INGUINAL HERNIA SURGERY
A PATIENT CENTERED APPROACH

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PART 1

Introduction

CHAPTER 1

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General introduction

An inguinal hernia is a protrusion of parietal peritoneum, 'the peritoneal sac', through a preformed or secondarily established defect in the inguinal area of the abdominal wall.[1] The risk of inguinal hernia is highest in males and increases with age reaching 22.8% in persons aged 60-74 year. The only therapy for inguinal hernia is surgical repair, which is one of the most common performed surgical procedures in the world.[2] In the United States, inguinal herniorrhaphy accounts for approximately 800,000 cases yearly.[3] Improvements on clinical outcome therefore have great medical and economic impact.

Historical evolution of inguinal hernia surgery

The history of hernia repair parallels closely the evolution in anatomical understanding and development of the techniques of general surgery. [4, 5]

Ancient era (to fifteenth century)

Inguinal hernias have first been described by the ancient Egyptians in the *Papyrus* of Ebers. The papyrus was written in about 1500 BC, but it is believed to have been copied from earlier texts, perhaps dating as far back as 3400 BC. The first anatomical studies of the inguinal region date back to Galen (131–210 A.D.).[6] Treatment for inguinal hernias was advised for pain, especially for young patients. Before the middle ages, the hernia sac was excised by barbers, rupture cutters and bathing masters via a scrotal incision, the wound left open to granulate [7] and some, like the Roman Celsus, included routine sacrifice of the testicle. During the dark Middle Ages, evolution in hernia surgery stagnated and it took about 13 centuries to reject the theory on excision of the testicle as an essential part of the operation. New surgical knowledge flourished during the Renaissance. Antonio Benivieni (1440-1502), founder of pathologic anatomy, wrote on inguinal hernias in 1507 (*Abditis Morborum Causis*). Ambroise Pare described the hernia repair in his book The Apologie and Treatise (*Apologie et Traité*) by reduction of abdominal organs into the abdominal cavity and sewing up the peritoneum.

Anatomic era (seventeenth to nineteenth centuries)

Knowledge culminated during the early nineteenth century in complete anatomic understanding of the inguinal canal by publications of Pott (1757), Richter (1785), Camper (1801), Scarpa (1814), and Morton (1841). Cooper's ligament, a pectineal part of the inguinal ligament and the fascia transversalis were defined by Cooper In 1804. He distinguished this layer from the peritoneum and demonstrated that it was the main barrier to herniation.[4] During the first half of the nineteenth century little progress was made despite increasing knowledge of anatomy and introduction of anesthesia in 1846, because of infectious complications and recurrence after opening the inguinal canal. [8]

Era of hernia repair under tension (nineteenth to mid-twentieth century)

After introduction of antiseptic spray (Lister 1870) and gloves (Halsted 1896) techniques of modern hernia surgery were developed. Marcy, a pupil of Lister, published on his repair in 1871: high ligation of the sac and narrowing of the internal ring. The Marcy repair still is the simplest non prosthetic repair performed today, for treatment of indirect inguinal hernias in children and young adults. Second half of the nineteenth century mortality rate was 2-7% and recurrence rate about 100% (Billroth 1890, Bull 1891). To prevent recurrence surgeons adopted the McBurney procedure again; they left the wound open to heal by secondary intention, to prevent sepsis and relying on scar formation to prevent recurrence. Bassini's reports from 1889 changed the way inguinal hernias were managed. He was the first to reconstruct the inguinal canal physiologically, recreating internal and external openings with anterior and posterior walls. The peritoneal sac could be dissected up into the iliac fossa for high ligation. His "triple layer" repair included the internal oblique muscle, transversus abdominis muscle and transversalis fascia. During World War II, the 1940's the Shouldice repair was developed by the Canadian Earle Shouldice[9]. This repair is a direct descendent of Marcy, Bassini, and Halsted's repair, consisting of a "four layer" tissue reconstruction of the posterior wall, using two separate continuous sutures, originally described with stainless steel.[10] Recurrence rates were superior and the technique was taken over in the USA and Europe. [11, 12] For many years, it became the standard operation.[13]

Era of tension-free hernia repair (mid-twentieth century to present)

The use of foreign material to the repair site is an alternative for tissue repair under tension. Marcy was the first surgeon to use animal tendon in 1887 for inguinal hernia repair (hernioplasty). During the 1930s and 1940s various natural organic prostheses and metallic materials were used with several complications. Fragmented metal formed sinuses and tissue eroded leading to hernia recurrence. The discovery of nylon by Wallace Carothers in 1935 led to the use of polyamide in hernia repair by Melick.[14] The darn repair using nylon (Moloney et al. 1948) became popular until the early 1990s.[15] In 1989 Lichtenstein and associates reported on 1000 consecutive patients with primary repair of inguinal hernia using a "tension-free" repair using a polypropylene mesh to reinforce the transversalis fascia without approximating the tissue defect. No recurrences and no infection were reported after 1 to 5 years follow up.[16] Lichtenstein made inguinal hernia repair everyday outpatient practice and pioneered the idea that inguinal hernia surgery is special and should be performed by an experienced surgeon. A tension-free hernia repair can also be accomplished by a preperitoneal approach via a low midline incision (Stoppa 1975).[17] With this concept a large Dacron (polyester) unsutured mesh is placed in the preperitoneal space of Retzius and Bogros. The mesh is fixated by intra-abdominal pressure on the muscular layers and later by tissue adhesion and in-growth into the mesh. Long-term recurrence rates were published of 1.4% among 604 repairs.[17] A third method for tension- free inguinal hernia repair is represented by plugging the inguinal canal with synthetic prosthetic materials.

The idea of plugging the inguinal canal was probably first described by Pierre Nicholas Gerdy during the mid-1830s using inverted fold of scrotal skin. In 1968 Lichtenstein began using a rolled cylindrical Marlex (polypropylene) mesh plug as treatment of femoral and recurrent inguinal hernias.[18] Later the design was improved by taking a flat piece of mesh and fashioning it into a cone or umbrella shape.

Era of endoscopy (end-twentieth century to the present)

The first laparoscopic hernia repair was reported in 1982 by the South African surgeon Ralph Ger. A clip was introduced laparoscopically to close the neck of the sac. Bogojavalensky introduced a laparoscopic mesh-plug technique in 1989. The first series of laparoscopic hernia repairs were published by Schultz in 1990. Since then, three endoscopic approaches have been established: IntraPeritoneal Onlay Mesh (IPOM, Fitzgibbons and Toy 1990), TransAbdominal Preperitoneal Procedure (TAPP; Arregui 1991) and Totally Extra Peritoneal repair (TEP; Dulucq 1991). [19]

The present era

It is estimated that worldwide each year over 20 million surgical procedures for inguinal hernias are performed.[2] In the Netherlands, in 2010 over 28.000 inguinal hernia repairs were performed, meaning 17 surgical repairs per 10.000 inhibitors per year (statline.cbs. nl). In the Netherlands inguinal hernia repair is performed according to the guidelines of the Dutch Society of Surgery and the European Hernia Society Guidelines (EHSG). The EHSG state that Lichtenstein or endoscopic repair should be the procedure of choice for both primary unilateral and bilateral inguinal hernias with the note that endoscopic repair should only be performed if expertise is available. The committee is of the opinion that TEP is preferred to TAPP in the case of endoscopic surgery and that except for the Lichtenstein and endoscopic techniques, none of the alternative mesh techniques have received sufficient scientific evaluation to be given a place in the guidelines.

Evolution of inguinal hernia repair in the Netherlands
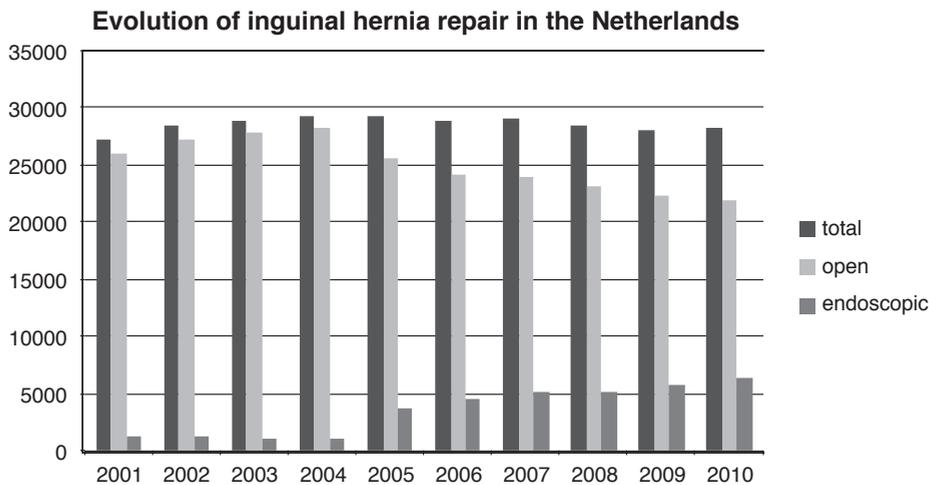
Until 2004 about 1000 endoscopic procedures per year were performed in the Netherlands.
Since then an increase is seen to almost 6.500 per year in 2010.

Chronic Postoperative Inguinal Pain (CPIP), defined as pain lasting for three months or more by the International Association for the Study of Pain (IASP)[20], is the most common complication of inguinal hernia repair, with large socio-economic impact because of the high incidence of inguinal hernia surgery. The high incidence of CPIP (up to 37%)[21-24] leads in 11% to 17% of patients to various types of social disability.[23] In 3 % of patients pain is severe or very severe and has profound effects on the patients' physical and social activities and limits patients' ability to participate in paid employment.[25] Worldwide that means every year up to 3.4 million people suffer from social disability caused by CPIP and about 600.000 people cannot participate in a paid employment and thereby CPIP has a large socioeconomic impact.

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Aim of the thesis

The introduction of surgical mesh to create a tension free repair in inguinal hernia surgery in the 1990s, was quickly implemented worldwide, because recurrence rates dropped dramatically. Debate on the best surgical approach for this tension-free mesh repair is ongoing. Chronic postoperative inguinal pain (CPIP) is currently the most common complication after inguinal hernia repair.

The aim of this thesis was to examine possible benefits of endoscopic compared to open mesh inguinal hernia repair and secondly to examine risk factors on CPIP.

Outline of the thesis

The studies presented in this thesis discuss the outcomes of endoscopic mesh repair compared to open mesh repair of an inguinal hernia in Part 1. Studies on risk factors on chronic postoperative inguinal pain (CPIP), the most frequent complication of tension-free inguinal hernia repair, are presented in Part 2 together with a score chart to predict patient's individual risk on CPIP.

Debate is still ongoing about the relative merits of endoscopic (TEP and TAPP) versus open mesh (mesh and plug) inguinal hernia repair. We therefore reviewed data on costs- effectiveness, time to return to work, quality of life and pain associated with endoscopic and open hernia repair in **Chapter 2**.
The TEP approach, - was compared with open mesh or sutured repair in a qualitative analysis of randomized trials in **Chapter 3**, with focus on operating time, hospital stay, return to work, major complications, recurrence rates and costs of TEP.

To compare the most common technique for open mesh repair (Lichtenstein) with the preferred minimally invasive technique (TEP) for surgical correction of inguinal hernia, a randomized controlled trial (RCT) was designed with postoperative pain, length of hospital stay, period until complete recovery, and quality of life as primary outcomes in **Chapter 4**. The long term evaluation of this RCT is documented in **Chapter 6**.

Chapter 5 represents the discussion on the best laparoscopic repair for inguinal hernia: TEP or TAPP in a letter to the editor and in Chapter 7 is discussed if open mesh repair with local anesthesia should be the standard of care for randomized trials.

In the RCT on TEP vs. Lichtenstein, we found a high incidence of CPIP. We therefore focused in PART 2 on risk factors of CPIP. To evaluate the role of the mesh in CPIP, a systematic review and meta-analysis of Shouldice/Bassini versus Lichtenstein is presented in **Chapter 8**.

Young age is described as risk-factor of chronic pain after surgery for other indications. The results of our study on the prognostic value of age for CPIP are presented in **Chapter 9**.

For use at the outpatient clinic, a score chart was created to assess the individual preoperative risk of a patient on CPIP, which is presented in **Chapter 10**.

In Chapter 11 and **12** the results of these studies are summarized and general conclusions are presented together with future perspectives on inguinal hernia repair.

PART 2

INGUINAL HERNIA REPAIR:
SURGICAL APPROACH

CHAPTER 2

Costs and quality of life after endoscopic repair of inguinal hernia vs. open tension-free repair: a review

M. Gholghesaei, H.R. Langeveld, R. Veldkamp, H.J. Bonjer.

Abstract

Background: The ongoing debate about the relative merits of endoscopic (EH) vs open mesh herniorrhaphy (OH) prompts the need for comparisons of outcome measures other than recurrence. Therefore, we reviewed data on the costs, time to return to work, quality of life (QoL), and pain associated with EH and OH. Methods: Studies comparing EH to OH and explicitly involving costs or QoL were identified and reviewed.

Results: Eighteen studies were included. Direct in-hospital costs were higher for unilateral EH. Direct out-of hospital costs were lower after EH in some studies. Indirect costs were lower for EH. Total costs were higher for EH in three studies and lower in one study. With EH, QoL was better, pain was less, operating time was longer and time return to work and other activities was shorter.

Conclusion: From a societal perspective, EH entails costs similar to OH but offers extra benefits to the patient in terms of QoL and pain.

Introduction

Inguinal herniorrhaphy is one of the most common surgical procedures performed today. However, the best surgical approach to the repair of inguinal hernias continues to be a subject of debate among surgeons. In recent years, mesh repair has been advocated because of its low recurrence rates in comparison to non–tension free repairs. [6] Endoscopic herniorrhaphy (EH) has been shown to have a recurrence rate comparable to open tension-free herniorrhaphy (OH), reducing the relative risk by 30-50% over conventional non-mesh procedures.[18] Given their similarity in terms of the recurrence rate, other issues associated with these surgical techniques become more important. Also, in the age of evidence-based medicine, health technology assessment mandates the full and explicit evaluation not only of efficacy and safety but also of every aspect that impacts on society.[28] Economic aspects become important when resources are scarce and choices have to be made by policy makers. Furthermore, patients are demanding effective treatments that also yield the maximum health-related quality of life (HRQoL). These new priorities for healthcare are reflected in the increasing number of studies reporting on costs, recovery, and quality of life (QoL). The aim of this paper was to review and synthesize the data on cost-effectiveness, quality of life, and other related issues associated with the endoscopic repair of inguinal hernias.

Materials and methods

We conducted a qualitative review of the literature reporting on cost-effectiveness and/or QoL associated with endoscopic repair of inguinal hernias. When possible and practical, the quality of reporting of meta-analyses (QUORUM) guidelines was adhered to.[21]. All literature reporting on the results of randomized controlled trials (RCT) explicitly involving cost-effectiveness and/or QoL were eligible for inclusion. In addition, trials reporting on outcome measurements associated with costs or QoL were also included. These outcome measurements include operating time, time to return to normal activities, and postoperative pain. A search of the literature was conducted using the electronic databases of MEDLINE and the Cochrane Central Controlled Trials Registry. The search comprised all entries from 1994 to present, without language restrictions. Search terms were selected so as to yield a large number of eligible studies. The following search terms were entered in MEDLINE: (endosc* OR laparosc*) AND hernia* AND (cost* OR quality*). Limits were set to 10 years, RCT, and title/abstract words only. Identical search terms were applied to the Cochrane databases. To simplify the somewhat complicated economic issue, costs and charges cited in the studies have been allocated to commonly used cost categories. Cost-driving items are divided into expenses directly related to the procedure (so-called direct costs) and costs to society associated with a procedure (indirect costs mainly due to production losses). Additionally, a useful subdivision for direct costs is one that differentiates between inhospital and out-of-hospital costs. This division is clarified in Table 1.

Table 1. Direct costs

Direct in-hospital costs	Direct out-of-hospital costs
Surgery	Out-patient visits
Anaesthesia	Medication at home
Operating time	Visits to family doctor
Personel	Home care
Equipment	Help in housekeeping
Instruments	Travel costs
Time in recovery room	
Hospital stay	
Medication	
Complications	

In some instances, this required recalculation and reallocation. Direct costs for which no division into in-hospital and out-of-hospital can be made are categorized as direct costs. To circumvent the issues of currency exchange rates, price indexing, and discounting, where possible, costs are calculated as an increase or decrease of EH over OH, depicted as a multiplying factor. Also, no distinction is made between actual costs and hospital charges even though charges do not necessarily reflect costs. Outcome measures for the included studies cannot be compared outright Because of this heterogeneity, no attempt at a more formal quantitative analysis was made.

Results

A MEDLINE search yielded 37 hits. Fourteen were discarded for involving non mesh techniques or hernias other than inguinal, for mentioning only trial design but lacking data, or for containing results derived from a previously included data set. In these latter cases, the most recently published papers based on the data set were included. Although one of the search criteria was "RCT," a number of prospective nonrandomized trials turned up. These were included. This review comprises both RCT and prospective nonrandomized research. The Cochrane databases rendered four additional articles, in total this review is based on 18 published papers. Study characteristics are shown in Table 2.

Table 2. Included studies

Author	Year	Country	Perspective	Design	Total cases	Endoscopic procedure	Open Procedure	Primary included	Bilateral included	Recurrent included
Barkun [1]	1995	Canada	Societal	RCT	92	TAPP/IPOM	Mesh and nonmesh	X	X	X
Beets [2]	1999	The Netherlands	Hospital	RCT	79	TAPP	GPRVS	—	X	X
Brooks [4]	1994	USA	Hospital	PNRT	100	TAPP	Mesh plug	X	X	X
Farinas [7]	2000	USA	Hospital	PNRT	112	TEP	Lichtenstein	X	X	X
Gainant [9]	2000	France	Hospital	RCT	117	TEP	Stoppa	—	X	—
Goodwin [10]	1995	USA	Hospital	PNRT	139	TAPP	Preperitoneal mesh	X	X	X
Heikkinen [11]	1998	Finland	Societal	RCT	40	TAPP	Lichtenstein	X	—	—
Johansson [13]	1999	Sweden	Societal	RCT	400	TAPP	Preperitoneal mesh	X	—	X
Lawrence [16]	1996	UK	Hospital	RCT	125	TAPP	Modified Maloney darn	X	—	—
Liem [17]	1997	The Netherlands	Societal	RCT	273	TEP	Mesh and nonmesh	X	—	X
Millikan [19]	1994	USA	Hospital	PNRT	106	TAPP	Lichtenstein (50%) Bassini, Shouldice	X	X	X
MRC Laparoscopic Groin Hernia	2001	UK /Ireland	Hospital	RCT	928	TAPP/TEP	Mesh repair (402), nonmesh (30), unknown (11)	X	X	X
Paganini [24]	1998	Italy	Hospital	RCT	108	TAPP	Lichtenstein	X	X	X
Payne [25]	1994	USA	Hospital	RCT	100	TAPP	Lichtenstein	X	X	X
Pikoulis [26]	2002	Greece	Hospital	PNRT	471	TA PP	Mesh plug	X	X	X
Schultz [29]	1995	USA	Societal	PNRT	63	TAPP	Mesh repair	X	—	—
Smith [30]	2001	USA	Hospital	PNRT	233	TEP	Lichtenstein	X	—	—
Wellwood [32]	1998	UK	Hospital	RCT	400	TAPP	Lichtenstein	X	X	X

RCT, randomized controlled trial; PNRT, prospective nonrandomized controlled trial; TAPP, transabdominal preperitoneal procedure; IPOM, intraperitoneal onlay mesh; TEP, totally extraperitonealtotally extraperitoneal procedure; GPRVS, giant prosthetic reinforcement of the visceral sac.

Most studies reported on direct in-hospital costs. In some cases, a detailed analysis was made, including, for example, the actual instruments that were used and the grade of staff employed; at the other end of the spectrum, a general rate was given for OR time with the usually used disposable instruments. Because herniorraphy frequently is performed in day care surgery, hospital stay is often left out of the equation. The results for direct in-hospital costs are shown in Fig. 1.

Fig. 1. Direct in-hospital costs. *Bilateral hernias only
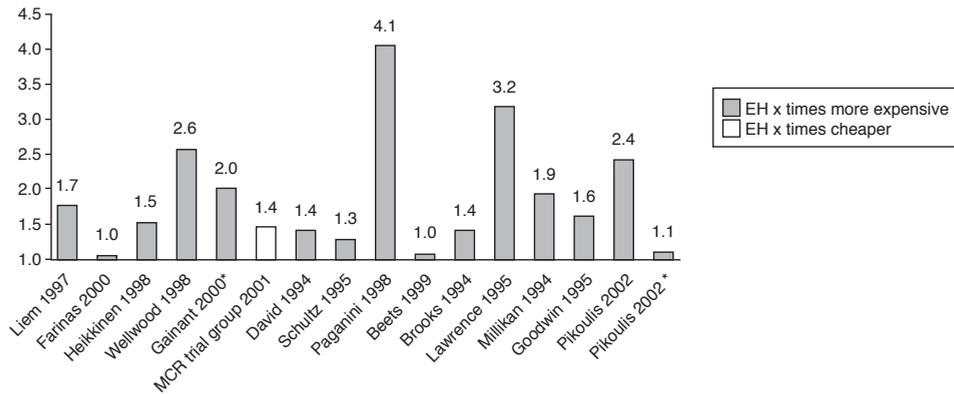
For the study of Johansson et al., no multiplying factor could be presented because they used a different method to report costs.[13] Costs were expressed as additional or incremental costs of EH and OH over conventional herniorrhaphy without mesh prosthesis. Regarding direct costs, EH carried additional costs of US $831over OH, and OH was US $52 more expensive than open repair without mesh prosthesis. Savings on indirect costs were 16 times greater for EH than OH. Additional total costs of EH over open repair without mesh prosthesis were US $749 compared toUS$44 for OH. In many studies, the use of expensive disposable instruments proved to be a major cause for the increased costs of the endoscopic procedure. Direct out-of-hospital costs are shown in Fig. 2.

