88/4426 (2%) recurrences were reported after mesh repairs compared with 187/3795 (4.9%) after conventional repairs in a meta-analysis of randomized studies on mesh vs. non-mesh[88].

There were no significant differences in the recurrence rates between the groups in this thesis (Paper I, II), but the numbers of patients in these studies do not allow an assessment of the methods regarding recurrence rates. In Paper III, only short-term follow-up is yet completed.

Pain and numbness

It has been suggested that other data than recurrence should be considered in the overall assessment of the outcome after inguinal hernia surgery[128]. In a Danish national study the incidence of chronic pain one year after hernia surgery was 28.7% and was associated with functional impairment in more than half of those with pain [128]. These factors must be addressed when discussing the surgical intervention of inguinal hernia. In the literature the incidence of chronic pain is 0-37% but the endpoints are not necessarily pain in these studies.

The risk of post-herniorrhaphy pain has been reported very low from dedicated hernia centers performing tension-free open mesh-repir[77, 129, 130].
Patients with prolonged early pain after 4 weeks have an increased risk of chronic pain[131]. In the study by Callesen et al 8% of the patients operated on with Lichtenstein had moderate or severe pain one year after surgery[131]. In a Scottish study of 5506 patients operated on with hernia repair the majority (84%) were operated on with open mesh-repair (4% had a laparoscopic repair[132]), 4062 patients returned a questionnaire after 3 months. Forty-three percent had mild or very mild pain and 3% (125) had severe or very severe pain. At a median follow-up of 30 months 26% of the patients with severe or very severe pain still had that pain, 45% had mild or very mild pain and the rest did not have any pain at the site of the hernia[133] In the latter patients there were no difference between mesh or non-mesh methods. Notable is that only one of the patients with chronic pain had had a laparoscopic repair. In a randomized study by Cunningham et al, 10.6% of the patients who were all operated on with open non-mesh techniques reported moderate to severe pain two years after surgery[134]. Gillion reported that 5% of the patients assessed their postoperative pain and discomfort as more troublesome than the hernia they had before[135].
Risk factors for the development of chronic pain has been stated to be: Young age[128, 136], operation for recurrent hernia[131, 136], preoperative pain, day-case surgery[136] and high initial pain scores[131, 133].

In a recent large meta-analysis of laparoscopic vs. open hernia repair the risk of numbness and persisting pain were lower after laparoscopic repair[114]. This was similar in the meta-analysis of mesh (laparoscopic or open) vs. non-mesh where the risk of persisting pain was decreased if mesh was used[88].
Gillion had the same experience in his evaluation with a lower rate of sensory changes after laparoscopic repair vs. open repair and lower in mesh vs. open non-mesh repair[135]. There may be an anatomic explanation to finding that the risk is higher in open repair. The nerves of the groin has a higher variability in their terminal course in the inguinal canal where open operations are performed than in the retro-peritoneum, where laparoscopic repair is done [137].
Postoperative persistent pain has been suggested to be prevented by division of the ileohypogastric nerve, with excellent results in a consecutive series [138].

There was no difference in pain or quality of life between the two meshes in Paper III during follow-up. However there was a tendency of more pain and neuralgia in the Prolene group. Having pain after a few months may increases the risk of chronic pain [133].

There was no statistically significant difference between the groups in the late complications in Paper I-III. Yet, there was a tendency to a higher incidence of pain and sensory loss in the Lichtenstein group than in the other groups in Paper II. This may be an important finding, which needs further investigation. One hypothesis is that the dissection and fixation in the Lichtenstein method is more extensive than the other two, which could increase the risk of nerve injuries leading to pain and/or sensory loss.

Intestinal obstruction (Paper IV)

The most important risk factor in Paper IV was earlier hospital admissions, particularly multiple admissions and operations, including earlier events with intestinal obstruction. These relative risks were the highest found in the study, suggesting that the most important risk factor for postoperative intestinal obstruction is a previous history of abdominal surgery or inflammation. This finding confirms clinical experience and further supports the importance of obtaining a detailed patient history, before considering surgery. The risk was also increased if the patient was more than 60 years old, or if the index operation was acute rather than elective. No other operation method but TAPP brought a significantly increased risk. The increased risk after TAPP is, however, moderate compared to other risk factors.

Female patients first appeared to be at higher risk in the univariate Cox analysis, particularly if they had femoral or other types of hernias. However, this was not significant in the multivariate analysis indicating that these factors do not contribute to the risk of developing of intestinal obstruction. No type of hernia operation brought an increased risk in the univariate analysis compared to the Lichtenstein reference method. However, the risk following a TAPP operation was significantly increased in the multivariate Cox analysis. Yet, this risk estimate was lower than all other significant risk factors, except acute hernia operations. This indicates that other factors than the operation method for hernia repair may be more important for the risk of postoperative intestinal obstruction. Previous laparotomies have been reported to predispose for later intra-abdominal adhesions and intestinal obstruction[139], which is in accordance with our findings, where previous admissions was the single most important risk factor.