Fig. 2. Direct out-of-hospital costs
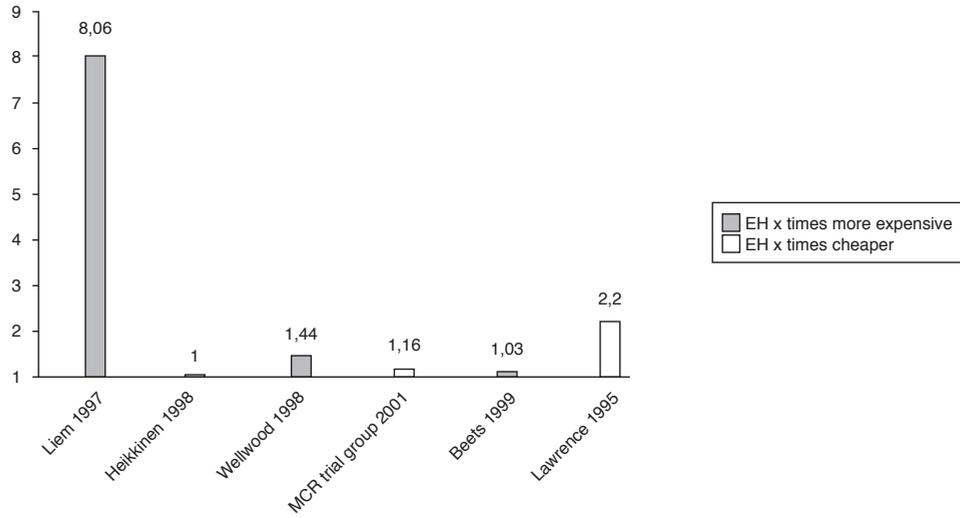
The results from Liem et al. are for the most part explained by an increased need for housekeeping in the OH group, partly attributable to one patient, as stated by the authors. [17] Total direct costs are shown in Fig. 3.

Fig. 3. Total direct costs
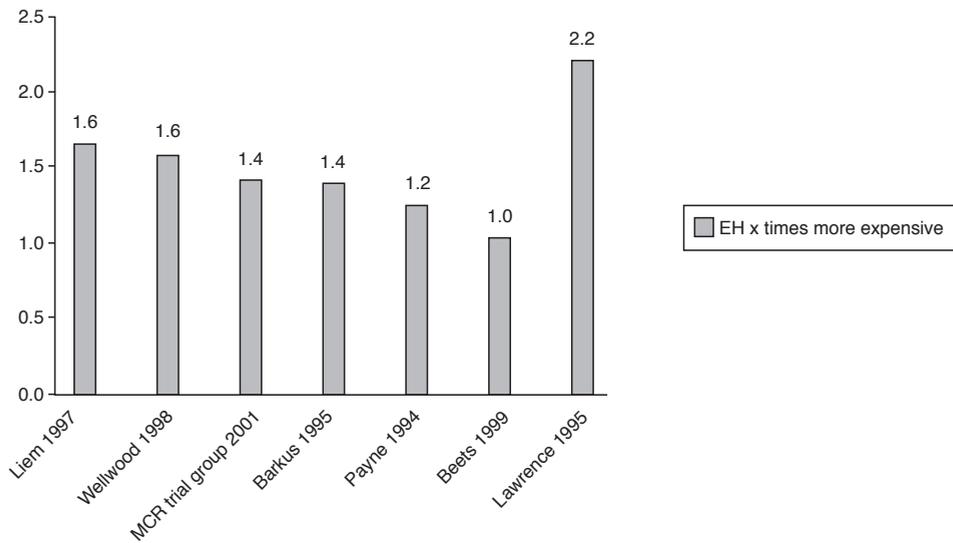
Even though indirect costs are responsible for a large chunk of all costs to society incurred by inguinal hernia repair, few studies have addressed this issue. Three studies agreed that EH was superior in this respect (Fig. 4).

Fig.4. Indirect costs
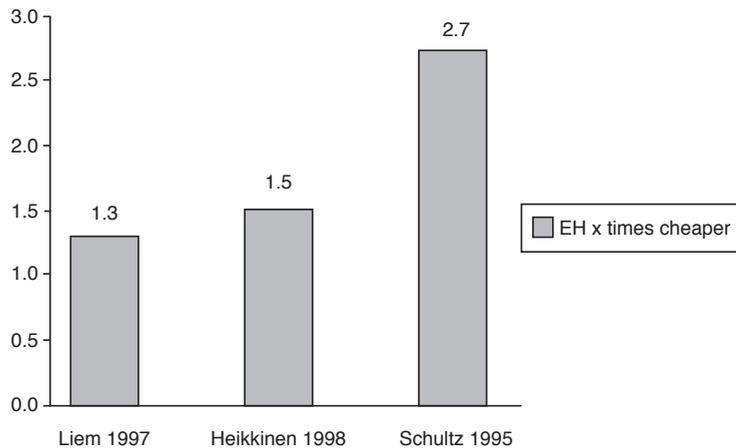
Subtracting the benefit of decreased indirect costs from the usually higher direct costs yields the total costs to society as a whole (Fig. 5).

Fig.5. Total costs
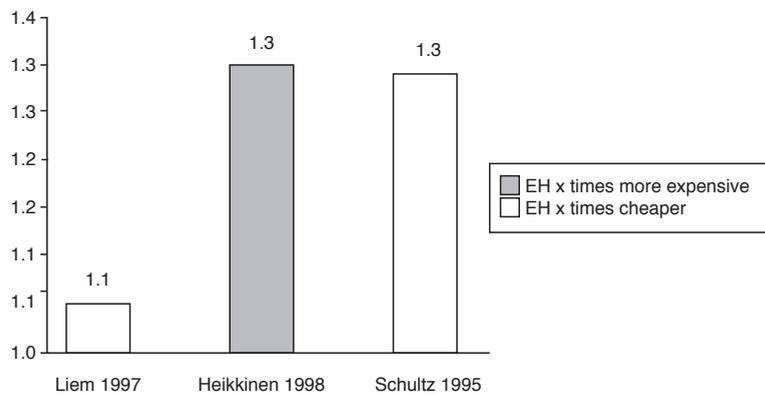
Heikkinen et al. concluded that EH cost less overall, whereas the other three studies found that OH was more economical. [11, 13, 17, 29] The Finnish results can be explained by an increase in indirect costs after OH. In this trial, it was argued that costs arising from the loss of production are grossly underestimated if salaries alone are used to represent these costs. The actual loss of revenue might be tripled if they were adjusted for the cost of substitute

workers, quality reduction, overtime, etc. Health-related quality of life was reported in five studies.[1, 16, 17, 22, 32] Validated standardized generic instruments were applied, including Short-Form 36, EuroQoL, and Nottingham Health Profile Questionnaire (NHPQ). These questionnaires yield profiles that describe health status or QoL of each patient. In this review, the profiles were lost due to aggregation of the different items and different time intervals of the measurements. All authors concluded that EH confers a greater improvement in HRQoL than OH. Pain was usually measured by the amount of analgesic medication or the duration for which it is required, or by through the postoperative administration of visual analogue scales. As shown in Table 3,

Table 3. Postoperative pain

EH favorable	EH equal to OH
Liem (1997)	Heikkinen (1998)
Wellwood (1998)	Brooks (1994)
Gainant (2000)[a]	Goodwin (1995)
MRC (1999)[a]	Smith (2001)
Johansson (1999)[b]	Pikoulis (2002)
Millikan (1994)	
Lawrence (1995)	
Beets (1999)	
Barkun (1995)[b]	
Paganini (1998)	

EH, endoscopic herniorraphy; OH, open mesh herniorraphy
[a] MRC Laparoscopic Hernia Repair Trial Group
[b] Pain was measured at different time intervals with different outcomes
but overall favoring EH

EH outperformed OH in reducing postoperative pain and discomfort. According to Wellwood et al., this effect can last for ≤ 2weeks.[32] On the subject of time to resumption of paid activities, there appears to be a consensus that OH causes a greater loss of productivity than EH, owing to, in most studies, a significantly longer period of sick leave in the OH groups (Table 4).

Table 4. Time to return to work

EH favorable	EH equal to OH
Liem (1997)	Barkun (1995)
Heikkinen (1998)	Paganini (1998)
Wellwood (1998)	Pikoulis (2002)
MRC (1999)a	Lawrence (1955)
Johansson (1999)	
Payne (1994)	
David (1994)	
Schultz (1995)	
Millikan (1994)	
Brooks (1994)	
Smith (2001)	
Beets (1999)	

EH, endoscopic herniorraphy; OH, open mesh herniorraphy

[a] MRC laparoscopic Hernia Repair Trial Group

The reported differences were on the order of 14 days (in the trial of the MRC Laparoscopic Groin Hernia Trial Group) to 39 days (as reported by Millikan et al.). [19, 22] Return to usual activities comprised very different activities in these studies. Activities ranged from driving a car for the first time postoperatively to getting out of bed unaided. Although the actual activities varied, recovery after EH appears to be more rapid (Table 5).

Table 5. Time to resumption of usual activities

EH favorable	EH equal to OH
Liem (1997)	Barkun (1995)
Wellwood (1998)	Paganini (1998)
Gainant (2000)[a]	Millikan (1994)
MRC (1999)[b]	Brooks (1994)
Johansson (1999)	Goodwin (1995)
Pikoulis (2002)	Lawrence (1995)
Beets (1999)	

EH, endoscopic herniorraphy; OH, open mesh herniorraphy

[a] Bilateral hernias only.

[b] MRC Laparoscopic Hernia Repair Trial Group

Significant differences ranged from 1 day to 23 days for bilateral repairs. [9, 32] Operating time was longer for hernia repair endoscopically (Table 6).

Table 6. Operating time

OH favorable	OH equal to EH
Gainant (2000)	Heikkinen (1998)
MRC (1999)[b]	Wellwood (1998)
Johansson (1999)	Barkun (1995)
Paganini (1998)[b]	Schultz (1995)
Beets (1999)	Smith (2001)
Liem (1997)	Payne (1994)
Brooks (1994)	
Goodwin (1995)	
Millikan (1994)	
Pikoulis (2002)	

OH, open mesh herniorraphy; EH, endoscopic herniorraphy

[a] MRC Laparoscopic Hernia Repair Trial Group

[b] Operating times for recurrent and bilateral Hernias equal

Some authors noted that the difference was reduced for patients who suffer from recurrent or bilateral hernias.[24, 32] Although ambulatory surgery is commonplace at the present time, hospital stay was subject to investigation in most of the papers. The results are shown in Table 7.

Table 7. Length of hospital stay

OH favorable	EH favorable	EH equal to OH
Heikkinen (1998)	Farinas (2000)	Liem (1997)
Wellwood (1998)	Gainant (2000)[a]	Barkun (1995)
Brooks (1994)	MRC (1999)[b]	Payne (1994)
	Millikan (1994)	Paganini (1998)
	Beets (1999)	Pikoulis (2002)

OH, open mesh herniorraphy; EH, endoscopic herniorraphy

[a] Bilateral hernias only

[b] MRC Laparoscopic Hernia Repair Trial group

Discussion

Although a formal review or even a meta-analysis would have been preferable, this approach was not possible because of the diversity of the study protocols, populations, techniques, and reimbursement or health care systems. Instead, an overview of the current state of cost analysis has been provided in which the overall results and conclusions of the studies are compared. Accurate assessment of costs and cost-effectiveness should be performed on a national level if it is to be used in actual policy making, because of marked differences among countries in health economics. It seems, however, that overall costs to society for EH need not be higher and in fact may be lower due to lower indirect costs. Disposable equipment accounts for much of the higher direct in-hospital costs. Making use of cheaper reusables may tip the balance in some instances to favor EH. [3, 17] Furthermore, more widespread application of EH may decrease costs by the principle of economy of size—for example, purchasing more specific instruments will make them less expensive to produce. Performing EH more rapidly is another way of reducing OR costs. Lawrence et al. and Lau et al. found a significant correlation between cumulative surgical experience and decreased operating times. [15, 16] An essential part of gaining this experience is completing the learning curve. The learning curve experienced by endoscopic surgeons had negative effects on the results of EH compared to OH in many clinical studies. Not only do operating times decrease, but recurrence rates continue to improve after 50–100 procedures.[8, 31] Results from a large recent study even suggest that there is a significant difference in recurrence rates between surgeons who <250 endoscopic repairs and those who have done >250, thus influencing the results of this trial. [23] Another subject impacting on recovery and costs to society is the matter of chronic inguinal pain or discomfort after hernia repair. Although it was initially an underreported complication, recent reports suggest that ≤ 38% of patients undergoing OH suffer from chronic pain. [14, 20] There is a tendency for EH to produce less chronic pain than OH. It has also been suggested that OH is comparable to the largely abandoned open suture repair in terms of its relatively high incidence of chronic pain, which has a significant effect on all daily activities, including work.[5, 27] Also, patients with endoscopically repaired hernias were less likely to consult with specialized pain clinics.[12] The mechanism of chronic pain has yet to be fully elucidated, but one possible explanation may be the nerve-sparing nature of the endoscopic technique, especially if mesh fixation is performed with special attention to the anatomic location of the nerves or with no fixation at all. The endoscopic approach clearly benefits QoL, making it the preferred technique from a patient perspective. For now, it seems that patient-centered outcomes favor EH over OH, at the expense of hospital budgets. If these higher initial costs can be reduced or reimbursed, EH should become the procedure of choice, given that it is superior from the perspective of the individual patient as well as offering cost benefits to society as a whole by mitigating losses in productivity.

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CHAPTER 3

Open or endoscopic total
extraperitoneal inguinal hernia repair?
A systematic review.

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Abstract

Background: Although a large number of surgeons currently perform endoscopic hernia surgery using a total extraperitoneal (TEP) approach, reviews published to date are based mainly on trials that compare laparoscopic transabdominal preperitoneal (TAPP) repair with various types of open inguinal hernia repair.

Methods: A qualitative analysis of randomized trials comparing TEP with open mesh or sutured repair.

Results: In this review, 4,231 patients were included in 23 trials. In 10 of 15 trials, TEP repair was associated with longer surgery time than open repair. A shorter postoperative hospital stay after TEP repair than after open repair was reported in 6 of 11 trials. In 8 of 9 trials, the time until return to work was significantly shorter after TEP repair. Hospital costs were significantly higher for TEP than for open repair in all four trials that included an economic evaluation. Most trials (n = 14) reported no differences in subsequent recurrence rates between TEP and open repair.

Conclusions: The findings showed that endoscopic TEP repair is associated with longer surgery time, shorter postoperative hospital stay, earlier return to work, and recurrence rates similar to those for open inguinal hernia repair. The procedure involves greater expenses for hospitals, but appears to be cost effective from a societal perspective. The TEP technique is a serious option for mesh repair of primary hernias.

Introduction

Inguinal hernia repair is one of the most common surgical procedures. In the United States alone, more than 700,000 of these procedures are performed each year, incurring approximately 3.5 billion dollars of hospital costs.[1] Optimizing surgical technique to improve short-term outcome and reduce the rate of recurrence is therefore of great value to health care. Over the past 20 years, several hernia repair techniques have been introduced.[2–4] Reducing the rate of recurrence has been the main incentive for the development of these new techniques. The introduction of the Lichtenstein tension-free hernioplasty, which uses a mesh to reinforce the abdominal wall, has decreased recurrence rates greatly.[5] Another advantage of the Lichtenstein hernia repair is that it is a relatively straightforward and easy-to-learn procedure requiring minimal dissection that can be performed using local anesthesia. In addition, because the technique is tension free, it is associated with significantly less postoperative pain and discomfort than conventional open repair.[6] Since the introduction of laparoscopic inguinal hernia repair, most of the ongoing discussion has focused on the choice between open or endoscopic surgery. Endoscopic inguinal hernia repair is associated with shorter recovery periods, earlier return to daily activities and work, and fewer postoperative complications.[7] Some authors suggest that endoscopic repair of recurrent hernia is easier because it is performed in virgin tissue. On the other hand, endoscopic hernia repair requires special skills to overcome limitations inherent to this type of surgery such as loss of depth perception, limited range of motion, and reduced tactile feedback. As a consequence, endoscopic hernia repair has a significant learning curve[8] and is associated with longer operating times.[9] Furthermore, some serious complications during laparoscopic transabdominal preperitoneal (TAPP) mesh repair have been reported,[10–13] some even resulting in the death of a patient.[11, 13] Some authors propose that these complications may have been avoided if an endoscopic extraperitoneal approach had been used.[11] Neumayer et al.[14] compared a mixed design of total extraperitoneal (TEP) and laparoscopic TAPP repair with anterior open inguinal repair according to the Lichtenstein method. Randomized clinical trials comparing only TEP repair with open repair are scarce. Although many surgeons have now adopted the TEP repair, reviews and meta-analyses published to date are based primarily on comparisons between both laparoscopic and endoscopic repair with open inguinal hernia repair.[15] In light of this, a systematic review was performed to examine all published and non-published randomized controlled trials comparing TEP with open mesh and suture repair.

Materials and methods

Randomized trials comparing TEP with open mesh or suture repair were included in this review. Studies that included both TEP and TAPP were not included. Relevant randomized controlled trials were identified through a systematic search of Pubmed, Medline, Embase, and Cochrane using the keywords "TEP" and "randomized controlled trial." Studies published as abstracts and presented at scientific meetings also were included in the review to minimize bias. A total of 23 randomized trials comparing TEP repair with open hernioplasty were identified. In some cases, different outcomes for the same trial were published in separate articles. Therefore, a total number of 29 publications had to be analyzed.[16–44] Of the 23 trials included in this review, 18 were reported as full articles and 5 as abstracts only. Most trials compared TEP with one method of open repair. In seven trials, TEP was compared with two or more open types of inguinal hernia repair (Table 1). Because of heterogeneity between studies (Table 1), it was not possible to pool the data. The divergences in trial designs were too great, and not all data needed to perform a quantitative statistical analysis were available. Therefore, we performed only a qualitative analysis. The current review focuses on operating time, hospital stay, return to work, major complications, recurrence rates, and costs of TEP, as compared with suture repair. Statistical significance was defined as a p value less than 0.05.

Table 1. Details on articles and abstracts regarding randomized controlled trials comparing TEP with open repair

Reference	Type of open repair	Follow-up (months)	No analysed
TEP vs open mesh			
Heikkinen et al. [16]	Lichtenstein	10 (median)	45
Andersson et al. [17]	Lichtenstein	12(97%)	168
Merello et al. ¶ [18]	Lichtenstein	"short"	120
Bilgin et al. ¶ [19]	PPOR 1	12/15 (median)*	60
Lal et al. [20]	Lichtenstein	13 (mean)	50
Payne et al. ¶ [21]	Lichtenstein	20 (median)	100
Colak et al. [22]	Lichtenstein	12/11 (mean)*	134
Bostanci et al. [23]	Stoppa	15 (mean)	64
Champault et al. [24]	Stoppa	20 (mean)	100
Champault et al. [25]	Stoppa	20 (mean)	100
Suter et al. [26]	Stoppa	—	39
Suter et al. [27]	Stoppa	—	39
Khoury et al. [28]	Mesh-plug	17 (median)	292
Bringman et al. [29]	Lichtenstein, Mesh-plug	20 (98%)	294
Wright et al. [30]	Lichtenstein, Stoppa	0.25	120
Wright et al. [31]	Lichtenstein, Stoppa	0.25	64
Simmermacher et al. [32]	Ugahary	—	162
TEP vs open non-mesh			
Nathanson et al. ¶ [33]	Shouldice	24 (mean)	184
Bessell et al. [34]	Shouldice, darn	7.3 (mean)	113
Decker et al. [35]	Shouldice	—	30
Fleming et al. [36]	Shouldice	16 (86% median)	231
Champault et al. [37]	Shouldice	12.3 (mean)	181
TEP vs open mixed			
Liem et al. [38]	Procedure of choice	20 (median)	994
Liem et al. [39]	Procedure of choice	1.5	105
Liem et al. [40]	Procedure of choice	20 (median)	237
Liem et al. [41]	Procedure of choice	44 (median)	994
Champault et al. [42]	Shouldice, Stoppa	48 (79% mean)	461
Wright et al. [43]	Lichtenstein, Stoppa & others	60 (mean)	300
Vatansev et al. [44]	Lichtenstein, Bassini, Nyhus	0.25	84

¶ Reported as abstract only

* TEP/open

Results

The 23 trials analyzed in the current review included a total of 4,231 patients. The follow-up periods ranged from 0 to 48 months.

Operating time

Data on the duration of surgery were compared in 15 of the trials. The TEP repair required significantly more time than the open methods of inguinal hernia repair in 10 of the trials. One trial reported a shorter operating time for TEP repair than for Lichtenstein hernioplasty. For three trials, no significant differences were found. Bilgin et al.[19] mentioned operating times, but did not state whether the differences observed were statistically significant (Table 2).

Table 2. Operating time

Reference	Operating time		p value
	TEP	Open	
Heikkinen et al. [16]	67.5 (40–88)*	53(42–78)*	0.001
Andersson et al. [17]	81 ± 27º	59 ± 20	<0.001
Bilgin et al. [19]	69 (25–150)^	85 (40–150)^	not stated
Lal et al. [20]	75.7 ± 31.6º	54 ± 15	<0.001
Colak et al. [22]	49.67 ± 14.11º	56.67 ± 11.67º	0.002
Bostanci et al. [23]	58 (40–85)	35 (20–65)	<0.05
Suter et al. [26, 27]	82 (50–135)^	54 (35–86)^	<0.001
Khoury et al. [28]	31.5 (5–80)*	30.5 (10–70)*	NS
Bringman et al. [29]	50 (25–150)^	36 (19–88;45 (24–100)^¶	<0.001‡
Wright et al. [30]	60 (53–72)*	45 (35–52)*	<0.0001
Liem et al. [38]	45 (35–60)*	40 (30–45)*	<0.001
Vatansev et al. [44]	58.6 ± 9.7º	54.7 ± 7.2; 51.9 ± 6.5; 59.4 ± 8.2º	NS
Decker et al. [35]	57.2 (38–78)^	53.1 (33–71)^	NS
Fleming et al. [36]	70 (30–145)*	56 (30–145)*	0.0001
Simmermacher et al. [32]	27^	39^	<0.001

* median (range); ^ mean (range); º mean ± standard deviation

¶ Mesh-plug; Lichtenstein

‡ significant difference between TEP\Lichtenstein versus Mesh-plug

Lichtenstein; Nyhus; Bassini

Hospital stay

In-hospital stay was mentioned in available data on 11 trials. Significant differences in favor of repair were found in six trials. Heikkinen et al.[16] found a longer hospital stay after TEP repair than after Lichtenstein tension-free hernioplasty (6.25 vs 4.75 h; p < 0.001). In two trials, no differences between groups were found, and in one study, p values were omitted (Table 3).

Table 3. Hospital stay

Reference	Hospital stay		p value
	Hospital stay	TEP Open	
Heikkinen et al. [16]	6.25 h (5.25–21)*	4.75 h (1.75–45)*	<0.001
Andersson et al. [17]	13.6 ± 6.9 h°	12.4 ± 6.3 h°	NS
Bilgin et al. [19]	1.3 days (1–4)^	3.2 days (1–7)^	not stated
Lal et al. [20]	1.48 days (1–2)^	1.40 days (1–2)^	NS
Colak et al. [22]	1.80 ± 0.65 days^	2.73 ± 1.62 days^	0.001
Champault et al. [24, 25]	3.2 days (1–6) ^	7.3 days (5–12)^	0.01
Suter et al. [26, 27]	2.2 (2–4)^	2.7 (2–4)^	0.02
Khoury et al. [28]	100% daycare	98% daycare	NS
Wright et al. [30]	1 day (0–1)*	2 days (1–2)*	<0.0001
Liem et al. [38]	1 day (1–2)*	2 days (1–2)*	<0.001
Fleming et al. [36]	68% daycare	48% daycare	0.0065

* median (range); ^ mean (range)
° mean ± standard deviation

Major complications

Only one major complication, a bowel obstruction, was reported among the patients undergoing TEP repair within the framework of a randomized trial. [17] Among the patients undergoing open surgery, no major complications occurred during or after the surgical procedure.

Return to work

In nine trials, return to work was compared between TEP and open repair. In eight of these trials, TEP repair was associated with significantly fewer workdays lost than open repair (Table 4).

Table 4. Return to work

| Reference | Return to work | | p value |
	TEP	Open	
Heikkinen et al. [16]	12 (3–21)*	17 (4–31)*	0.01
Andersson et al. [17]	8 ± 5º	11 ± 8	0.003
Merello et al. [18]	11^	26^	not stated
Lal et al. [20]	12.8 ± 7.1º	19.3 ± 4.3º	<0.001
Champault et al. [24, 25]	17 ± 11º	35 ± 14º	0.01
Khoury et al. [28]	8 (5–13)*	15 (11–21)*	<0.01
Bringman et al. [29]	5 (0–30)*	7 (0–150); 7 (0–70)*¶	0.02‡
Liem et al. [38]	14 (7–21)*	21 (12–33)*	0.001
Fleming et al. [36]	14 (3–42)*	30 (7–84)*	0.0001

* median (range); º mean ± standard deviation

¶ Mesh-plug; Lichtenstein

‡ Significant difference between TEP and Lichtenstein repair only

Recurrence rates

Recurrence rates were reported in 15 trials. Liem et al. [41] reported a significantly lower rate of recurrence after TEP than after various methods of open mesh and open nonmesh repair (p = 0.006). In the remaining 14 trials, no significant differences were found (Table 5).

Table 5. Recurrences

| Reference | Recurrences | | p value |
	TEP	Open	
Heikkinen et al. [16]	0/22	0/23	NS
Andersson et al. [17]	2/78	0/85	NS
Merello et al. [18]	0/60	0/60	NS
Bilgin et al. [19]	1/30	0/30	NS
Lal et al. [20]	0/25	0/25	NS
Colak et al. [22]	2/67	4/67	NS
Bostanci et al. [23]	0/32	0/32	NS
Champault et al. [24, 25]	3/51	1/49	NS
Suter et al. [26, 27]	1/20	0/19	NS
Khoury et al. [28]	3/150	4/152	NS
Bringman et al. [29]	2/92	2/104; 0/103¶	NS
Liem et al. [41]	21/487	43/507	0.006
Champault et al. [42]	7/107	8/64; 2/19‡	NS
Wright et al. [43]	3/149	3/151	NS
Fleming et al. [36]	2/93	5/106	NS

¶ Mesh-plug; Lichtenstein
‡ Shouldice; Stoppa

Costs

An economic evaluation was performed in only four trials.[16, 17, 36, 40] In the trial by Heikkinen et al.[16] hospital costs were significantly higher for TEP endoscopic repair than for Lichtenstein repair ($1239 vs $782; p < 0.001). Total costs, defined as direct and indirect costs caused by absence from work, were however higher with open repair ($3,912 vs $4,661 for TEP vs Lichtenstein, respectively; p = 0.02). The cost-effectiveness analysis by Andersson et al.[17] showed similar results, namely, higher direct costs for TEP than for Lichtenstein repair ($2,085 vs $1,480; p < 0.001), but no difference in total costs, including costs of sick leave ($4,408 vs $4,757; p = 0.21). In the study by Liem [40], TEP repair was found to involve higher hospital costs: Dfl 2,417.24 ($1,309.13) vs Dfl 1,384.91 ($750.05). However, societal costs were lower for endoscopic repair, resulting in total costs that were only Dfl 251.50 ($136.21) higher for TEP repair. Fleming et al. [36] reported nearly 40% higher costs for TEP repair than for Shouldice, mainly caused by the high costs of laparoscopic equipment and disposables.

Table 6. Qualitative analysis

Outcome	No of trials	Significant advantage*	
		TEP	Open
Duration of operation	15	10	1
Hospital stay	11	6	1
Return to work	9	7	1
Recurrences	15	1	0

* $p < 0.05$

Discussion

Laparoscopic hernia surgery has been criticized because of its complexity, high costs, risk of major complications, and need for general anesthesia. The majority of randomized trials compare a laparoscopic TAPP repair with open methods of inguinal hernia repair. As a consequence, systematic reviews and meta-analyses published to date have been based primarily on a comparison between TAPP and open groin hernia repair. Because most surgeons have now adapted the endoscopic extraperitoneal approach, a review of all trials comparing TEP with open mesh and nonmesh repair was performed. Most of the randomized trials in the current review reported longer surgery time for TEP than for open repair. Possible reasons for these prolonged operative times are the intricacy of the procedure and the need for general anesthesia. A major drawback of the laparoscopic approach for inguinal hernia repair is the risk of major complications. The TEP procedure for hernia repair is performed within the preperitoneal space. The peritoneal space is avoided, presumably leading to a considerable reduction in the risk of major vascular complications, intestinal obstructions, and perforations. In the current review, only one major complication was reported among the patients undergoing TEP hernia repair.[17] This patient experienced a small bowel obstruction 3 days after surgery. A loop of the small intestine had herniated through a peritoneal tear. These peritoneal defects occur in approximately 10% to 47% of endoscopic hernia repairs.[38, 45, 46] However, herniation occurs rarely and can be prevented by closing the peritoneal defect, for example, through the use of endoscopic stapling or pretied suture loop ligation.[46] Proponents of laparosopic inguinal hernia repair often refer to the shorter hospital stay and the earlier return to daily activities and work associated with this approach. Obviously, hospital stay and return to work are very important outcome measures given that many patients who undergo inguinal hernia repair are of working age. The majority of trials in the current review showed earlier hospital discharge and quicker return to work after TEP than after open hernia repair. In a systematic review by the Hernia Trialist Collaboration.[47] which included mainly trials comparing TAPP with open procedures, no significant difference in

length of hospital stay was observed between groups (p = 0.50). However, return to normal daily activities was found to be earlier after minimally invasive surgery (p < 0.001). The economic benefits to society of reduced absence from work are clearly indicated by the differences in direct and total costs. Whereas in-hospital costs are significantly higher for TEP than for open hernia repair, no differences exist in total costs, including costs associated with workdays lost. Although endoscopic TEP hernia repair is more expensive for hospitals, it appears long-term recurrence rates and morbidity have not been included in the economic evaluations performed to date. In a recent meta-analysis of randomized trials comparing open and laparoscopic inguinal hernia repair [7], a trend toward an increase in the relative probability of short-term hernia recurrence after laparoscopic repair was detected. However, this trend was found only for TAPP compared with open hernia repair and not for trials comparing TEP with open hernia repair. None of the differences observed were statistically significant. In the current analysis of 23 trials comparing TEP repair with open mesh and sutured repairs, only one trial reported a significant difference in the number of recurrences.[41] Among 994 patients undergoing inguinal hernia repair, a lower recurrence rate after TEP than after open repair using various techniques was observed (21/507 vs 43/487; p = 0.006). None of the other trials showed any significant differences in recurrence rates between the different techniques. A possible reason for this is that these trials were not adequately powered to detect significant variances of this magnitude. Future large trials may show up such differences, which are not apparent in most of the studies analyzed in the current review. Neumayer et al. [14] compared both the TAPP and TEP repair techniques with the open Lichtenstein method and concluded that the open technique is superior to the laparoscopic technique for mesh repair of primary hernias. Endoscopic TEP repair tends to be superior to TAPP repair, because of less morbidity as well as lower recurrence rates and complications.[48, 49] Endoscopic TEP repair seems to be associated with longer surgery time, shorter hospital stay, and earlier return to work than open inguinal hernia repair. (Table 6) Although TEP is associated with higher hospital costs, it does not seem to produce an increase in total expenses, including costs of sick leave. Recurrence rates after TEP repair seem to be comparable with, if not better than, rates after open methods of repair.

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CHAPTER 4

Total extraperitoneal inguinal
hernia repair compared with Lichtenstein
(the LEVEL-Trial): a randomized
controlled trial.

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Abstract

Background: This randomized controlled trial was designed to compare the most common technique for open mesh repair (Lichtenstein) with the currently preferred minimally invasive technique (total extra peritoneal, TEP) for the surgical correction of inguinal hernia.

Methods: A total of 660 patients were randomized to Lichtenstein or TEP procedure. Primary outcomes were postoperative pain, length of hospital stay, period until complete recovery, and quality of life (QOL). Recurrences, operating time, complications, chronic pain, and costs were secondary endpoints. This study was registered at www.clinicaltrials.gov and carries the ID: NCT00788554.

Results: About 336 patients were randomized to TEP, and 324 to Lichtenstein repair. TEP was associated with less postoperative pain until 6 weeks postoperatively (P =0.01). Chronic pain was comparable (25% vs. 29%). Less impairment of inguinal sensibility was seen after TEP (7% vs. 30%, P= 0.01). Mean operating time for a unilateral hernia with TEP was longer (54 vs. 49 minutes, P =0.03) but comparable for bilateral hernias. Incidence of adverse events during surgery was higher with TEP (5.8% vs. 1.6%, P <0.004), but postoperative complications (33% vs. 33%), hospital stay and QOL were similar. After TEP, patients had a faster recovery of daily activities (ADL) and less absence from work (P = 0.01). After a mean follow-up of 49 months, recurrences (3.8% vs. 3.0%, P =0.64) and total costs (€3.096 vs. €3.198) were similar.

Conclusion: TEP procedure was associated with more adverse events during surgery but less postoperative pain, faster recovery of daily activities, quicker return to work, and less impairment of sensibility after 1 year. Recurrence rates and chronic pain were comparable. TEP is recommended in experienced hands.

Introduction

Correction of inguinal hernias is one of the most common surgical procedures.[1] The optimal method for repair remains a matter of debate, despite extensive research. The use of prosthetic mesh, to create tension-free repair, is preferable over non mesh techniques because of reduced recurrence.[2–7] The mesh can be placed with either open or endoscopic surgery. The hernia repair according to Lichtenstein is the most commonly used mesh technique in open surgery.[8] The total extraperitoneal inguinal hernioplasty (TEP) is the current preferred endoscopic mesh technique. A large randomized head to head comparison of only TEP and Lichtenstein repair has not previously been performed. We therefore designed a randomized trial; the "LEVEL"-trial, to compare TEP with Lichtenstein regarding postoperative pain, length of hospital stay, period until recovery, and quality of life. A long-term evaluation with 660 patients was performed in which we focused largely on postoperative pain.

Methods

Six hospitals, including 1 university hospital in the Netherlands participated in the "LEVEL"-trial. All centers obtained approval of their Medical Ethical Committee for participating. Adults presenting with primary or recurrent inguinal hernias, uni- or bilateral, with an indication for elective correction, were eligible for randomization. Exclusion criteria were scrotal hernia, pregnancy, and communicative or cognitive limitation that prevented informed consent. A medical history of prostatectomy, pfannenstiel incision, preperitoneal procedure, or abdominal bladder operation were other reasons for exclusion. Written informed consent was obtained before randomization. Randomization for TEP or Lichtenstein was carried out by telephone or fax at the outpatient clinic, by the central study coordinator, according to a balanced and stratified computer-generated list. Stratification was by center, recurrence state (primary, first recurrence, or ≥ second recurrence), uni- or bilateral hernia and clinical or day-care treatment. The trial is registered at www.clinicaltrials.gov with number NCT00788554.

Surgical Technique

Surgeons and residents were experienced with both procedures or were supervised by an experienced surgeon. For TEP, a surgeon who previously performed a minimum of 100 laparoscopic interventions and a minimum of 30 endoscopic corrections of inguinal hernias had to be present in the operating room throughout the whole procedure. Experience of the surgeon or resident who performed the operation was registered. Experience was reported as: "Level 1" (experience with less than 10), "Level 2" (10 –25), or "Level 3" (more than 25 procedures). Both procedures were performed under standardized techniques. Use of prophylactic antibiotics was up to the surgeon and reported. The open tension-free mesh hernioplasty was performed according to Lichtenstein.[2,8] General, local, or spinal

anesthesia was used. The hernia sac was dissected and reduced to the preperitoneal space except when the contents of the hernia were fixed to the hernia site. To close the hernia site, a polypropylene mesh of 7,5 x 15 cm (Prolene or Marlex), was fashioned and placed with an overlap of the pubic bone. The mesh was fixed with a monofilament non absorbable suture (Prolene 2-0). The surgeon had to report whether the ilioinguinal nerve and the iliohypogastric nerve were identified and spared. The external oblique fascia was closed with absorbable polyglactin sutures (Vicryl 3-0). The TEP hernioplasty was performed under general anesthesia. Through a subumbilical incision the preperitoneal space was created using balloon dissection. Carbon dioxide was insufflated through a blunt tip trocar (pressure, 12–15 mm Hg). A second trocar was placed halfway the umbilicus and pubic bone. The space of Bogros was created with isolation of the spermatic cord. The third trocar was placed medial of the anterior superior iliac spine. A 12 x 15 cm polypropylene (Prolene or Marlex) mesh was placed over the myopectineal orifice of Fruchaud. Mesh fixation was not performed routinely, but it was recorded if the mesh was fixed to Coopers ligament with tackers. Instructions were given to all patients, to resume normal daily activities and return to work as soon as possible, irrespective of the operative method.

Endpoints

The primary endpoints were postoperative pain, length of hospital stay, period until complete recovery, and quality of life. Secondary outcomes were: duration of the procedure, complications, period until return to work and daily activities, economic costs, and recurrence.

Follow-up and Data Collection

Baseline characteristics of patients were recorded by the surgeon or surgical resident. Data regarding the surgical procedure was filled out in the operating room on a standard form. Operation time was defined as time from the first incision to complete closure of the skin. Postoperative complications and length of hospital stay (defined as length of stay in days including the day of surgery) were reported after 1 week at the outpatient clinic control. Postoperative pain was measured by a 10 cm Visual Analogue Scale (VAS), ranging from no pain (0) to unbearable pain (10), preoperative and postoperative after 24, 48, 72 hours and after 1 and 2 weeks. The wound was inspected, analgesic consumption reported. Wound infection was defined: "light" with erythema present, "medium" with pus and "severe" with pus and fever. After 6 weeks, 1 and 5 years the patient was seen back at the outpatient clinic. Chronic pain, sensibility disorders, recurrences, and reoperations were documented. Pain in general and a specification of the pain regarding the inguinal area, scrotum, incision site, upper leg or other areas were reported. Physical examination was performed by a resident or surgeon for inspection of the incision site, sensibility disorders, testis atrophy, and recurrences. The last follow-up was 5 years postoperatively. Recurrences and reoperations during the follow-up interval from 1 to 5 years were reported to the central study coordinator,

at time of diagnosis. Activities of daily life (ADL) were assessed preoperative and 1 and 4 weeks postoperative, with a questionnaire from a Dutch.

Figure 1. Flowchart.
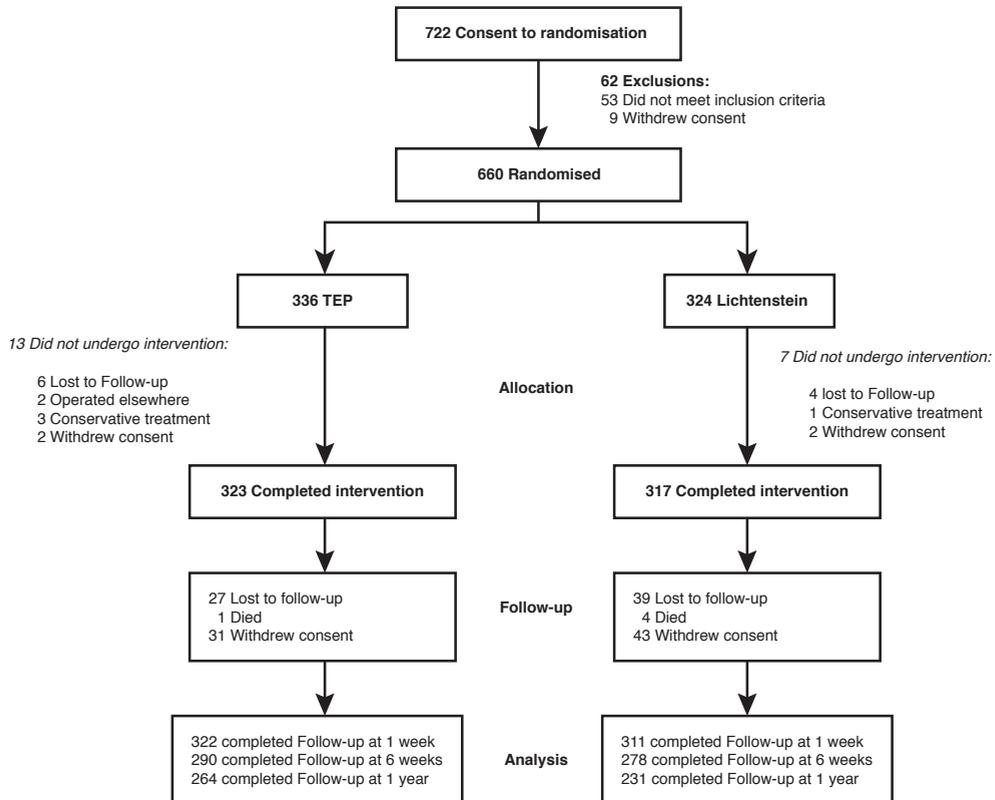
Health Survey.[9, 10] In the survey, questions were asked about walking, bowing, carrying things, etc. Date of return to work and normal daily activities was written down by the patient. Visits to the general practitioner, outpatient clinic, use of homecare, and care of family and friends were also reported. Quality of Life (QOL) was measured preoperative and 4 weeks postoperative with Euroqol.[11] The SF-36 questionnaire (acute version of SF-36 Health Survey, Medical Outcomes Trust, Boston, MA 02116) was used preoperative and postoperative after 1 and 4 weeks. A sub study was performed with the first 450 patients included in the trial to calculate costs. A differentiation was made in medical costs, societal costs, and costs for the patient. Medical costs were costs of hospital stay, day-care, operation, general practitioner, outpatient clinic, and home care. Societal costs were costs of absence of work and activities because of illness. Costs for the patient were costs for private homecare. The economical evaluation was made with the guidelines and index prices for economical evaluations of the

college of health insurances.12 Costs of hospital stay was 343.63 euro per day and daycare 219 euro. Costs for the operation included costs of the employees and the use of the instruments and equipment in the operation room. During the first 450 operations all materials used in the operation room were documented. Costs of a visit to the outpatient clinic were 50.71 euro, costs for homecare 26.70 euro per hour.

Statistical Analysis

The sample size was calculated such that a difference of 0.7 points on the VAS according to pain could be detected with a 80% power and an α error of 0.05 (2 sided). This required a sample size of 600, 300 in each arm, based on the variance of the VAS scores reported by Liem et al.9 With the sample size of 600, it was also possible to detect a difference of 0.29 days in hospital stay, 2.0 days in the period until return to normal daily activities and 4.1 days until return to work with a 80% power and an α error of 0.05 (2 sided). Categorical outcomes were analyzed with x^2 tests. Continuous outcomes were analyzed with a Mann-Whitney-U test. Analysis of covariance was used for pain scores, with correction for preoperative use of analgesics. All analyses were made using SPSS version 11.5 (Chicago, IL). Primary analysis was performed on an intention to treat basis. No interim analyses were performed.