Laparoscopic surgery is associated with fewer adhesions postoperatively than open operations[140]. In an experimental study, the authors showed that open herniorrhaphy was associated with fewer intraperitoneal adhesions than TAPP operations [141]. The proportion of intestinal obstruction after laparoscopic surgery in a retrospective study of 10 327 patients was 0.11-2.5% [142] with the highest risk after a TAPP operation and the lowest after laparoscopic cholecystectomy. The risk reported in that study was higher than we found after TAPP. In a study of the risk of intestinal obstruction after appendectomy, the control group had an accumulated risk of being operated on for intestinal obstruction of 0.003% after one year and 0.06% after ten years[143], which is lower than our results.

Mortality (Paper IV)

The crude mortality within 30 days after hernia surgery in the SHR has been reported to be 0.3% [144] and the SMR (standardized mortality rate) following both inguinal and femoral procedures to be increased five to ten-fold, after acute procedures. It was decreased after elective inguinal hernia surgery in men[144]. We found that the crude mortality within 30 days was 0.3%, i.e. identical to that previously reported in the SHR. A similar mortality rate (0.4%) after inguinal, femoral and incisional hernias has been reported from Scotland[145]. Among our patients, one third had inguinal or femoral

hernia either with or without intestinal obstruction or intestinal obstruction only, as the causes of death. To our knowledge no other studies have reported causes of death in patients operated on for hernia.

The Swedish National Inpatient Register has a complete set of data on all admissions and a high validity[146]. Follow-up of mortality in Sweden is also almost complete [147]. The Swedish Hernia Register is validated regularly[47, 48] and now include the majority of the groin hernia operations in Sweden. By combining these large national registries we believe that our results give valid estimates of the postoperative risk of intestinal obstruction after hernia repair. We believe that it is important to include all hernia operations in a national register and we recommend regular linking to the national patient register, to monitor the quality of hernia surgery.

MESH

In Lichtenstein's operation there is a possible risk of injuring or catching the sensory nerves (ileoinguinal, genital branch of genitofemoral, ileohypogastric) when suturing the mesh, or during the fibroblastic in-growth postoperatively.

Even though there is data showing that the risk of pain with mesh-repairs is actually decreased compared to non-mesh repairs[88], there seems to be a concern for mesh-repairs to increase the risk of long-term pain and discomfort[136, 148, 149]. If the risk actually is increased in the long run, we might have changed the problem of recurrence to another problem: chronic pain and discomfort.

The extent of the foreign body reaction with its provoked scar tissue depends on the amount and structure of the incorporated material[150]. Accordingly, mesh with a 30% amount of polypropylene, higher elasticity, and larger pores (VYPRO®) was developed for incisional hernia repair[151]. This mesh proved to be favorable in both experimental and clinical studies with a reduced inflammatory reaction and a better abdominal wall function[152, 153]. Yet, this mesh is probably not suitable for inguinal hernia repair due to a too complicated intra-operative handling and placement of the mesh.

In consideration of the benefits of this mesh, a new mesh with a temporarily increased stiffness was developed for inguinal tension-free repair (VYPROII®). This mesh consists of 50% polyglactin and 50% polypropylene. It has been proven favorable in experimental studies[150]. When comparing Prolene with VyproII in Paper III there were no significant differences in the short-term outcome. The time of absorption of polyglactin is estimated to be eight weeks [154]. During eight weeks follow-up we did not find any clinically relevant differences between the two meshes. When the fibroblastic in-growth is completed possible differences between the meshes may be apparent. This may be shown in the planned one-year follow-up.

A lighter and softer mesh may be beneficial concerning nerve entrapment and/or pain by creating less fibrosis[150] and also appear softer against the surrounding tissues. Another possibility to decrease the risk of nerve entrapment is to use laparoscopic preperitoneal hernioplasty (TEP) where the mesh is situated further from the nerves of the groin and no sutures or staplers are used as showed in Paper II.

THE FUTURE

Education

The rapid changes that have been witnessed in prosthetic materials, open-approach operations and laparoscopic techniques have made hernia surgery a most interesting field of endeavor that demands renewed discipline and dedication[35]. Hernia surgery is reconstructive surgery[155] and it is important to concentrate hernia surgery on those who shows an interest in it[155]. This is probably beneficial for the patients. Patients operated on in dedicated hernia services experiences less pain and have a shorter convalescence [47]. An important task for experienced hernia surgeons is to educate surgeons in training since the latter should not make the same mistakes as their mentors made[111]. This is applicable both for laparoscopic and open hernioplasty. Anatomic knowledge is of great importance not only in preperitoneal hernia surgery, but also in tension-free open operations.

NICE (National Institute of Clinical Excellence, UK) states that laparoscopic surgery for inguinal hernia should only be undertaken in those units with appropriately trained operating teams which regularly undertake these procedures[156].

Open or laparoscopic

Both NICE and EU Collaboration recommend laparoscopic repair in recurrent and bilateral hernias. In the SHR, 11.4% of the operations were for recurrent hernias and 3.4% were bilateral operations 2001[48]. According to the recommendations, these operations should preferably be operated on by a laparoscopic technique. But, only 7,1% of the patients were operated laparoscopically 2001, including primary, recurrent and bilateral operations (5,6% TEP and 1,5% TAPP)[48]. The situation in Denmark is similar, with only 5% of the patients operated on laparoscopically when 17% are operated on for recurrence[127].