Results

Between August 2000 and March 2004, 722 patients consented to randomization (Fig. 1). Fifty-three patients did not meet the inclusion criteria and 9 patients withdrew consent. This resulted in 336 randomizations for TEP and 324 for Lichtenstein. Thirteen patients from the TEP group and 7 from the Lichtenstein group did not undergo the intervention. The 1-week follow-up was completed in 99% (633) of the 640 patients who underwent surgery. Follow-up after 6 weeks was completed in 89% (568) and 1 year in 77% (495). One-year follow-up was completed in 82% in the TEP group and 73% in the Lichtenstein group. Reasons why patients were not analyzed included 66 patients lost to follow-up (10%), 74 withdrew consent (12%), and 5 died of unrelated causes (0.8%). Hernia characteristics were comparable. Patients were generally male, presenting with primary unilateral hernias. Patients' baseline characteristics were comparable in general aspects (Table 1). There were more patients with Chronic Obstructive Pulmonary Disease (COPD) in the TEP group (8.2% vs. 4.4%). The use of corticosteroids (7.4% vs. 4.3%) was comparable.

Table 1. Baseline Characteristics

|	TEP (336)	Lichtenstein (324)
General characteristics		
Age (yr, median, interquartile range)	55	56
Gender (% male)	99	98
Body mass index (mean)	25	25
ASA (mean)	1	1
Medical history		
COPD (%)	27 (8.0)	14 (4.3)
Diabetes (%)	6 (1.8)	9 (2.8)
Abdominal surgery (%)	71 (22)	81 (26)
Corticosteroid use (%)	24 (7.1)	13 (4.0)
Preoperative analgesic use (%)	16 (4.8)	11 (3.4)
Sensibility abnormality (%)	2 (0.6)	2 (0.6)
Testis abnormality (%)	7 (2.1)	9 (2.7)
Hernia characteristics		
Primary hernia (%)	293 (91)	295 (93)
First recurrence (%)	23 (6.8)	18 (5.5)
≥ Second recurrence (%)	6 (1.8)	3 (0.9)
Unilateral (%)	284 (88)	292 (92)
Bilateral (%)	39 (12)	25 (7.7)

Table 2. Complications

	TEP (323)	Lichtenstein (317)	P
Peroperative complications and adverse events			
Hypercapnia (%)	1 (0.3)	0 (0.0)	
Material failure (%)	2 (0.6)	0 (0.0)	
Allergic reaction to Kefzol (%)	0 (0.0)	1 (0.3)	
Arrhythmia (%)	1 (0.3)	0 (0.0)	
Hypertension (%)	1 (0.3)	0 (0.0)	
Ligation vas deferens (%)	1 (0.3)	0 (0.0)	
Bladder lesion (%)	1 (0.3)	0 (0.0)	
Bleeding epigastric vessels (%)	12 (3.7)	4 (1.3)	
Total (%)	19 (5.8)	5 (1.6)	< 0.004
Early postoperative complications			
Wound infection "light" (%)	6 (1.9)	11 (3.4)	
Wound dehiscence (%)	3 (0.9)	2 (0.6)	
Seroma (%)	20 (6.2)	24 (7.5)	
Hematoma (%)	67 (21)	65 (21)	
Airway infection (%)	1 (0.3)	0 (0.0)	
Urinary tract infection (%)	5 (1.5)	1 (0.3)	
Urinary retention (%)	6 (1.9)	1 (0.3)	
Flebitis (%)	2 (0.6)	1 (0.3)	
Epididymitis (%)	1 (0.3)	0 (0.0)	
Total (%)	107 (33)	104 (33)	0.93

Operative Results

In both groups most procedures were performed by residents or surgeons with Level 3 experience. Prophylactic antibiotic use was administered in 46% for TEP and in 50% for Lichtenstein. Cephalosporins (40% Cefuroxime and 33% Cefazolin) were mainly chosen. All patients in the TEP group received general anesthesia. For Lichtenstein, 44% general anesthesia, and 51% spinal anesthesia was used. Local anesthesia or a combination of the above was used in 5%. There were more lateral hernias diagnosed during TEP; 59% versus 46% (P =0.01). Mean operating time was 5 minutes longer for primary unilateral hernias in TEP procedure than Lichtenstein (54 minutes [interquartile range: 16–130]vs. 49 minutes [interquartile range: 20–101, P = 0.03]). Mean operating time for primary bilateral hernias was comparable (69 minutes for TEP [interquartile range: 35–120] and 72 minutes for Lichtenstein [interquartile range: 48–110, P =0.5]). There were 21 conversions (6.5%). Two operations were converted to a transabdominal preperitoneal procedure (TAPP). Other TEP procedures were converted to Lichtenstein. Reasons for conversion were: lack of overview because of problems with adhesions or local anatomy (38%), peritoneal tears (14%), bleeding (14%), large peritoneal sac or accrete hernia (19%), or combined and other reasons (14%). Two operations in the Lichtenstein group were converted, one to a Shouldice procedure and

one bilateral hernia operation to a Bassini/Mc Vay. The overall rate for complications and adverse events during surgery was 5.9% for TEP and 1.6% for Lichtenstein repair (P <0.001, Table 2). Important complications in the TEP group were one ligation of the vas deferens, one arrhythmia and one bladder lesion. All patients recovered well.

Figure 2. VAS pain score
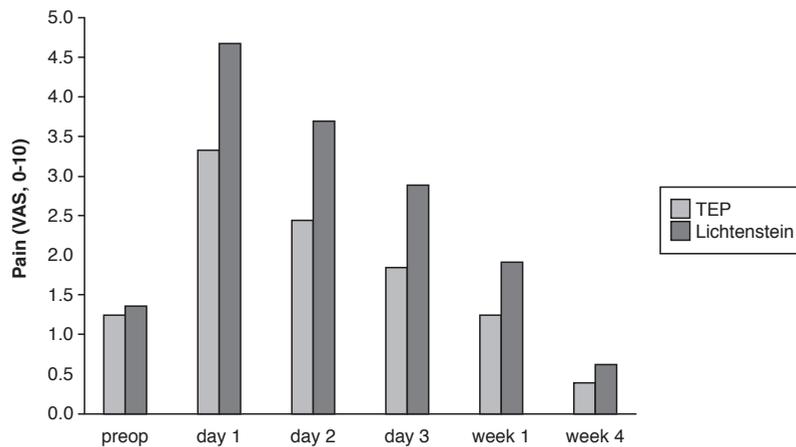
Postoperative Results

There was no difference in length of hospital stay (1.6 days in both groups, P =0.6) and early postoperative complications were comparable (33% in both groups, P =0.8). The pain score for TEP was significantly lower on the visual-analogue scale (VAS) on day 1, 2, 3, 1 week, and 4 weeks (overall P < 0.001, Fig. 2). Analgesics were used less the first 3 days postoperative after TEP (day 1 P = 0.001, day 2 P = 0.003, day 3 P = 0.001). After 6 weeks significantly less pain was seen after TEP (23% versus 32% P =0.01, Table 2). Activities of daily life (ADL) were resumed earlier after TEP than Lichtenstein (Table 3) and the period of sick leave was shorter (1.0 vs. 1.4 week, P = 0.001). Evaluation of quality of life using Euroqol did not show a difference (P= 0.35).

Medical costs were higher for TEP procedure than for Lichtenstein (€1.758 vs. €1.333), explained mainly by costs of disposable materials and equipment used in TEP procedure. Social costs because of sick leave were lower for TEP than Lichtenstein (€1.327 versus €1.839). Patient costs were €11 after TEP and €17 after Lichtenstein. Therefore total costs were €3.096 for TEP and €3.198 for Lichtenstein.

Table 3. Long-term Follow-up

	TEP	Lichtenstein	P
Recurrences			
6 wk	1	2	
1 yr	3	5	
Total recurrences at mean FU 49 mo	10/264 (3.8)	7/231 (3.0)	0.53
Reasons for second operations			
Recurrence	7	4	
Bleeding	1	1	
Femoral hernia	1	1	
Fibrosis scar	1	1	
Persistent pain	1	1	
Total second operations (%)	11/264 (4.2)	8/231 (3.5)	0.68
Pain/sensibility			
Pain after 6 wk (%)	64/282 (23)	87/269 (32)	0.011
Pain after 1 yr (%)	65/264 (25)	65/231 (28)	0.34
Pain at the scar(s) after 1 yr (%)	6/264 (2.3)	15/231 (6.5)	0.019
Impairment of inguinal sensibility after 1 yr (%)	19/264 (7.2)	69/231 (30)	0.001
Recovery			
Sick leave (mean wk)	1.0	1.4	0.01
ADL			
Problem to carry 5 kg 10 m (%)			
Preoperative	26	32	0.001
1 wk	42	57	
4 wk	11	23	
Problem to bow and pick up (%)			
Preoperative	35	32	0.042
1 wk	56	73	
4 wk	18	26	
Problem to walk (%)			
Preoperative	19	30	0.013
1 wk	24	54	
4 wk	7.1	14	
Problem to walk fast 100 m (%)			
Preoperative	66	67	0.023
1 wk	83	94	
4 wk	50	61	
Problem to get dress/ undressed (%)			
Preoperative	8.7	9.3	0.037
1 wk	21	42	
4 wk	2.0	5.6	
Problem to get in/out bed (%)			
Preoperative	3.2	7.4	0.086
1 wk	20	40	
4 wk	1.6	4.2	
QOL (VAS euroqol, median)			
Preoperative	80	85	0.192
4 wk	90	90	0.353

Figure 3. Experience.
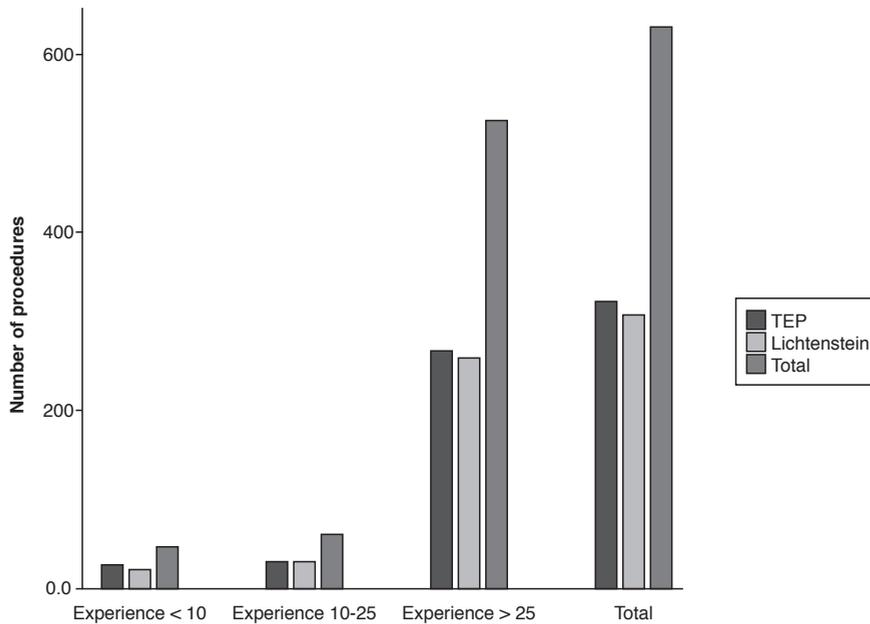
Long-Term Follow-up

After a mean follow-up of 49 months, 10 recurrences were seen after TEP (3.8%) versus 7 after Lichtenstein (3.0%, P = 0.53; Table 3). Micturation- and erection problems occurred in 1.9% of the cases in both groups. A second operation was performed in 11 patients from the TEP group and 8 from the Lichtenstein group (P =0.68, Table 3). Pain sensations after 1 year were reported in similar rates; 25% after TEP and 28% after Lichtenstein (P = 0.34, Table 3). However, pain located at the scar after 1 year was significantly higher after Lichtenstein (6.5% after Lichtenstein and 2.3% after TEP, P = 0.19). The ilioinguinal nerve and iliohypogastric nerve were identified in 67% and preserved in 64% of the procedures. Single nerve identification took place in 11% for the ilioinguinal nerve and 1.4% for the iliohypostric nerve. In 20% no nerves were

identified. Neither identification nor nerve sparing surgery influenced chronic pain (P = 0.4 and P = 0.3). Impairment of inguinal sensibility 1 year postoperatively was reported in 30% after Lichtenstein versus 7.2% after TEP (P <0.001). Patients reported "numbness" of the scar and a "pulling sensation." "Numbness" was reported in 24% after Lichtenstein procedures where the nerves were sacrificed versus 12% after nerve sparing surgery (P = 0.3).

Surgeons Experience

In both groups most procedures were performed by residents or surgeons with Level 3 experience (Fig. 2). This was comparable for TEP and Lichtenstein. With TEP, more recurrences (8.0% vs. 1.9%) and second operations (12% vs. 1.9%) were found in the group of patients that were operated by surgeons or residents with Level 1 experience, compared with the group operated by surgeons with Level 3 experience (P =0.02 and P = 0.004, respectively). For Lichtenstein these differences were not found (P =0.5 and P = 0.5). The number of complications during surgery in the TEP group was comparable for patients operated by a surgeon or residents with Level 1 experience or Level 3 experience (12% vs. 9.4%, P = 0.5). As stated earlier all procedures were supervised by a well experienced surgeon.

Dicussion

Although several randomized studies have been published regarding inguinal hernia repair, most of them compared a number of different techniques for open or endoscopic repair within one trial.[13–17] Most studies used the transabdominal preperitoneal approach (TAPP). With this technique the peritoneal cavity is entered, which is avoided in TEP repair. Several studies and a Cochrane review suggested that TAPP is associated with higher incidence of port-site hernias and life-threatening visceral injuries compared with TEP, and some studies found higher recurrence rates after TAPP. Therefore, TEP is generally preferred to TAPP.[18–21] Few randomized studies comparing Lichtenstein with the TEP technique were published.[22–27] In most of these studies, either follow-up was short23 or less than 200 patients were included.[22, 24–26] Recently, Eklund et al published long-term results of their study on recurrences.[27] However, the issue of chronic pain was not addressed in their study. As was shown in our study, 25% to 29% of all patients still had sensations of pain after one year. Chronic pain is therefore to be considered to be an important issue in inguinal hernia repair. We present a large randomized study comparing Lichtenstein with TEP with a follow-up over 1 year postoperatively. In the present study, more complications were seen during TEP mainly because of bleeding of epigastric vessels (3.7% after TEP). However, blood loss was less than 45 mL and no blood transfusions were needed. In addition, incidence of postoperative hematoma was comparable in both groups. Lau et al.[25] did not find any complications during TEP procedure and Eklund et al.[23] reported bleeding of the epigastric vessels in only 1% of patients. Peritoneal tears were reported as reason for conversion in 14% in this trial. Data suggest that peritoneal tears in most of cases may be safely managed without peritoneal closure and where therefore not considered a complication.[28] However the high conversion rate suggest to avoid peritoneal tears. The mean duration of operation was 5 minutes longer in the TEP group. The duration of TEP procedure was influenced by the relatively high conversion rate (6.5% in the present study, compared with 2% in the study of Eklund et al and 0% in the study of Lau et al) resulting in one operating time of 130 minutes after conversion to a Lichtenstein procedure. Postoperative recovery was significantly better in the TEP group, with less pain until 6 weeks postoperatively, faster recovery of ADL and quicker return to work. These findings are in accordance with other studies.[13, 22, 23, 25] Recurrence rates in Lichtenstein and TEP procedure were low (3.0% and 3.8%, respectively). In the TEP group, most of these recurrences were found in the patients who were operated by surgeons or residents with Level 1 experience, even with supervision of an experienced surgeon. This finding stresses the longer learning curve for TEP repair compared with Lichtenstein repair. The learning curve for laparoscopic repair is reported between 30 and 250 operations.[13, 29, 30] A Cochrane review suggested that surgeons become experienced between 30 and 100 procedures.[19] Neumayer et al. reported that recurrence rates among surgeons who had performed fewer than 250 laparoscopic hernia repairs (both TEPP and TAP) were consistently above 10%.13 Regarding chronic pain, in both procedures,

25% to 29% of the patients still had sensations of pain after one year. In our trial nerve sparing surgery during Lichtenstein procedure did not result in less chronic pain or less impairment of sensibility. A recent review on nerve management during open hernia repair suggested that nerves should probably be identified to prevent damage caused by sutures placed near the nerves.[31, 32] In conclusion, the TEP technique could be recommended as the optimal technique for inguinal hernia repair in experienced hands. TEP was associated with less postoperative pain, less impairment of inguinal sensibility after 1 year, a faster recovery of ADL and a quicker return to work, despite more adverse events during surgery. The authors suggest to avoid peritoneal tears because they are a reason for a high conversion rate. The longer learning curve might be considered a drawback of the TEP procedure and in less experienced hands the Lichtenstein procedure is a good alternative with comparable recurrence rates and incidence of chronic pain.

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CHAPTER 5

The best laparoscopic hernia repair: TEP or TAPP.

H.R. Langeveld , J.F. Lange, J. Jeekel, M. van 't Riet.

TAPP procedure is easier to learn; however there are many possible advantages to using the TEP approach. There is less chance of visceral damage because the abdominal cavity is not entered. In case of bilateral hernias, minimal further dissection is needed and, because the peritoneum is not violated, adhesion formation from the mesh to the visceral organs is avoided. The Cochrane database on TAPP versus TEP included only 1 small randomized controlled trial.[1] In 1996, Schrenk et al published a report on 28 patients randomized for TAPP versus 24 patients for TEP.[2] Only length of stay was significantly shorter for TEP. No differences between TAPP and TEP were seen in terms of length of operation, hematomas, time to return to usual activities and hernia recurrence. Data about complications were obtained from additional non-RCT studies and these results appear to be broadly consistent. The non-RCT studies suggest that an increased number of port-site hernias and visceral injuries are associated with TAPP rather than TEP. These non-RCT studies consisted of 5 studies with concurrent comparators and 3 case series. These were mainly large studies: Lepere with 1290 TAPP versus 692 TEP procedures[3], and Felix with 733 TAPP versus 382 TEP procedures.[4] The case series varied from 2500 to 5707 procedures.[5-7] Therefore, although the learning curve for TAPP is shorter and the conversion rate is higher for TEP [8], the Dutch guideline on inguinal hernia repair prefers TEP over TAPP.[9] However, well-rando-mized controlled multicenter trials comparing TAPP versus TEP are lacking indeed. For the future, more research on this subject is encouraged.

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CHAPTER 6

Randomized clinical trial of total extraperitoneal inguinal hernioplasty vs Lichtenstein repair: a long-term follow-up study.

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Abstract

Hypothesis: Mesh repair is generally preferred for surgical correction of inguinal hernia, although the merits of endoscopic techniques over open surgery are still debated. Herein, minimally invasive total extraperitoneal inguinal hernioplasty (TEP) was compared with Lichtenstein repair to determine if one is associated with less postoperative pain, hypoesthesia and hernia recurrence.

Design: Prospective multicenter randomized clinical trial.

Setting: Academic research.

Patients: Six hundred sixty patients were randomized to TEP or Lichtenstein repair.

Main Outcome Measures: The primary outcome was postoperative pain. Secondary end points were hernia recurrence, operative complications, operating time, length of hospital stay, time to complete recovery, quality of life, chronic pain, and operative costs.

Results: At 5 years after surgery, TEP was associated with less chronic pain (P = .004). Impairment of inguinal sensibility was less frequently seen after TEP vs Lichtenstein re- pair (1% vs 22%, P <.001). Operative complications were more frequent after TEP vs Lichtenstein repair (6% vs 2%, P <.001), while no difference was noted in length of hospital stay. After TEP, patients had faster time to return to daily activities (P <.002) and less absence from work (P = .001). Although operative costs were higher for TEP, total costs were comparable for the 2 procedures, as were overall hernia recurrences at 5 years after surgery. How- ever, among experienced surgeons, significantly lower hernia recurrence rates were seen after TEP (P <.001).

Conclusions: In the short term, TEP was associated with more operative complications, longer operating time, and higher operative costs; however, total costs were comparable for the 2 procedures. Chronic pain and impairment of inguinal sensibility were more frequent after Lichtenstein repair. Although overall hernia recurrence rates were comparable for both procedures, hernia recurrence rates among experienced surgeons were significantly lower after TEP. Patient satisfaction was also significantly higher after TEP. Therefore, TEP should be recommended in experienced hands.

Trial Registration: clinicaltrials.gov Identifier: NCT00788554

Introduction

Chronic pain and hypoesthesia after inguinal hernia repair are increasingly gauged, and hernia recurrence rates have decreased as a result of the use of prosthetic mesh.[1-6] Incidence rates of chronic pain up to 37% have been reported after open inguinal hernia repair.[7] Surgical technique may have a significant role in the occurrence and reduction of chronic pain, with some studies [8,9] demonstrating less pain and hypoesthesia after endoscopic repair. Large randomized clinical trials having long- term follow-up periods that compare chronic pain and hypoesthesia associated with open vs endoscopic inguinal hernia repair are rare.[10,11] Particularly scarce are randomized clinical trials comparing minimally invasive total extraperitoneal inguinal hernioplasty (TEP) with Lichtenstein repair. We report results of a long-term follow-up study of a prospective multicenter randomized clinical trial comparing TEP vs Lichtenstein repair for postoperative pain, hypoesthesia, and hernia recurrence rates among 660 patients.

Methods

Study Design

Between July 18, 2000, and April 28, 2004, adult patients with a primary or recurrent inguinal hernia were eligible for inclusion in the study and were randomly assigned to TEP or Lichtenstein repair. Only patients scheduled for elective repair were included. Patients were excluded if they were pregnant, had a scrotal hernia, or had communicative or cognitive limitations to give informed consent. Other exclusion criteria were a medical history of prostatectomy, Pfannenstiel incision, previous preperitoneal operation, or abdominal bladder operation. The study protocol was approved by the ethics committees of 6 participating centers. Primary end points were postoperative groin pain, length of hospital stay, and time to complete recovery. Secondary end points were hypoesthesia, hernia recurrence, operative complications, operating time, time to return to daily activities and work, and operative costs. Randomization was achieved at the ward by telephone call or fax from the central study coordinators (H.R.L. and M.v.R.) using a stratified and balanced computer-generated list. Patients were stratified by center, hernia recurrence (primary, first recurrence, or second recurrence or more), unilateral or bilateral hernia, and inpatient or outpatient treatment. All participating centers were experienced in both hernia repair procedures. The experience of the operating surgeon was registered as level 1 (<10 procedures), level 2 (10-25 procedures), or level 3 (>25 procedures). During each TEP, an experienced surgeon who previously had performed a minimum of 30 TEP procedures was present in the operating room. Both procedures were standardized and well documented in the study protocol. Polypropylene prosthetic meshes were used for both procedures. Whether the ilioinguinal and iliohypogastric nerves were identified and spared was reported. More detailed descriptions of the procedures have been published

previously.[11] Long-term follow-up visits occurred at 1 year and 5 years after surgery. All the patients were invited to visit the ward to undergo physical examination, performed by 2 independent physicians (H.H.E. and P.J.K.) who were unaware of each other's findings or of data from the medical records. The inguinal region was examined for any symptomatic or asymptomatic hernia recurrences on the operated or contralateral side. All the patients were asked about symptoms of chronic pain, sensibility disorders, sexual dysfunction, other hernia occurrences, and hernia recurrences. Postoperative pain and chronic pain in the inguinal and scrotal region were measured using a 10-cm visual analog scale, ranging from no pain (0 cm) to unbearable pain (10 cm). Reoperations during the follow-up period for a recurrent inguinal hernia were recorded. Ultrasonographic examination was performed when findings on physical examination were inconclusive. Patient satisfaction with the surgical procedure and with cosmetic results was assessed using a numeric rating scale, ranging from worst outcome (0 points) to best outcome (10 points).

STATISTICAL ANALYSIS

A 2-tailed test was performed with 80% power and an a α=.05 to determine a difference of 0.7 cm on the visual analog scale for pain. A minimum sample size of 300 patients in each group (TEP vs Lichtenstein repair) was required to detect this difference, resulting in a total number of 600 patients. Considering an estimated dropout rate of 10%, we aimed to include 660 patients. Continuous variables were compared using Mann-Whitney test. Categorical variables were compared using χ^2 test or Fisher exact test. Cumulative hernia recurrences were calculated using Kaplan-Meier method and were compared using the log-rank test. All the statistical tests were 2-sided; $P \leq .05$ was considered statistically significant. The primary analysis was performed on an intent-to-treat principle; that is, patients remained in their assigned group even if during the procedure the surgeon judged a patient to be unsuitable for the technique to which he or she was allocated. All the analyses were performed using commercially available software (SPSS for Windows, version 15; SPSS, Inc).

Results

Between July 18, 2000, and April 28, 2004, a total of 722 patients consented to randomization, of whom 62 patients (8.6%) were excluded. Among these, 9 patients withdrew consent, and 53 patients did not meet the inclusion criteria. The remaining 660 patients were randomized and analyzed within the groups to which they were allocated to, based on the intent-to-treat principle. Of 660 patients, 336 were randomized to TEP and 324 to Lichtenstein repair. Twenty-one conversions (6.3%) occurred in the TEP group, 19 to Lichtenstein repair and 2 to a transabdominal preperitoneal procedure. Two conversions (6.6%) occurred in the Lichtenstein group, one to Shouldice repair and another to Bassini-McVay repair. The mean (SD) age of patients at the time of study inclusion was 55 (16) years, with no significant difference between the 2 study groups. No differences were found between the 2 study groups in sex, body mass index, American Society of Anesthesiologists score, comorbidities, or primary vs recurrent hernias. Baseline characteristics of the patients are given in Table 1.

Table 1. Patient Characteristics

Variable	TEP (n = 336)	Lichtenstein Repair (n = 324)
Age, mean, y	55	56
Male sex, %	99	98
Weight, mean, kg	80	78
Height, mean, cm	179	178
BMI, mean	25	25
Diabetes mellitus, No. (%)	6 (1.8)	9 (2.8)
Chronic obstructive pulmonary disease, No. (%)	27 (8.0)	14 (4.3)
Sensibility disorder, No. (%)	2 (0.6)	2 (0.6)
Testicular pain, No. (%)	7 (2.1)	9 (2.7)
American Society of Anesthesiologists score, No. (%)		
1	252 (75)	225 (69)
2	77 (23)	91 (28)
3	7 (2)	8 (3)
4	0	0
Primary hernia, No. (%)	293 (91)	295 (93)
Hernia recurrence, No. (%)		
First recurrence	23 (6.8)	18 (5.5)
≥Second recurrence	6 (1.8)	3 (0.9)
Hernia side, No. (%)		
Unilateral	284 (88)	292 (92)
Bilateral	39 (12)	25 (7.7)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); TEP, minimally invasive total extraperitoneal inguinal hernioplasty.

During the long-term follow-up period, 44 patients died, 21 in the TEP group and 23 in the Lichtenstein group (Figure 1). No death was related to inguinal hernia repair. At a median follow-up time of 5.0 years (interquartile range, 2.3-5.8 years), 482 of the 640 patients (75.3%) completed their long-term follow-up visit. The median follow-up periods were comparable for both groups. The cumulative hernia recurrence rates were 4.9% (12 of 247) after TEP and 8.1% (19 of 235) after Lichtenstein repair (*P*=.10) (Figure 2).

Figure 1. Patients screened for participation in the study. TEP indicates minimally invasive total extraperitoneal inguinal hernioplasty.
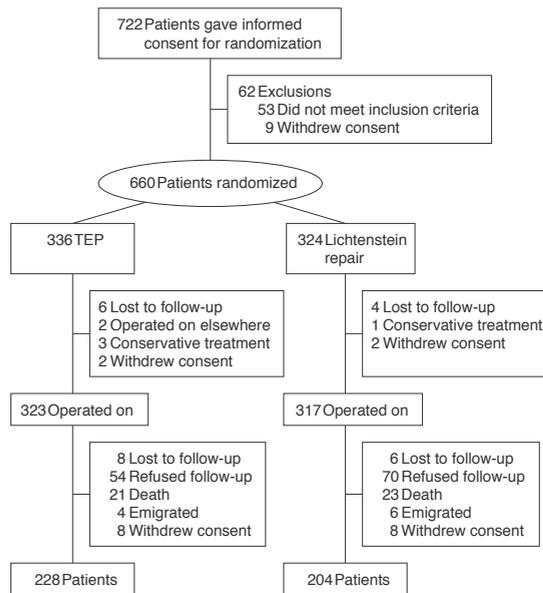
Figure 2. Kaplan-Meier curves for hernia recurrence based on physical examination findings at the outpatient clinic. TEP indicates minimally invasive total extraperitoneal inguinal hernioplasty.
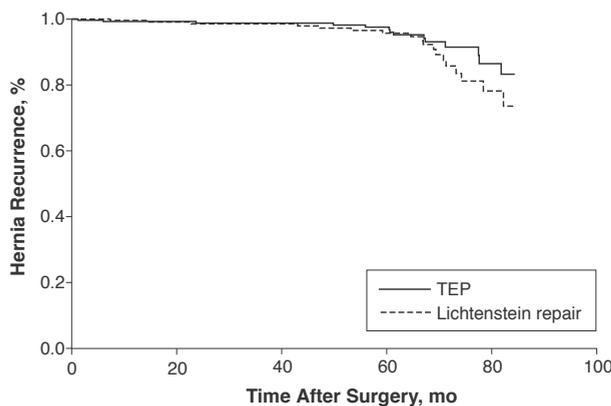
During the follow-up period, 15 patients underwent reoperation for hernia recurrence, 6 after initial TEP and 9 after initial Lichtenstein repair. The experience level of the operating surgeon was reported by 457 operating surgeons (71.4%; 457 of 640). Twenty-eight operating surgeons were classified as level 1 surgeons, 27 as level 2 surgeons, and 402 as level 3 surgeons. The overall hernia recurrence rate after 5 years for both procedures performed by experienced residents or surgeons (level 3) was significantly lower than that for inexperienced residents or surgeons (level 1) (2.4% vs 14.3%, P=.001). When only TEP procedures were analyzed, the differences in hernia recurrence rates between experienced residents or surgeons (level 3) and inexperienced residents or surgeons (level 1) were more obvious (0.5% vs 25.0%, P=.001) (Table 2). The hernia recurrence rates varied between 4.1% and 9.1% among centers but were not statistically different (P=.67). When only procedures performed by experienced residents or surgeons (level 3) were evaluated, significantly lower hernia recurrence rates were seen after TEP than after Lichtenstein repair (0.5% vs 4.2%, P=.04) (Table3).

Table 2. Hernia Recurrence Rates at 5 Years After Surgery by Experience Level of Operating Surgeons[a]

| | Hernia Recurrence, % | | | |
Procedure	Level 1 (n = 28)	Level 2 (n = 27)	Level 3 (n = 402)	P Value
TEP	25.0	6.7	0.5	<.001
Lichtenstein repair	0	8.3	4.0	.55
Total	14.3	7.4	2.2	.001

Abbreviation: TEP, minimally invasive total extraperitoneal inguinal hernioplasty.
[a]Experience level 1 is fewer than 10 procedures, level 2 is 10 to 25 procedures, and level 3 is more than 25 procedures.

Table 3. Hernia Recurrence Rates at 5 Years After Surgery by Procedure

| | Hernia Recurrence, No. (%) | | |
Experience Level[a]	TEP (n = 235)	Lichtenstein Repair (n = 222)	P Value
1 (n = 28)	4 (25.0)	0	.26
2 (n = 27)	1 (6.7)	1 (8.3)	>.99
3 (n = 402)	1 (0.5)	8 (4.2)	.04

Abbreviation: TEP, minimally invasive total extraperitoneal inguinal hernioplasty.
[a]Experience level 1 is fewer than 10 procedures; level 2, 10 to 25 procedures; and level 3, more than 25 procedures.

The number of patients operated on by level 1 and level 2 residents or surgeons was too small to discern any differences between the 2 study groups. At 5 years after surgery, the incidence of chronic pain was significantly higher in the Lichtenstein group (28.0%) compared with the TEP group (14.9%) (*P*=.004). The visual analog scale scores for pain were significantly higher in the Lichtenstein group (1.5 cm) compared with the TEP group (0.9 cm) (*P*=.03) (Figure 3).

Figure 3. Visual analog scale scores for postoperative pain. TEP indicates minimally invasive total extraperitoneal inguinal hernioplasty.
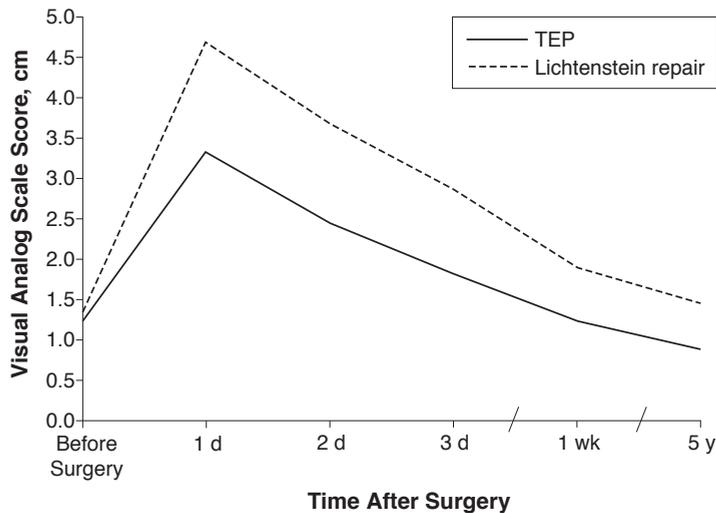
No significant differences were found in testicular pain between the study groups (*P*=.09). Identification and preservation of the ilioinguinal and iliohypogastric nerves had no influence on the incidences of inguinal pain and sensibility disorders (*P*=.10 and *P*=.07, respectively). Whether inguinal nerves were identified was reported for 339 patients: both inguinal nerves were recognized in 199 patients (58.7%), the ilioinguinal nerve in 33 patients (9.7%), the iliohypogastric nerve in 4 patients (1.2%), and no nerves in 103 patients (30.4%). Whether inguinal nerves were preserved was reported for 293 patients: both inguinal nerves were preserved in 163 patients (55.6%), the ilioinguinal nerve in 20 patients (6.8%), the iliohypogastric nerve in 7 patients (2.4%), and no nerves in 103 patients (35.2%). Sensibility disorders and numbness were more frequently reported in the Lichtenstein group. At 5 years after surgery, 21.7% of patients in the Lichtenstein group reported sensibility disorders compared with 1.2% of patients in the TEP group (P <.001). On a scale of 0 to 10, patient satisfaction with the surgical procedure was significantly higher after TEP compared with Lichtenstein repair (8.5 vs 8.0 points, *P*=.004). Patients were also more satisfied with their operative scars after TEP (8.8 vs 8.4 points, *P*=.02).

Comment

For many decades, inguinal hernia repair has been based on "the radical cure of inguinal hernia" according to Bassini[12] and subsequent other herniorrhaphy techniques based on suture repair developed during the 20th century, such as the McVay and Shouldice techniques. However, these procedures were often associated with severe postoperative pain and high inguinal hernia recurrence rates. The introduction of tension-free repair using prosthetic mesh represented a new era in inguinal hernia repair.[13] By reducing hernia recurrence rates, other long-term complications, such as postoperative pain and chronic pain, were addressed.

Our study is not the first evaluation of recurrence rates and chronic pain after open or endoscopic inguinal hernia repair.[10,14-19] Several randomized trials [10,14-19] comparing open and laparoscopic repair have been published,but most enrolled few patients or compared various open techniques with endoscopic techniques. Some studies [14,18] had short follow-up periods or did not report chronic pain and sensibility impairment. The follow-up methods of previous investigations have been variable or even suboptimal because hernia recurrences were often determined using questionnaires. Vos et al[20] compared follow-up results using questionnaires and physical examination and found that at least half of the hernia recurrences were missed using questionnaires only. The accuracy of hernia recurrence rates in our study is ensured because every patient in our study had a clinical follow-up visit with physical examination performed by 2 independent physicians.

Our long-term follow-up data after inguinal hernia repair show that overall recurrence rates seem to be comparable after TEP and Lichtenstein repair. However, the experience level of the surgeon was found to be an independent risk factor for hernia recurrence. Significantly lower hernia recurrence rates were found among experienced surgeons (level 3) after TEP vs after Lichtenstein repair (0.5% vs 4.2%, $P = .04$).

In our study design, we tried to eliminate learning curve bias by assuring that during every endoscopic procedure in this study a surgeon with substantial experience in laparoscopic surgery participated by supervising or operating. In retrospect, we wonder if the requirement of 30 procedures was sufficient. Since the beginning of our study, some authors [14,15,21-23] have reported 80 to 250 procedures before notable improvements occur in surgical outcomes after TEP.

Hernia recurrence rates are expected to increase with longer follow-up periods because recurrences may occur up to 10 years after initial repair.[4] Some earlier investigations comparing open vs endoscopic repair found lower hernia recurrence rates after TEP.[15] Other researchers have reported that hernia recurrence rates were significantly lower after

Lichtenstein repair.[18] A Cochrane review[24] and a meta-analysis[25] comparing open vs laparoscopic herniorrhaphy showed no difference in recurrence rates. Meta-analyses comparing TEP alone with Lichtenstein repair are needed to determine which technique is associated with the lowest hernia recurrence rate.

Chronic pain seems to be the most frequent long-term complication after open inguinal hernia repair. Particularly, if inguinal nerves are not recognized and preserved, the incidence of chronic pain increases considerably.[26] However, an advantage of recognition and preservation of inguinal nerves could not be confirmed in our study. In the present study, [11] postoperative pain was significantly less after TEP (23%) than after Lichtenstein repair (32%) ($P = .01$), measured at intervals of 1, 2, or 3 days and 1 week and 4 weeks after surgery. Postoperative pain was evaluated as pain vs no pain. Earlier results demonstrated that return to work was quicker and recovery of daily activities was faster after TEP than after Lichtenstein repair.[11] Another important finding herein was that impairment of inguinal sensibility in the groin region seemed to be less frequently observed after TEP than after Lichtenstein repair (1% vs 22%, $P < .001$).

These positive outcomes for TEP are counterbalanced by its association with a significantly higher incidence of operative complications.[11] However, none of these operative complications affected the long-term outcomes of patients. During long-term follow-up periods, the incidence of chronic pain, severity of chronic pain, and impairment of inguinal sensibility seemed high in the Lichtenstein group (28%, 1.5 cm, and 22%, respectively) and were significantly lower in the TEP group (15%, 0.9 cm, and 1%, respectively) ($P = .004$, $P = .03$, and $P < .001$, respectively).

A strength of our study is that it was a multicenter randomized clinical trial that included many patients, randomizing between only Lichtenstein repair for open surgery and TEP for endoscopic repair. The fact that physical examination of each patient was performed by 2 independent physicians increases the reliability of our hernia recurrence rates.

In summary, this randomized controlled trial shows in a long-term follow-up study that the overall incidences of hernia recurrence after TEP and Lichtenstein repair are comparable at 5 years after surgery. Among experienced surgeons, the hernia recurrence rates were significantly lower after TEP than after Lichtenstein repair. Experience level of the surgeon was found to be an independent risk factor for hernia recurrence after inguinal hernia repair. Postoperative pain in the short term and chronic pain at 5 years after surgery were significantly greater after Lichtenstein repair vs TEP (32% vs 23% and 28% vs 15%, respectively), as was impairment of inguinal sensibility (22% vs 1%). Patients are more satisfied after TEP with the surgical procedure and with their operative scars. Therefore, TEP should be recommended in experienced hands.

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CHAPTER 7

Should open mesh repair with local anesthesia be the standard of care for randomized trials?

H.R. Langeveld, M. van't Riet, J.F. Lange, J. Jeekel.

Local anesthesia for inguinal hernia repair is a good alternative type of anesthesia. However, because the use of local anesthesia requires greater expertise and surgical skills, it is only successful if the surgeon is thoroughly familiar with the technique.[1] In the Netherlands, inguinal hernia repair is generally not performed in specialized centers and the average Dutch surgeon is not familiar with the technique for local anesthesia. In the Netherlands, national guidelines are implemented, and the guidelines regarding inguinal hernia repair were published in 2003.[2] Regarding local anesthesia, the guidelines are based on Amid's 1994 publication.[3] The exact technique for local anesthesia is explained, combined with how to treat the patient verbally and what preoperative medicine should be used. However, also stated is the fact that there is only a slight advantage for local anesthesia and that local anesthesia can be annoying to the patient and the surgeon. This was based on randomized trials published by Song and O'Dwyer.[4, 5] Higher satisfaction, quicker discharge from the hospital and slightly lower costs were seen with the use of local anesthesia. The second trial did not show differences. As a consequence, it is still not clear what type of anesthesia is best, and therefore the guidelines do not recommend either kind of anesthesia. However, we actually came up with the same questions about the potential advantages regarding local anesthesia. Therefore, in 2004, directly after the inclusion was stopped for our trial on TEP versus Lichtenstein, a new randomized controlled trial was enrolled from our hospital that focused on Spinal versus Local anesthesia in Lichtenstein Hernia repair. R. van Veen et al. published the results of the trial in Annals of Surgery, March 2008. [6] The main results were that in 100 randomized patients, there was less pain shortly after the operation in the group treated with local anesthesia. More urinary retention and more overnight admissions for the spinal anesthesia group were observed. Total operating time was shorter for the local anesthesia group. They concluded that local anesthesia in primary, inguinal hernia repairs should be the method of choice.[6] Altogether, although Dutch surgeons are still not very familiar with the technique, we agree that the use of local anesthetics for the Lichtenstein technique should be advocated, probably best in specialized hands or clinics.

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PART 3

RISK FACTORS ON CHRONIC
POSTOPERATIVE INGUINAL PAIN

CHAPTER 8

The effect of the mesh on chronic postoperative inguinal pain:
a systematic review and meta-analysis comparing Shouldice/Bassini and Lichtenstein techniques for inguinal hernia repair.

H.R. Langeveld , Y. Vergouwe , J.F. Lange.

Abstract

Background: Chronic Postoperative Inguinal Pain (CPIP) is the most common complication of inguinal hernia repair. A tension-free repair with a mesh is standard treatment nowadays to decrease recurrence rates. The mesh however is thought to be one of the causes of CPIP. The Lichtenstein-, Bassini- and Shouldice techniques both have the same anterior approach to reinforce the transversalis fascia with a mesh used in the Lichtenstein technique only. Our hypothesis: incidence of CPIP is higher after Lichtenstein than after Shouldice or Bassini repair because of introduction of the mesh.

Objectives: To evaluate the mesh, used in the Lichtenstein technique, as a cause of CPIP.

Methods: A systematic review and meta-analysis were performed to compare the Shouldice and Bassini suture techniques with the Lichtenstein mesh repair for inguinal hernia repair related to CPIP. Random effects models were used to estimate odds ratios (OR).

Results: Five randomized controlled trials were included. In total, 758 elective Shouldice Bassini repairs and 863 Lichtenstein repairs were performed for inguinal hernia in adults. No difference in CPIP was seen after Shouldice/Bassini vs. Lichtenstein (Odds Ratio 0.88, 95 CI 0.39 – 1.98, I^2=0.48).

Conclusion: From the available data the mesh cannot be regarded as a significant cause of CPIP. However, methodological quality of most included trials is low and length of follow-up differs, therefore no clinical conclusion can be drawn by this data.