The risk of chronic pain and numbness is higher in open hernioplasty than in laparoscopic[114]. Laparoscopic operations and open operations with mesh both have a lower risk of recurrence than open non-mesh repair[88, 114].

In laparoscopic hernioplasty the routine is to use general anesthesia even though some authors have used epidural anesthesia[157]. Open hernioplasty is possible to perform under local anesthesia. However, a minority of the operations in Sweden and Denmark were done under local during the past years. In both the SHR 2001 and in the Danish Hernia Database 1998-2000, about 18% of the operations were under field-block, infiltration anesthesia or both[48, 127]. In the SHR 2001 58% of the operations were performed under general anesthesia[48]. Hence, by operating a larger proportion of inguinal hernias with laparoscopic hernioplasty in Sweden, would not necessarily increase the proportion of operations under general anesthesia.

TEP or TAPP

TEP has been suggested to be superior to TAPP, not in randomized, but in prospective studies [32, 34, 158]. The findings in Paper IV also supports that TEP should be done instead of TAPP since the risk of postoperative intestinal obstruction was increased in TAPP. The EU Hernia Trialists Collaboration proposes TEP and NICE recommends TEP when a laparoscopic repair is undertaken [88, 156]. TEP is considered technical complex with a long learning curve, 30-50 operations[38, 57, 111, 112](Paper I). Even though it is a logical step to operate via a posterior route if the previous operation was an anterior repair, it is still more difficult to perform a laparoscopic repair on a recurrent hernia than on a primary

one, because of adhesions from the previous suture or mesh. Bilateral laparoscopic hernioplasty can also be more technically demanding than unilateral[65]. It is probably not possible to learn and practice TEP only by operating on recurrent and bilateral hernias.

In 1996 20.5% of the hernias in the SHR were operated with TEP (9.3%) or TAPP (11.2%)[159]. It is time to increase the use of laparoscopic hernia repair in Sweden again, not only in recurrent and bilateral hernias but also in primary inguinal hernias. The risk of chronic pain and numbness may be reduced. The risk of recurrence may not be increased compared to open mesh-operations and it may be reduced compared to non-mesh operations[88, 114]. The postoperative rehabilitation would be shorter with less pain, faster return to work and activities [114] (Paper II). It is possible to perform a laparoscopic repair with only reusable instruments (Paper I, II) and to use the same mesh as in open tension-free repair (Paper I-III). The same laparoscopic equipment that is used for laparoscopic cholecystectomies can be used for inguinal hernias. General anesthesia is needed, but since a majority of the inguinal hernia operations in Sweden already are performed under general anesthesia, the direct cost (hospital cost) would not be increased. The operating time is not longer than Lichtenstein (Paper II) or Mesh-plug [64] after the learning curve.

Future studies

A crucial question in hernia research today is chronic pain and numbness after different repairs. To perform a long-term follow-up of the studies in Paper I and II, would probably give more knowledge in this important field.

If the material of the mesh influences the chronic pain incidence is too early to answer yet. When the one-year follow-up of the study in Paper III is completed, we will have more information about that.

If VyproII is superior to Prolene in Lichtenstein hernioplasty it might also be beneficial in laparoscopic hernia surgery. In a short time we have included the calculated number of patients in two internet-based studies:

1. TEP with VyproII vs. Prolene in recurrent hernias.
2. TEP with VyproII vs. Prolene in bilateral hernias.

The results after laparoscopic hernia surgery in randomised studies have been good or excellent in spite of being performed early in the learning curve. It would be interesting to conduct a large multi-center trial on TEP beyond the learning curve vs. tension-free open repair. The hypothesis is that TEP is even more superior to open tension-free repair than we already know, concerning chronic pain and numbness, rehabilitation and also operating time. That study should of course be carried out through the Internet, just like in Paper III, with all the benefits experienced in that study.

The issue of pain can also be addressed in further epidemiological studies using data from the SHR, analysing the risk of chronic pain and numbness after different methods of repair considering other risk factors.

CONCLUSIONS

The use of a dissection balloon can be helpful during the learning curve, but in experienced hands it just adds costs to the operation, without offering additional benefits.

Laparoscopic hernioplasty (TEP) is superior to tension-free open herniorrhaphy with Mesh-plug and patch or Lichtenstein's operation in terms of postoperative pain and rehabilitation.

Lichtenstein's operation with either Prolene or VyproII is safe and well tolerated with an acceptable postoperative rehabilitation time and a high quality of life, two months after surgery.

The use of a database through the Internet is feasible and may facilitate a clinical multi-center trial.

The risk of post-operative intestinal obstruction after hernia surgery is low and preperitoneal laparoscopic hernioplasty (TEP) do not bring an increased risk of postoperative intestinal obstruction. Transabdominal laparoscopic hernioplasty (TAPP) increases this risk.

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