Introduction

Nowadays, a patient diagnosed with an inguinal hernia would probably do a search on the internet for 'inguinal hernia surgery'. Since most patients do not know about 'evidence based medicine', search engines on the worldwide web will lead them to websites like the free encyclopedia Wikipedia (www.wikipedia.org). Frequent (>10%) complications of mesh repair i.e. foreign-body sensation, pain, ejaculation disorders, mesh folding and migration, meshoma, infection, adhesion formation, and also erosion of meshes into organs with abscesses, fistulas or obstruction apart from recurrence are mentioned. And in the long term: risk of stiffness, chronic pain, obstructive azoospermia and even cancer transformation. After reading all this, the patient has to be very courageous to undergo inguinal hernia surgery with the use of mesh.

Until the 1990s the standard procedure for inguinal hernia repair was represented by the open suture repair with recurrence rates of about 0.8-2.5% in specialized centers. [1, 2] These acceptable percentages could not be reproduced in general surgery departments where recurrence rates of about 15% were seen.[3, 4, 5]. It is because of these high recurrence rates, that the tension free hernia repair with the use of mesh was introduced. The mesh can be placed with either an open or a laparoscopic approach. Since then, a decrease in hernia recurrence is seen to less than 2% even in non-specialized surgery departments.[6, 7] Research on inguinal hernia repair in the 1980-90's focused mainly on recurrence rates. After recurrences decreased, research nowadays focuses mainly on complications. Searching the literature, the most common complication of inguinal hernia surgery is chronic postoperative inguinal pain (CPIP) with incidences reported up to 40%. CPIP can be neuropathic because of damage to inguinal nerves or non-neuropathic because of the mesh or other factors. The mesh is often considered a cause of CPIP, because of interference of the mesh with the surrounding tissues and inguinal nerves. Therefore we questioned that maybe with suture repair less CPIP might be seen compared to tension free repair with mesh, also considering that patients or even society as a whole might prefer the risk of a recurrence over CPIP.

The inguinal nerves run in the plane anteriorly to the transversalis fascia. Therefore we wanted to compare techniques which use this specific surgical plane for either the mesh insertion or the suture repair. In 1887 Bassini introduced a musculoaponeurotic repair for inguinal hernia, representing an open repair of the transversalis fascia with use of sutures. The technique was modified by Shouldice in 1945. The Bassini and Shouldice techniques were the mostly commonly used techniques in suture repair. Nowadays the 'golden standard' is represented by the open tension-free mesh Lichtenstein technique, first described by Lichtenstein et al.[9] in 1989 In this technique a mesh is placed anteriorly to the transversalis fascia which is the same surgical plane as used with the Shouldice and Bassini-repairs. The endoscopic approaches for tension-free mesh repair (Total Extraperiotoneal Procedure: TEP and Trans Abdominal Preperitoneal Procedure: TAPP) were left out of this analysis,

because with these endoscopic approaches the mesh is placed posteriorly to the transversal fascia in the preperitoneal plane and thereby not in the same plane as the inguinal nerves. Recently Fischer proposed that mesh repairs should be abandoned and the transversalis or Shouldice repair be adopted. It was stated that recurrence rates reported in large series in the 1980's were no more than 4% to 6% and the incidence of CPIP was 2% to 4%. No references are given however.[8]

 A systematic review on the Shouldice or Bassini open suture repairs versus the Lichtenstein open mesh repair was performed to compare incidences of CPIP with the hypothesis that the incidence of CPIP is higher after Lichtenstein technique, because of the mesh.

Methods

A qualitative analysis of randomized trials comparing the open mesh Lichtenstein technique with the sutured (Shouldice or Bassini) repairs was performed with use of the PRISMA guidelines (www.prisma-statement.org).[10] Included were adult patients with a primary inguinal hernia. The primary endpoint was: CPIP, defined as groin pain persisting longer than 3 months. Electronic databases PubMed and Ovid/Medline were searched for relevant randomized clinical trials or quasi-randomized trials. All trials were analyzed using the 'intention to treat' principle. The following search strategy was used: SEARCH: Pubmed: 'Lichtenstein' AND 'Bassini', with the filters activated: Randomized Controlled Trial, Humans, English and Adult: 19+ years, Field: Title. The same search with the filters was performed for 'Lichtenstein' AND 'Shouldice', 'Lichtenstein' AND 'non-mesh', 'Lichtenstein' AND 'tension', 'mesh' AND 'non-mesh'. For the search 'mesh' AND 'suture repair' and the search 'mesh' AND 'suture repair' we added: NOT 'laparoscopy' NOT 'endoscopy' NOT 'umbilical' NOT 'vaginal' NOT 'pilonidal' NOT 'incisional' NOT 'ventral', with the same filters activated. EMBASE/MEDLINE was searched with the same strategy. Further, the Cochrane Central Register of Controlled Trials (CENTRAL) was searched and trials were sought from the reference lists of reports of known trials.

Statistics

The odds ratio (OR), its standard error and 95% confidence interval were calculated based on the reported numbers. Random effect models were used to pool the ORs from individual studies if a statistically significant heterogeneity was found, otherwise, a fixed effect model was used.[11] analyses were performed with R statistical software version 2.14.2

Results

There were 249 records identified through database searching and other sources (Fig 1). After screening and removing duplicates 24 full text articles were assessed for eligibility. Eighteen full text records were excluded because other surgical techniques were used, follow up was less than 3 months or no assessment of CPIP was performed. Some records had multiple causes of exclusion. Only one reason for exclusion per record is mentioned in the flowchart (Fig 1). The remaining 6 records were included in a qualitative synthesis. [12-17] One record was not included in the meta-analysis because it was not possible to distract data on the Shouldice only of all non-mesh types. [17] The five remaining records included only Shouldice vs. Lichtenstein.[12-16] Follow up varied between 3 months and 6-9 years. [15, 16]

Identification	245 records identified through database searching	4 additional records identified through other sources

Screening	147 records after duplicates removed

	147 records screened	118 records on title/abstract + 5 records abstract only

Eligibility	24 full-text articles assessed for eligibility	19 full-tekst articles excluded: • 6: other technique • 5: Follow up < 3months • 1: not possible to extract the data • 7: CIP not assessed

	5 studies included in qualitative synthesis

Included	5 of studies included in quantitative synthesis (meta-analysis)

CHARACTERISTICS OF INCLUDED STUDIES

Koninger 2004		
Methods	Single center, three arms RCT; Shouldice vs. Lichtenstein vs. TAPP (not in current analysis) Randomization: sealed envelope. Generation of sequence not stated. Follow up: median 52 (range 46–60) months. Analyses by standardized form, face-to-face interview , VAS; 0 to 100	
Participants	Country: Germany Single hospital specialized in inguinal hernia repair Total enrolled patients: 186: Shouldice (93), Lichtenstein (93). Mean age: Shouldice: 53; Lichtenstein 56. Inclusion criteria: male, age >18, primary inguinal hernia, elective. Exclusion criteria: not known. Demographic and baseline data reported: comparable for age, type of hernia	
Interventions	Shouldice (93), technique not specified, Lichtenstein (93), standard technique. Experience surgeon: >100 Lichtenstein and Shouldice interventions each.	
Outcomes	Chronic pain and its limitations to quality of life	
Notes	Follow up assesed by resident surgeon by physical examination in 150 patients (80.6%). Conflict of interest: not reported Sources of funding: not reported	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation conceal-ment (selection bias)	Low risk	A - Adequate

Nordin 2002		
Methods	Single center, two arms RCT; Shouldice vs. Lichtenstein. Randomization: sealed envelopes, generation sequence by computer generated in blocks of ten patients. Follow-up: 37-77 months.	
Participants	Country: Sweden Single center, two arms RCT; Shouldice vs Lichtenstein. Total enrolled patients: 297 Shouldice (148), Lichtenstein (149). Mean age: nm Inclusion criteria: 25-75 yrs., unilateral primary inguinal hernia. Exclusion criteria: irreducibility, coagulation abnormalities, anti-coagulant therapy, pt. unsuitable for anesthesia. Age, type of work, type of hernia, equally distributed.	
Interventions	Shouldice Standard (n=148). 4 rows Prolene. Lichtenstein (n=149). Standard technique; Marlex mesh, 2/0 Prolene. Surgeon thoroughly familiar with both techniques.	
Outcomes	recurrence rate, technical difficulty, convalescence and chronic pain	
Notes	Follow up by an independent surgeon in 284 patients. Conflict of interest: not reported. Sources of funding: not reported	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation conceal-ment (selection bias)	Low risk	A - Adequate

McGillicuddy 1998		
Methods	Single center, two arms RCT; Shouldice vs. Lichtenstein Randomization: coin tossed, allocation concealment not adequate Follow-up 52 weeks, lost to follow-up:251 (35,5%) Intention to treat.	
Participants	Country: USA Setting: private center specialized in hernia repair. Total enrolled patients: 672 pt 717 hernias Age: 20-90 mean not reported Inclusion criteria: inguinal hernia. Demographic and baseline data reported: discomfort, age, work activity: comparable, data not reported	
Interventions	Shouldice standard (n=337) 4 layers. Non-absorbable monofila- ment. Lichtenstein standard (n=371). Polypropylene mesh	
Outcomes	Recurrence rates, symptoms, infection	
Notes	Follow-up by the operating surgeon. Conflict of interest: not reported. Sources of funding: not reported	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation conceal- ment (selection bias)	High risk	C-inadequate

Miedema 2004		
Methods	Single center, three arms RCT; Shouldice vs Lichtenstein vs Mc Vay (not in current analysis). Randomization: generation of sequence by random digit table; allocation list maintained by a person unassociated with the study. Follow up: 7 years. Exclusions after randomizations: not reported. Losses to follow up: 29 Analyses by protocol.	
Participants	Country: USA. Setting: center not specialized in hernia repair. Total enrolled patients: 101(52 Shouldice, 49 Lichtenstein) Mean age: 62 Shouldice, 63 Lichtenstein. Inclusion criteria: primary inguinal hernia. Exclusion criteria: age <18 years, female, use of systemic steroids, incarcerated/ recurrent hernia, collagen/vascular disease, ASA 4 / 5, allergy to acetaminophen or codeine. Demographic and baseline data: comparable for age, prostate abnormalities, smokers, constipation	
Interventions	Shouldice modified (n=41). 4 layers. Polypropylene. Lichtenstein standard (n=39).	
Outcomes	long term recurrence and groin pain	
Notes	Experience surgeon: 1st, 2nd-yr residents, supervision: general surgeon experienced Physical exam at 6-9 years follow up assessed by general surgeon or senior surgical resident in 121 patients (29 lost to follow up). Conflict of interest: not reported. Sources of funding: not reported.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	A-Adequate

Hetzer 1999	
Methods	Two centers, two arms RCT; Shouldice vs. Lichtenstein. Randomization: by day of intervention. Allocation concealment inadequate. Follow up: 3 months. Analyses by protocol. Losses to follow up: none. Jadad quality score: 1.
Participants	Country: Switzerland Setting: 2 centers not specialized in hernia repair. Total enrolled patients: 385 patients; number of hernias: 410 (171 Shouldice vs. 239 Lichtenstein). Mean age: Shouldice 53 (SD 16-77); Mean age:Lichtenstein 58 (17-36) Inclusion criteria: male, age>18, primary elective inguinal hernia Exclusion criteria: incarceration, previous operation, coagulopathy, diabetes, prostate hypertrophy and wish for general anesthesia. Demographic and baseline data: comparable for age, type of hernia
Interventions	Shouldice Standard (n=171). 4 layers, PDS 2/0. Lichtenstein (n=239). Polypropylene mesh. Polypropylene 2/0
Outcomes	OR time, hospital stay, time to return to work , complications, pain, recurrence
Notes	Experience surgeon: > 8o% trainees under supervision of an experienced surgeon Conflict of interest: not reported. Sources of funding: not reported.
Risk of bias	

Bias	Authors' judgement	Support for judgement
Allocation conceal-ment (selection bias)	High risk	C-inadequate

Of the 5 records analyzed, significant differences in CPIP were found in the Miedema study which favored Shouldice (7 %(2/28) vs. 38%(11/29); OR 0.13 95% CI 0,02-0.64, p< 0.05) and the Hetzer study which favored Lichtenstein (12.3% (21/171) vs. 6.3 %(15/239); OR 2.09, 95% CI 1,04-4,19, p< 0.05)[15,16]. A total of 758 patients were included in the Shouldice group and 863 patients in the Lichtenstein group. The pooled data showed an OR of 0.88 (95%CI 0.39 – 1.98, I^2=0.44)) in the random effect meta-analysis. Therefore no difference was seen in CPIP after Shouldice vs. Lichtenstein.

Study	OR
Koniger:	1.25
Nordin:	1.13
Miedema:	0.13
Hetzer:	2.09
McGillicuddy:	0.27
Summary	0.88

0.1   0.5   1.0 1.52.0 3.0
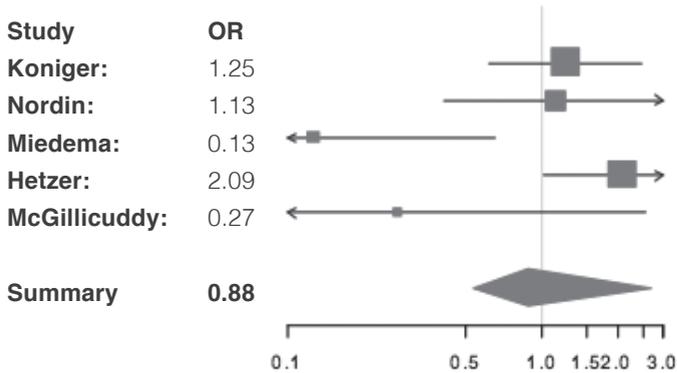
1. Koniger:	OR 1.24	95%CI 0.64-2.43
2. Nordin:	OR 1.13	95%CI 0.42-3.02
3. Miedema:	OR 0.13	95%CI 0.02-0.64
4. Hetzer:	OR 2.09	95%CI 1.04-4.19
5. McGillicuddy:	OR 0.27	95%CI 0.03-2.46
Total:	OR 0.88	95% CI 0.39-1.98

Discussion

There were five randomized controlled trials on Lichtenstein vs. Shouldice with the outcome on CPIP, none on Bassini vs. Lichtenstein on the outcome on CPIP to evaluate the role of the mesh in CPIP. Two out of these five trials had a high risk on selection bias. [14, 16.] The hypothesis that the incidence of CPIP is higher after Lichtenstein versus Shouldice or Bassini repairs, because of the mesh used in Lichtenstein could not be confirmed by our meta-analysis. No difference was seen in CPIP after Shouldice vs. Lichtenstein (OR 0.88, 95% CI 0.39-1.98). A drawback of this review however is the small number of eligible records and the different follow up periods and inconsistency of pain evaluations.

The PubMed database was searched for other records with regard to the Bassini, Shouldice and Lichtenstein techniques with regard to the outcome of CPIP. The search ´Bassini chronic pain´ resulted in 11 records. In three records the rate of CPIP of pooled data of different open approaches was given and it was not possible to distill the rates for Bassini only. Other records were not on inguinal hernia surgery for adults (n=4) or rates of CPIP for the Bassini technique not mentioned (n=3). There was one German retrospective article which showed 3.7% CPIP (29/920) after the Bassini technique.[18]

The search: 'Shouldice chronic pain' resulted in 23 records. Nine records (RCT's, meta-analyses, retrospective studies etc.) recorded on CPIP rates/numbers after the Shouldice technique. In the other records, rates/numbers of CPIP with regard to the Shouldice technique were not mentioned (n=6), one was a duplicate, different indications for surgery (n=3) or other technique/ outcome (n=3)). In the remaining nine records, rates of CPIP varied between 1.4% [19] and 36% [20]. No other records came up with comparable high rates of CPIP. The second highest rate (16.1%, n= not mentioned) was found in a questionnaire.[21] All other rates are in between 1.4%-7.1%. In total there were 336 (5.1%) patients with CPIP in 5140 Shouldice surgeries in the nine articles which recorded rates on CPIP.

For 'Lichtenstein chronic pain' 173 records came up, of which 65 clinical trials and 23 reviews. Ten of these reviews reported on CPIP rates, of which one was a retrospective study. Two were duplicates, records in which CPIP was not mentioned (n=6), other subject (n=3), or recurrent hernias only (n=2). Looking at the reviews and pooled data of meta-analyses only (fixation of the mesh with glue vs sutures, TEP vs. Lichtenstein, heavy vs. lightweight mesh etc.) incidences of CPIP varied from 0% [22] to 23.1%. [23] Pooled results of data of the 10 reviews showed 1104 patients with CPIP in 7647 Lichtenstein procedures (16.4%). Although we realize this is not a not a proper statistical analysis, it does show roughly the incidence of CPIP after Lichtenstein and that this incidence seems to be higher than in Shouldice/ Bassini.

As a consequence looking at the literature, the incidence of CPIP in Lichtenstein is probably higher than in our review, also in contrary to a 2002 Cochrane review on mesh vs. non-mesh suggesting that CPIP was less frequent after mesh repair than after non-mesh repair (01.10, overall Peto OR: 0.68, 95%CI: 0.47 to 0.98).[24] Furthermore, the 'Hernia Trialist Collaboration' stated that "The use of synthetic mesh substantially reduces the risk of hernia recurrence irrespective of placement method and a mesh repair appears to reduce the chance of persisting pain rather than increase it".[25] In both meta–analyses the included trials used different surgical planes for mesh placement and therefore rules out a good comparison regarding CPIP caused by the mesh.

Best quality of life for patients with inguinal hernia should be pursued. The introduction of mesh for inguinal hernia repair showed the advantage of lower recurrence rates. With the current systematic review on Shouldice versus Lichtenstein, the mesh seems not to be a cause of CPIP. However, with the incidence of 16.4% of CPIP after Lichtenstein repair found in the literature, compared to the lower incidence found regarding Shouldice repair (5.1%), further research on the mesh as a cause of CPIP is warranted.

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CHAPTER 9

Prognostic value of age for chronic
postoperative inguinal pain.

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Abstract

Purpose: Chronic postoperative inguinal pain (CPIP) is considered the most common and serious long term problem after inguinal hernia repair. Young age has been described as a risk factor for developing chronic pain after several surgical procedures. Our aim was to assess if age has prognostic value on CPIP.

Methods: The database of a randomized trial: the LEVEL trial, 669 patients, TEP versus Lichtenstein, was used for analysis. Data on incidence and intensity of preoperative pain, postoperative pain and CPIP at 1 year were collected. The association of age with incidence and intensity of pain was assessed with regression analysis. Further, hernia type and surgical technique were studied in combination with age and CPIP as possible risk factors on CPIP over age alone.

Results: Younger patients (18-40 years) presented more often with CPIP than middle-aged patients (40-60 years) and elderly (>60 years): 43% vs. 29% vs. 19%; overall 27%. Younger and middle-aged patients had more frequently preoperative pain: 54% vs. 55% vs. 41% and intensity of pain was higher during the first three post-operative days (VAS on day 1: 5.5 vs. 4.5 vs. 3.9 and on day 3: 3.8 vs. 2.9 vs. 2.6). Indirect type hernias were seen more often in younger patients (77% vs. 51% vs. 48%) and were not related to CPIP nor was surgical technique.

Conclusions: Almost one out of three patients experienced CPIP. The younger the patient, the higher the risk of CPIP. Hernia type and surgical technique did not influence CPIP.

Introduction

Inguinal hernia repair is one of the most common operations in general surgery. Incidence and prevalence are unknown, it is however estimated that worldwide each year over 20 million surgical procedures for inguinal hernias are performed. Operation rates vary between countries and range from 100 to 300 procedures per 100.000 people per year.[1] The lifetime risk of inguinal hernia is approximately 27% for men and 3% for women.[2] Since the introduction of tension free mesh repair with either an open or endoscopic technique, the incidence on recurrence rates decreased from 15-30 % to 1-5%.[3] Therefore focus in research on adult hernias has changed from recurrence to other aspects. 'Chronic postoperative inguinal pain' (CPIP) is now considered the most common and serious long term problem after inguinal hernia repair.[4] This reflects the acceptance of CPIP as an important outcome of inguinal hernia surgery with clinical consequences. In the literature there is still debate on incidence, pathogenesis, treatment as well as the definition on CPIP. CPIP was defined as pain lasting for three months or more by the International Association for the Study of Pain (IASP).[5] Multiple studies report on CPIP with incidences reported up to 37%.[6-9] The high incidence of CPIP leads in 11% to 17% of patients to various types of social disability.[8] In 3 % of patients, pain is severe or very severe and has profound effects on the patients' physical and social activities and limits patients' ability to participate in paid employment.[10] Worldwide that means that every year up to 3.4 million people suffer from social disability caused by CPIP and about 600.000 people cannot participate in a paid employment, thereby large socioeconomic losses being created. Identification of risk factors on the development of CPIP is therefore clinically important. More detailed preoperative information could be provided to the patient regarding his/her surgery for inguinal hernia at the outpatient clinic; therefore patients' expectations of surgical results will be more realistic. In addition, by identifying risk factors and getting more insight on causes of CPIP, we expect that better indications for surgery can be made and surgical techniques to be refined, which might prevents or reduces the prevalence of CPIP and thereby reduces socioeconomic costs. Some research has been done to identify risk factors on the development on CPIP. Age might be a possible risk factor for CPIP as it is suggested in the inguinal hernia literature for open as well as endoscopic techniques. In addition younger age is a risk factor for chronic pain after several other surgical procedures, such as mastectomy, surgery for cutaneous melanoma and thoracotomy.[11-13] Dickinson et al. identified young age as a risk factor in a retrospective study on transabdominal preperitoneal (TAPP) inguinal repair and total extraperitoneal procedure (TEP) in 881 patients.[14] Nienhuys et al. identified young age as a risk factor using data of 334 patients from a randomized trial which compared three open techniques for inguinal hernia repair: Prolene Hernia System, mesh plug repair and the Lichtenstein procedure.[15] Poobalan et al. studied on a cohort of 500 patients, mesh versus non mesh also identified young age as risk factor.[9] Identification of age as a risk factor on CPIP, however, has not been described yet in a setting of patients treated with either TEP

or the Lichtenstein procedure. Furthermore, the systematic calculation of the influence of different characteristics on pain after hernia surgery in different age groups has not been investigated before. Aim of this study was to assess the prognostic value of age on CPIP in a population of patients operated with TEP or Lichtenstein procedure.

Material and Methods

Patients and study design

For current analyses, the database of the LEVEL-trial was used. In this randomized multicenter trial, 669 patients were randomized between the open sutured Lichtenstein technique [16] and the minimally invasive TEP (Trial Registration: clinicaltrials.gov Identifier: NCT00788554.[17, 18] Detailed methodology on this trial has been reported previously.[17] In short: in the original trial adults were included presenting with uni- or bilateral, primary or recurrent inguinal hernias. Both surgical procedures were performed with the use of a polypropylene mesh in six hospitals. Preoperative data (baseline characteristics), perioperative data (hernia type, complications, conversions, etc.) and postoperative data (pain, recurrences, etc.) were reported. Patients were followed up at the outpatient clinic and they kept a diary for Quality of Life: EuroQol.[19] and the SF-36 questionnaire (acute version of SF-36 Health Survey, Medical Outcomes Trust, Boston, MA 02116) and Visual Analogue Scale (VAS) scores for pain.

Pain measurements

Primary endpoint in the trial was postoperative pain. Pain was registered preoperative, the first 3 days postoperative and after 1 and 4 weeks, using the 10 cm VAS scores, ranging from no pain (0) to unbearable pain (10). Further, after 1 and 6 weeks and 1 year the patient was seen at the outpatient clinic where pain, sensibility disorders, recurrences and reoperations were documented. The presence of pain and the localization of pain were reported. Physical examination was performed by a surgical resident or surgeon. The incision site was inspected on sensibility disorders and recurrences. Analysis of incidence of pain was done for the group that completed follow up at 1 year. Patients, who underwent a second operation in the inguinal area for recurrence or other causes before they visited the outpatient clinic for their 1 year follow-up, were left out of the analysis because of possible registration on acute pain instead of CPIP. An exception was made for two patients who were operated on within 24 hours after the initial operation because of a bleeding. For analysis of hernia type, age and pain only patients with a primary unilateral hernia were included.

Statistical Analysis

Continuous outcomes (preoperative VAS scores) were analysed with linear regression analysis; binary outcomes (presence of preoperative pain and pain at 1 year) were analysed with logistic regression analysis. For the estimates of the regression coefficients, 95% confidence intervals were calculated. All regression models were adjusted for hospital. Sixteen missing values for age were imputed once with the aregImpute procedure for R software.[20] All analyses were performed with R statistical software version 2.14.2.

Results

Six hundred forty-six patients were operated. Follow-up at the clinic was completed in 96% (n=620) after 1 week and 76% (n=493) after 1 year. The mean (SD) age of patients at the time of study inclusion was 55 (15.5) years (range: 19-89 years). Most patients were male (n=651: 98%), presenting with a unilateral inguinal hernia (n=600: 90%). Most hernias were indirect type hernias (n=321: 53%), also for the contralateral hernia in case of a bilateral hernia (Table 1) Three hundred twenty eight patients received a TEP and 318 a Lichtenstein procedure.

Table 1. Baseline Characteristics (n=669)

General characteristics		
Age,years[a]		55 (15.5)
	18-40 years	117 (17)
	40-48 years	279 (42)
	>60 years	257 (41)
Gender	Male	651 (98)
	Female	11 (2)
Hernia characteristics		
Hernia	Primary	615 (92)
	Recurrence	48 (7)
	Primary and recurrence	6 (1)
Hernia side(s)	Unilateral	600 (90)
	Bilateral	68 (10)
Hernia Type	Direct	223 (33)
	Indirect	347 (53)
	Both	89 (14)
Pain characteristics		
Preoperative pain	No	238 (51)
	Yes	228 (49)
Preoperative VAS[a]	All pt	0.0 (0.0-2.1)
Preoperative VAS[a]	Pt with pain	2.2 (1.0-4.0)
Surgical characteristics		
Surgical procedure	TEP	328 (51)
	Lichtenstein	318 (49)

All values are given number (%) unless indicated otherwise
[a] Median (IQR)

Pain Incidence

About one in two patients (228 out of 466: 49%) experienced pre-operative pain (Table 1, 2).
Four weeks after surgery this was 30% (141 out of 465) and 27% of all patients (130 out of 489) had CPIP after 1-year follow-up (Table 2).

Age and Incidence

Preoperative pain was experienced in 54% (32 out of 59) of young patients, 55% (117 out of 213) of middle-aged patients and in 41% (79/194) of older patients. Four weeks postoperatively, 36% (21 out of 59) of young patients, 36% (76 out of 212) of middle-aged patients and 23% (44 out of 194) of older patients still had pain. After 1 year 43% (29 out of 67) of the young patients reported CPIP. This was more often reported than for the other age groups (43% vs. 29% (63 out of 216) vs. 19% (38 out of 206), p<0.001, Table 2).

Table 2. Incidence of pain % (N) for the different age group during follow-up

Age group	Preoperative	4 Weeks	6 Weeks	1 Year
18-40	54 (32/59)	36 (21/59)	30 (25/82)	43 (29/67)
40-60	55 (117/213)	36 (76/212)	32 (72/225)	29 (63/216)
>60	41 (79/194)	23 (44/194)	23 (54/238)	19 (38/206)
Total	49 (228/466)	30 (141/465)	32 (151/466)	27 (130/489)
P Value	0.7	0.2	0.06	<0.05

Age and risk of pain

Figure 1 shows the association of age and incidence of pain preoperatively and after 1-year follow-up. Young patients have a higher risk of preoperative pain (p = 0.001) and CPIP (p < 0.001) compared to older patients (Fig.1a, b).

Figure 1a. Risk of preoperative pain by age for the whole population (n=466)
Figure 1b. Risk of pain at 1 year for tje whole population (n=489)
Confidence bands are 95% confidence limits.
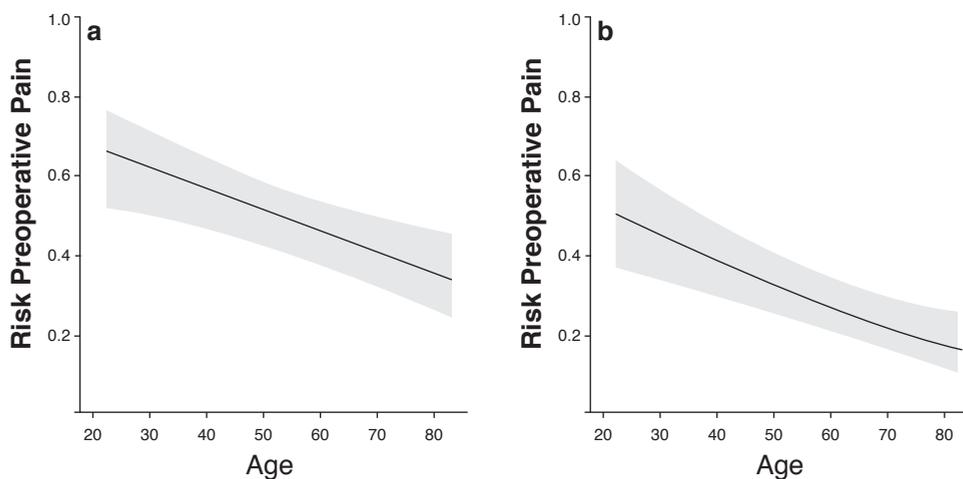
Pain Intensity

The median preoperative VAS score for the whole study group was 0.0. The preoperative VAS score is given in Table 1 as a median because 51% of the study group did not have any preoperative pain and therefore the distribution was not normal. The distribution of the group patients with preoperative pain (49%) was skewed to the right (median (IQR) = 2.2 (1.0–4.0)). Two hundred and three values were missing for preoperative VAS.

Age and intensity

It is more clinically relevant to assess intensity of pain in the group of patients that experienced pain, instead of the whole group. Therefore analysis exclusively for patients who reported pain is shown in Table 3. The observed median intensity of preoperative pain was comparable for the different age groups (overall=2.2; n=438). Postoperatively younger patients experienced more intensive pain than older patients, VAS: 5.4 vs. 4.3 vs. 3.4 (middle vs. young P=0.009, old vs. young p<0.001) on the first postoperative day (n=466). This difference in intensity remained during the first 3 postoperative days. After that, VAS scores decreased and were similar for the different age groups 4 weeks post-surgery (2.1 vs. 1.5 vs. 1.7) after 1 week (middle vs. young P=0.29, old vs. young P= 0.48) and 1.3 vs. 0.9 vs. 1.0 after 4 weeks (middle vs. young P=0.58, old vs. young P=0.48, Table 3).

Table 3. Median VAS scores for age groups *with pain* during follow up

	VAS-preop	VAS-d1	VAS-d2	VAS-d3	VAS-w1	VAS-w4
18-40 years (n=57)	1,8	5,4	4,6	3,6	2,1	1,3
40-60 years (n=207)	2,3	4,3	3,2	2,5	1,5	0,9
>60 years (n=174)	2,1	3,4	2,9	2,1	1,7	1,0
Overall (n=438)	2,2	4,1	3,2	2,4	1,7	0,9

Pain Localization

CPIP (n=130) was mostly localized in the groin (77%: n=100). Pain localized in the scrotum and at the scar was reported in 20 (15%) and 21 (16%) cases. Pain localized at the upper leg or other areas was reported in 16 (12%) and 14 (11%) cases.

Age and Localization

All age groups mainly suffered from groin pain (86% vs. 76% vs. 71%, middle vs. young P=0.007, old vs. young p<0.001). We found that younger patients had pain localized at the scrotum more often than the other age groups (24% vs. 13% vs. 13%, middle vs. young P=0.04, old vs. young P=0.01), although numbers were small. Older patients might experience less pain in the upper leg: 5% versus 14% versus 16%, middle vs. young P=0.30, old vs. young P=0.01) numbers being again small.

Hernia type

The indirect type hernia has a congenital etiology and therefore afflicts mainly young patients compared with the acquired direct hernia, which is seen more often in elderly patients.[21] We therefore studied whether hernia type had additional prognostic information on CPIP over age alone. In our trial patients of all three age groups had more indirect than direct hernias; however indirect hernias were mostly seen in young patients (77% vs. 51% vs. 48%, middle vs. young p<0.001, old vs. young *P*=0.002). As a result, direct hernias were less observed in young patients and more often in middle aged and elderly patients (18% vs. 36% vs. 36%, middle vs. young *P*=0.002 old vs. young *P*= 0.002, Table 4).

Table 4. Hernia type by age group, N (%)

Age group	Direct	Indirect	Both
18-40 years	18 (18%)	76 (77%)	5 (5%)
40-60 years	84 (36%)	120 (51%)	32 (14%)
>60 years	75 (36%)	101 (48%)	34 (16%)
Total	117 (33%)	297 (55%)	71 (13%)

Age and hernia type

We compared direct and indirect hernias in terms of preoperative VAS score, risk of preoperative pain and risk of pain after 1 year. When a difference was found between the two types of hernias, we studied whether it could be explained by differences in age. The preoperative VAS score for all patients with indirect hernias (1.3) was similar to the score for patients with direct hernias (1.0) (95% CI, 0 to 0.8, p = 0.14). When we considered only patients with pain, the difference in VAS scores was 0.1 (3.5 vs. 3.4, 95% CI, 0 to 0.9, p = 0.70). After controlling for age, these numbers did not change. Consequently, preoperative VAS scores for direct and indirect hernias were not influenced by differences in age. The risk of preoperative pain for direct and indirect hernias showed the same pattern and was not influenced by age. No difference in CPIP was found between direct and indirect hernias after 1-year follow-up.

Surgical technique

The surgical techniques were equally allocated for the three age groups. Fifty two percent (61/117) of patients in the young group received surgery using TEP versus 52% (141/273) and 49% (123/251) in the middle aged and older patients.

Surgical technique and age

The age groups within the two different surgical techniques were compared in terms of preoperative VAS score and risk of pain after 1-year follow-up. Median preoperative VAS scores for patients with pain were similar for both techniques (2.0 for TEP vs. 2.4 for Lichtenstein). Forty-four percent (17/39) of patients in the group with young patients who underwent TEP developed CPIP versus 40% (10/25) after Lichtenstein (P=0.87). For the middle aged group this was 26% (29/110) after TEP and 34% (32/94) after Lichtenstein (P=0.39). In the group patients >60 years, this was 16% (17/108) and 22% (23/106, P=0.24). Therefore surgical technique in regard to the different age groups was not related to CPIP.

Discussion

We found CPIP to be a common complication with almost 30% of patients who were randomized for TEP or Lichtenstein in the original study, still having pain one year after surgical correction. The risk for CPIP was higher in younger patients. The prevalence of chronic pain in general is known to increase with advancing age. It is estimated that over 50% of older adults suffer from some sort of persistent pain[22] It is therefore remarkable that after several surgical procedures, young people have a higher risk of chronic pain.

'Chronic postoperative inguinal pain' (CPIP) has a variety of interpretations in the literature. The International Association for the Study of Pain uses the definition: 'pain persisting for more than three months'.[5] This definition is disputable because it regards non-surgical chronic pain. The use of synthetic mesh in hernia repair causes an inflammatory response as a result of a foreign body reaction, which may last a couple of months. In this manuscript data were analyzed of patients seen at the outpatient clinic after 1 year. With the former theory on the inflammatory response, we do not consider this a problem.

CPIP has been described in other studies, however pain was not the primary outcome parameter in most studies and pain intensity was not always assessed.[8-10] The randomized trial of this study did have pain as primary outcome, intensity was assessed and in addition patients were randomized between TEP and Lichtenstein procedures which have not been used for analysis of risk factors on CPIP in previous publications. For analysis of pain intensity, we used VAS scores. These individual 0–10 pain intensity ratings have sufficient psychometric strength to be used in chronic pain research, especially research that involves group comparison designs with relatively large sample sizes.[2] VAS scores were taken preoperatively and during the early postoperative period. The patient filled in their VAS scores in a diary. Not all patients however received this diary and not all diaries were handed in after six weeks, hence data is missing. Because we assume this happened random, we do not consider this a problem. After one year patients were seen at the outpatient clinic. They were asked whether they had pain: 'yes' or 'no' and where the pain was localized; VAS scores were not taken. The course of intensity of pain in time can therefore not be measured accurately in our study for the long term. In addition it is important to give the right interpretation of VAS scores. VAS ratings of 0 to 4 mm can be considered no pain, 5 to 44 mm mild pain, 45 to 74 mm moderate pain and 75 to 100 mm severe pain.[2] Moderate pain was found in our trial during the first and second postoperative day in young and middle aged patients. Severe pain was not found. One year postoperatively, almost a third of patients (27%) still experienced pain (Table 2). Although we did not measure VAS scores after one year, we expect them to be lower than the preoperative VAS scores (mean VAS 2.7) since pain was mild four weeks postoperatively (mean VAS score 1.6) (see Table 3, Figure 2). We found an increase in risk of CPIP in younger patients in our report. Interpretation of these results is hindered by lack of data on patients' physical activities. Final data on QOL was collected only four weeks after surgery. It is however, important to know how pain

influences patient's daily activities and QOL. It might be different between the age groups and consequently with regard to their complaints.[24] Five years after surgery patients were asked how satisfied they were with their surgery, which might reflect on QOL. On a scale of 0 to 10 patient satisfaction (n=307) with the surgical procedure was 8.5 (SD 1.34). Younger patients were equally satisfied with their surgery compared to the middle-aged and elderly patients (*P*=0.94).

In this manuscript, no separate analysis on gender and age in regard to CPIP was performed. Because of the low number of females this would be statistically incorrect. The risk of pain for women does not influence the effect of age on pain. The latter was the objective of this study. We could have chosen to leave the female patients totally out of the analysis. Exclusion of female patients would not have made a statistical difference however, because female patients showed similar results regarding pain compared to male patients in our study.

Age was identified as a risk factor of CPIP in our trial, however other risk factors related to development and intensity of CPIP have been suggested in the literature: psychological status, preoperative and acute postoperative pain, intraoperative nerve handling, surgical technique (open vs. laparoscopic), surgery for recurrences and nerve injury.[3-7] In order to give 'custom made' information on the outcome of surgery to inguinal hernia patients, all risk factors should be taken into account. More research needs to be done for identification of other risk factors and to assess the relative importance or impact of each risk factor in a group as compared to the other items in the group.

The lower risk of preoperative pain, less intense acute postoperative pain and less risk of CPIP in older patients might be explained by the fact that aging affects functional and electrophysiological properties of the peripheral nerve system. There is a decline in nerve conduction velocity, muscle strength, sensory discrimination, autonomic responses and endoneural blood flow. In addition, after injury there is also a decline in nerve regeneration and the density of the regenerating axons decreases in aged animals. Further a reduction in terminal and collateral sprouting of regenerated fibers is seen with ageing, which further limits the capabilities for target re-innervation and functional restitution.[25] Currently, inguinal hernias in older patients are operated less often because often a wait-and-see policy is used. As we observed in our trial, 41% of patients over 60 years had preoperative pain related to their inguinal hernia. After surgery this percentage decreased to 19%. This is a larger decrease than for the other age groups. Inguinal pain in combination with an inguinal hernia in older patients therefore seems a good indication to perform surgery. This suggests a wait-and-see policy should be used for symptomless patients only.

Severe preoperative and immediate postoperative pain is considered a strong predictor of the development of chronic pain following a variety of surgical procedures.[26-29] The reason for this association remains unclear. Nowadays it is one of the motives for the use of perioperative regional anesthesia: to block nociception and subsequent sensitization.[30] Patients in our trial had mild preoperative pain (mean VAS 2.7). The risk of preoperative

pain was higher in young patients and also immediate postoperative pain was more intense in the young and middle aged patients (mean VAS 5.5 vs. 4.9 vs. 3.9 on day 1 postoperatively). CPIP was experienced also more often in young patients (43% vs. 29% vs. 19%), therefore we think perioperative anesthesia might benefit young people most on their outcome on CPIP. Young patients in our trial mainly had indirect inguinal hernias, conform the literature. The possibility that not age was the actual risk factor of CPIP, but rather the indirect hernia, was also investigated. Equal incidences of CPIP were reported among patients with direct and indirect hernias therefore CPIP seems not to be related to surgery for indirect hernias. A correlation with surgical technique could also not be demonstrated; therefore age is concluded to be associated with CPIP and can be used as prognostic factor.

In order to decrease the number of patients with CPIP and thereby the large socioeconomic losses created by CPIP, it is necessary to understand causes and risk factors of CPIP. Awareness by health professionals of the association between young age and CPIP will contribute to more accurate preoperative information to patients with inguinal hernias about the outcomes of their surgery. In addition, in order to reduce or try to prevent CPIP, we think there is an indication for perioperative regional anesthesia as standard care for young patients with inguinal hernias. The identification of age as a risk factor could also give direction in future research on the pathogenic mechanisms of CPIP.

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CHAPTER 10

A risk prediction model for chronic postoperative inguinal pain.

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Abstract

Aim: Chronic Postoperative Inguinal Pain (CPIP) is the most common complication of inguinal hernia surgery. Our aim was to identify risk factors of CPIP and to develop a risk model to predict patient's individual risk on CPIP.

Methods*: Data was analysed of 489 patients from a randomised controlled trial in which the endoscopic Total Extraperitoneal Procedure' (TEP) was compared with open Lichtenstein surgical correction for inguinal hernia repair. Predictors for CPIP were combined with multivariable logistic regression analysis. The risk prediction model was internally validated with a bootstrapping procedure.

Results: One year after surgical correction, 27% of patients experienced CPIP. The strongest preoperative predictors of CPIP were: young age, preoperative pain, bilateral hernia and higher 'American Society of Anesthesiologists' (ASA) score. The combination of these four was used to create a predictive model for CPIP. The area under the receiver operating characteristic curve was 0.65 after correction for optimism. Peri- and postoperative risk factors on CPIP were: low level of experience of the surgeon, conversion and postoperative pain after 1 and 3 days and 1 and 4 weeks sensibility disorders in the groin six weeks postoperative.

Conclusion: Seven predictors of CPIP were found: age, preoperative pain, bilateral hernia, ASA-classification, low level of surgical experience, postoperative pain and postoperative groin sensibility disorders. A prognostic model that included the four preoperative risk-factors (age, pain, bilateral hernia and ASA-classification) provides a more individualised risk of CPIP. The model's predictions may preoperatively inform patients and physicians on the risk of CPIP.

Introduction

Chronic Postoperative Inguinal pain 'CPIP' or inguinodynia is the most common complication of inguinal hernia surgery, with incidences reported up to 37% [1-9]; leading in 11-17% of patients to various types of social disability.[7] In about 3-10% of patients, pain is severe or very severe which has profound effects on patient's physical and social activities and can even limit patient's ability to participate in paid employment.[10-12] It is estimated that worldwide each year over 20 million surgical procedures for inguinal hernia are performed; therefore CPIP has large socio-economic consequences.[13] Although inguinal hernia repair is one of the most frequently performed surgical operations, elective surgery is no longer recommended in minimally symptomatic cases, due to the low risk of incarceration (<0.2% per year) and the significant risk (10–12%) of post herniorraphy pain syndrome.[14]

Several factors have been addressed to be related to the development of CPIP: young age, cognitive factors, preoperative pain, depression, intraoperative nerve handling and nerve injury, surgical technique (open vs. laparoscopic), surgery for recurrences, acute postoperative pain and intensity of postoperative pain.[11,15-19] Little is known on patients' individual risk on CPIP. Our goal is to identify risk-factors on CPIP in the preoperative, perioperative and postoperative phase and to combine the preoperative variables in a risk prediction model for use at the outpatient clinic to assess patient's individual risk on CPIP.

Methods

Patients and study design

The database of the 'LEVEL-trial' was analyzed for identification of risk factors and the strongest factors were combined in a prediction model. This randomized multicenter trial, was originally designed to compare the (open) tension-free 'Lichtenstein-procedure'[20] with a minimally invasive (endoscopic) tension-free procedure; the Total Extraperitoneal Procedure (TEP) (Trial Registration: clinicaltrials.gov Identifier: NCT00788554)[21] In short; pain was studied in 669 adults with primary or recurrent inguinal hernias in 6 hospitals. Polypropylene mesh was used for repair of the defect in both procedures. Preoperatively patient and hernia characteristics, history and physical examination were recorded. Perio-peratively, surgeons experience, nerve management, complications and conversions were recorded. Patients were followed-up at the outpatient clinic, after 1 week, 6 weeks, 1 year and 5 years for an interview and physical examination. Patients filled out Visual Analogue Scale (VAS)-scores and questionnaires on 'Quality of Life' (QoL), preoperatively and the first 3 days postoperatively and 1 and 4 weeks after surgical correction. Preoperative mood was recorded in SF-36 (acute version of SF-36 Health Survey, Medical Outcomes Trust, Boston, MA 02116) and Euroqol questionnaires.[22] Detailed methodology and results of this trial have been reported previously.[21,23]

In order to assess risk-factors on CPIP we studied data of patients who completed their

1 year follow-up. Patients, who underwent a second operation in the inguinal area for recurrence or other causes within the 1 year follow-up, were left out of the analysis, because they might experience 'normal' postoperative pain and not CPIP. An exception was made for two patients who were operated on within 24 hours after the initial operation because of bleeding.

The following potential preoperative risk factors were assessed: age, gender, 'Body Mass Index' (BMI), diabetes, ASA score, hernia type (primary or recurrent, direct or indirect, uni- or bilateral), mood (depressed, nervous, worried), inguinal pain and sensibility disorders in the inguinal area. For analysis of preoperative depression with SF-36, patients were categorized in two groups: 'always; most of the time; or often' depressed vs. 'sometimes; rarely; or never' depressed. Nervousness was categorized in ´a bit; or very worried; sad or unhappy' versus ´not worried, sad or unhappy. The following potential perioperative risk factors were analyzed: technique, nerve handling, surgeon's level of experience, bleeding and conversion. Potential postoperative risk-factors analyzed were: direct postoperative pain, pain after 3 days, pain after 1 and 4 weeks, wound infection and postoperative sensibility disorders.

Statistical analysis

Missing values were imputed with multiple imputations.[24] Logistic regression analysis was used to estimate univariable and multivariable regression coefficients and odds ratios with 95% confidence intervals. The nature of the association between continuous predictors and risk of CPIP was studied with restricted cubic splines with three knots (two df). The restricted cubic splines were plotted and approximated with simple transformations. The simplest transformation is a linear term. Other possible transformations included the natural logarithm, square and square root. A full multivariable model was fitted that included all candidate predictors with chosen transformations. The strongest predictors were selected with backward stepwise selection. We used a p value of 0.20 for predictor selection. Further, the backward selection procedure starts with a limited number of candidate predictors with continuous variables studied in their original form (i.e. continuously). Dichotomising or categorizing continuous variables may be seen as introducing an extreme form of rounding, with an inevitable loss of information. The regression coefficients in the final model were multiplied with a shrinkage factor, which was estimated with bootstrapping. [25] Shrinkage is applied to obtain accurate predictions for new patients; without shrinkage, predictions can be too extreme, resulting in low predictions being too low and high predictions too high. The final model with the shrunken regression coefficients was presented as a score chart to facilitate clinical application. Discrimination was used as a measure for model performance. The area under the ROC curve was corrected for optimism with the use of a bootstrap procedure. All analyses were performed with R statistical software version 2.14.2. The described analytical strategy to develop the prediction rule is in accordance with the

current state of the art.[25,26] The strategy aims to develop a prediction rule that can provide accurate predictions for future patients rather than predictions that are correct for patients of the development dataset.

Results

Baseline characteristics

We analyzed 489, mainly male patients (99%), with a median age of 58 years and a median BMI of 25kg/m², with primary (91%), unilateral (88%) hernias (Table 1). Almost half of the patients had preoperative pain, with a median VAS score of 2. Identification of both the ilioinguinal and iliohypogastric nerves during the Lichtenstein procedure (N=225) was performed in 63%, the nerves being preserved in 59% of cases. Surgeon's level of experience was > 25 procedures in 88% of cases. Almost all patients had direct postoperative pain (89%). Incidence of pain decreased to 29% after 4 weeks and 27% after 1 year.

Table 1. Characteristics of patients treated with TEP or Lichtenstein for inguinal hernia repair, N=489.

CHARACTERISTICS	N	MEASURE OR CATEGORY	
Age, years	485	Median (25 and 75 percentile)	58 (47–68)
Gender	488	Male	483 (99%)
BMI, kg/m2	406	Median (25 and 75 percentile)	25 (23-26)
Diabetes	477	Yes	11(2%)
ASA	471	ASA 1	337(72%)
		ASA 2	126(27%)
		ASA 3	8(2%)
Number of hernia	489	Prima ry	446(91%)
		Recurrence	43(9%)
Location of hernia	489	Unilateral	430(88%)
		Bilateral	59(12%)
Type of hernia	457	Indirect first site	153(33%)
		Direct first site	237(52%)
		Both first site	67(15%)
	44	Indirect contralateral site	19 (43%)
		Direct contralateral site	22 (50%)
		Both contralateral site	3 (7%)
Mood	392	Depressed (SF-36)	17 (4%)
	392	Nervous (SF-36)	33 (5%)
	393	Worried/sad/unhappy (Euroqol)	56 (14%)
Preoperative pain, VAS	385	Inguinal pain (VAS>0)	182(47%)
		Median (25 and 75 percentile)*	2.0(1.0-2.5)
Sensibility	462	Inguinal sensibility disorders	4(1%)
Technique	482	TEP	257(53%)
		Lichtenstein	225(47%)
Nerve identification	224	None	56(25%)
		Ilioinguinal	24 (11%)
		Iliohypogastric	3(1%)
		Both	141(63%)
Nerve sparing	195	None	59(30%)
		Ilioinguinal	16 (8%)
		Iliohypogastric	5 (3%)
		Both	115 (59%)
Level of experience	336	1 (<10 procedures)	19 (6%)
		2 (10-25 procedures)	20 (6%)
		3 (>25 procedures)	297 (88%)
Intraoperative complications	486	None	427(88%)
		Bleeding	15 (3%)
		Conversion	18(4%)
Postoperative		Wound infection	1(2%)
complications	444	Inguinal sensibility disorders at 6wks	87(20%)
Pain 1 day post-surgery	385	Yes (Vas > 0)	385(89%)
		Median (25 and 75 percentile)*	4.0 (2.4-6.2)
Pain 3 days post-surgery	387	Yes (Vas > 0)	307(79%)
		Median (25 and 75 percentile)*	2.4 (1.1-4.0))
Pain 4 weeks post-surgery	383	Yes (Vas > 0)	111(29%)
Persistent pain 1 year post-surgery	489	Yes	130(27%)

* If VAS >0

Preoperative risk factors

Age showed an association with CPIP, see Figure 1. The younger the patient was at time of surgery, the greater the risk of CPIP (47 year vs. 68 years, OR 2.0(1.5-2.9)). Male gender tended to be associated: OR 1.9 (0.3-11.5, 95% CI), although the number of female patients was too low (n=5) to assess statistically significant results (Table2). Patients with normal BMI had the lowest risk of CPIP (Figure 1). This difference was not significant with multivariate analysis. Other positive associations for CPIP were found for ASA 1 compared to ASA 3 (OR 1.7 (0.7-10.5, 95% CI) and bilateral hernia compared to unilateral hernia (OR 1.7 (1.0-3.2, 95% CI) (Table 2). No association could be demonstrated between CPIP and surgery for recurrence or type of hernia (Table 2). Patients with depressed feelings preoperatively were at higher risk for CPIP, although numbers were low (SF36: 53% (9 out of 17) vs. 24% (90 out of 375), OR 2.2 (0.95-5.11). Nervousness was not of influence on CPIP (SF36: 30% (10 out of 33) vs. 25% (89 out of 359), OR 1.22 (0.58-2.57). Table 1,2. Analysis of Euroqol showed that patients who preoperatively were worried, sad or unhappy were more at risk for CPIP (Euroqol: 39% (22 out of 56) vs. 23% (78 out of 337), OR 1.81 (1.022 3.230)). In the multivariable analysis however, this difference was not significant. Preoperative pain was also associated with CPIP; patients with preoperative VAS-scores > 3 were more at risk for CPIP, see Figure1. Preoperative sensibility disorders in the groin: OR 1.9 (0.4-8.1, 95% CI, n=4) were not associated with CPIP.

Table 2. Associations between predictors and CPIP at 1 year, n = 489

Characteristics	Coding	Odds ratios (95% CI)	
		Univariable	**Multivariable**
Preoperative			
Age	47* versus 68 years (Interquartile range)	1.8 (1.3-2.4)	2.0(1.5-2.9)
Gender	Male* vs. female	1.9 (0.3-11.5)	
BMI	26* vs. 23 kg/m2	1.6 (1.0-2.6)	
Diabetes	Yes vs. no*	0.4 (0.1-1.5)	
ASA classification	ASA 1* vs. ASA 2	1.2 (0.7-1.9)	1.7(1.0-2.9)
	ASA 1* vs. ASA 3	2.8 (0.7-10.5)	
Hernia type	Primary* vs. recurrence	0.7 (0.3-1.5)	
	Unilateral vs. bilateral*	1.7 (1.0-3.2)	1.7(0.9-3.2)
	Indirect* vs. direct	0.9 (0.6-1.5)	
Mood	Nervous* vs. not (SF-36)	1.2 (0.58-2.57)	
	Depressed * vs. not (SF-36)	2.2(0.95-5.11)	
	Anxious/depressed* vs. not (Euroqol)	1.8 (1.0-3.2)	
Preoperative Pain	Yes* vs. no	1.8 (1.2-2.8)	
	VAS 2.5 vs. 1.0 (Interquartile range)	1.4 (1.2-1.7)	1.4(1.2-1.7)
Inguinal sensibility disorders	Yes* vs. no	1.9 (0.4-8.1)	
Perioperative			
Technique	TEP vs. Lichtenstein*	1.3 (0.8-1.9)	
Nerve identification	None* vs. ilioinguinal	1.7 (0.7-4.2)	
	None * vs. iliohypogastric	0.9 (0.2-3.7)	
	None* vs. both	1.6 (0.7-3.4)	
Nerve sparing	None* vs. ilioinguinal	1.8(0.8-3.9)	
	none* vs. iliohypogastric	0.2 (0.0-1.9)	
	none* vs. both	1.0 (0.5-1.8)	
Level of experience surgeon**	1* vs. 2	1.3 (0.4-4.5)	x
	1* vs. 3	1.7 (0.7-4.3)	
Bleeding	Yes* vs. no	0.5 (0.1-1.9)	x
Conversion	Yes* vs. no	3.0 (1.1-7.9)	x
Postoperative			
Pain; day 1	Yes* vs. no	2.0 (0.9-4.2)	
	VAS 6.2 vs. 2.4 (Interquartile range)	1.6 (1.2-2.1)	
Pain; day 3	Yes* vs. no	2.1 (1.2-3.7)	
	VAS 4.0 vs. 1.1 (Interquartile range)	1.8 (1.3-2.5)	
Pain; 4 weeks	Yes* vs. no	3.2 (1.9-5.3)	x
	VAS 1.8 vs. 0.4 (Interquartile range)	Not relevant	
Wound infection	Yes* vs. no	0.9 (0.3-3.0)	x
Sensibility disorders at 6 wks	Yes* vs. no	1.8 (1.1-2.8)	

* = reference category
**Level of experience surgeon: 1= < 10, 2=10-25, 3 = > 25 procedures

Figure 1. Form of association of the continuous predictors (age, BMI, preoperative pain and pain after 7 days) with persistent pain at 1 year.
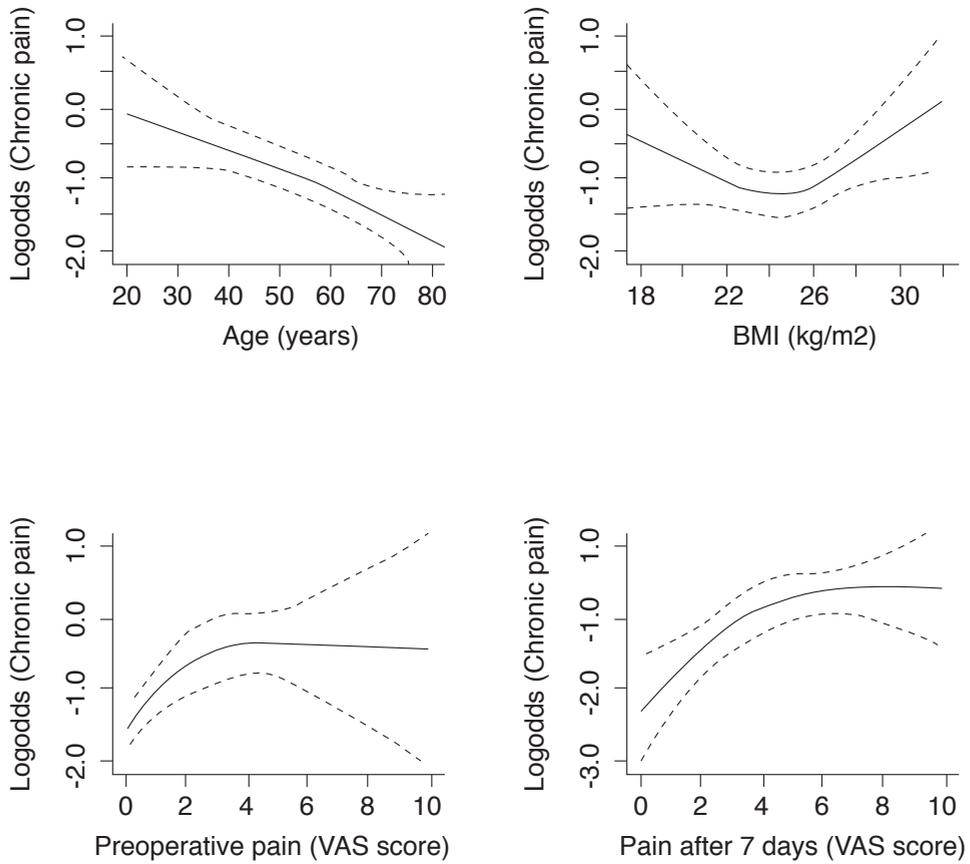
Discrimination AUC = 0.70, after correction for optimism: 0.65

Perioperative risk factors

An increased risk of CPIP was seen, for patients operated by inexperienced surgeons (< 10 procedures) versus surgeons with experience over 25 procedures: OR 1.7 (0.7-4.3, 95% CI). Another positive association was found for conversion (OR 3.0 (1.1-7.9, 95% CI) although numbers were low (n=18).The technique of hernia repair used (i.e. TEP or Lichtenstein) was not associated with CPIP. Further neither nerve identification nor nerve preservation in the Lichtenstein technique showed an association with CPIP (Table 2).

Postoperative risk factors

Direct postoperative pain was associated with increased risk on CPIP for higher VAS scores (VAS 6.2 vs. 2.4, OR 1.6 (1.2-2.1 95%CI). The risk on CPIP increased if this postoperative pain was still present 4 weeks after surgical repair (OR 3.2, 1.9-5.3, 95% CI) (Table 2). Figure 1 shows a positive association for pain 7 days after surgery and CPIP and in addition it shows that this risk increases with higher VAS scores. Patients, who had inguinal sensibility disorders six weeks after surgery, also had an increased risk on CPIP (OR 1.8 (1.1-2.8, 95% CI)).

Risk prediction model

Based on multivariable modelling, the strongest predictors on CPIP found, were the four preoperative risk factors: young age, preoperative pain, bilateral hernia and ASA classification. A score chart for prediction of CPIP was created with these four preoperative risk factors for CPIP (Figure 2). Other risk factors did not add value to the chart if included. Furthermore, the score chart is meant for use at the outpatient clinic in the preoperative phase for the physician and the patient to be informed on the patient's preoperative risk on CPIP. Therefore perioperative and postoperative risk factors are not included. As shown, the predicted risk on CPIP 1 year after surgery varies between 16% and 52% depending on the four preoperative risk factors. (Figure 2)

Figure 2. Score chart for persistent pain at 1 year after inguinal hernia repair.

Characteristic	Value	Score				
Age	58 or younger	1				
Preoperative pain*	Yes	1				
Hernia	Bilateral	1				
ASA classification	2 or 3	1				
Total score		**0**	**1**	**2**	**3**	**4**
Risk of persistent pain at 1 year		16%	23%	31%	41%	52%
* VAS>3						

Discussion

We identified eight risk factors on CPIP in our analysis. The four strongest preoperative risk factors: young age, bilateral hernia, ASA classification and preoperative pain, were combined to create a risk prediction model for use at the outpatient clinic. One perioperative risk factor was identified: little surgical experience and two postoperative risk factors: pain after surgery (one and 3 days), with increasing risk on CPIP when pain persists at 1 and 4 weeks and sensibility disorders at 6 weeks. Young age and preoperative pain both have been described as risk factor on CPIP before.[9, 17, 19] Although it seems plausible that surgery for bilateral hernia has a higher risk on CPIP than for unilateral hernia, it has not been reported before. High ASA classification has also not been reported as a risk factor however most studies have not addressed this item. What is new in this manuscript is that we combined the identified pre-operative risk factors in a model for counselling patients on outcome of their individual inguinal hernia surgery in terms of CPIP. The model created is simple to use and gives good insight in patient's individual preoperative risk on CPIP. Other predictive factors found in our study were: the level of experience of the surgeon and acute postoperative pain and pain after 3 days and 4 weeks. These predictive factors were not included in the score chart because they are not of use for preoperative counselling at the surgical outpatient clinic. They are however important outcomes.

Surgeon's inexperience, in our opinion, is an unacceptable cause of CPIP. The difficulty is however, that all surgical procedures have learning curves. There is an inter-variability of learning curves between surgeons because of different backgrounds and skills and in addition different outcomes have different learning curves; the point where the surgeon reaches an acceptable recurrence rate differs for example from the point where OR-time reaches a steady state. It is therefore hardly impossible to identify a specific number of procedures at where a surgeon in general has 'gone through' the learning curve. The learning curve for TEP in literature is long and varies between 20-250 procedures, however different outcomes were addressed.[31-34] In our case of CPIP, the risk of CPIP was higher before 10 procedures and therefore it should be recommended that at least the first 10 procedures should only be performed on patients with proctors, but rather on virtual reality trainers and anatomical phantoms.

The other postoperative predictors on CPIP found in our study: acute postoperative pain, pain after 3 days and 4 weeks are also important general risk factors on CPIP. Anaesthetists could consider additional forms of pain management or prolonged pain management for patients preoperatively counselled as high risk patients on CPIP. For example an additional inguinal nerve block, local anaesthesia, prolonged oral pain medication etc. Noteworthy is that in our study the chosen surgical approach was not associated with CPIP. This result is confirmed by the meta analysis by Koning et al (2013) who saw no significant effect of

TEP compared with Lichtenstein on the number of patients with CPIP in a random-effects model (RR 0.80; 95% confidence interval (CI) 0.61 to 1.04; p=0.09)[31] With a longer follow-up however, these results might change. In the long term follow-up study of the LEVEL-RCT it was shown that after five years, incidence on pain was lower after TEP: 15% versus Lichtenstein: 28% (*P*=0.004) with lower VAS scores (0,9 vs. 1,5, *P*=.03).[23] Whether these low VAS-scores have any clinical relevance is questionable. Other studies showed a decrease in incidence of CPIP after TEP and Lichtenstein after long term follow-up as well.[32-35] So, there is a possibility that with time to a large extent, CPIP will fade out while the rate of dysesthesia will probably remain constant.[34] The most common explanation is that with the Lichtenstein-procedure the inguinal nerves can be damaged because the mesh is placed in the same anatomical plane as the inguinal nerves in contrast to the endoscopic TEP were the mesh is placed in the preperitoneal plane. In our analysis neither nerve identification nor was nerve sparing surgery (in case of Lichtenstein) however a predictor of CPIP. A drawback of the study is that the identification of the genitofemoral nerve was not included in the study. In general, it is recommended by the 'International guidelines for prevention and management of post-operative chronic pain following inguinal hernia surgery (2011)' to identify and preserve all three inguinal nerves (ilioinguinal, iliohypogastric and genitofemoral nerves) to reduce the risk of CPIP.[36]

In conclusion, more focus on the avoidance of CPIP after inguinal hernia surgery is urgently needed as it is the most significant complication nowadays. In this respect a risk prediction model as defined from the data of a large RCT on inguinal hernia surgery seems relevant.

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PART 4

SUMMARY
FUTURE PERSPECTIVES

CHAPTER 11

Summary

Summary

PART I   INTRODUCTION

Part 1 of this thesis presents a historical review on inguinal hernia surgery. This is presented together with the aims and outline of this thesis.

PART 2   INGUINAL HERNIA REPAIR: SURGICAL APPROACH

Chapter 2 presents a review based on 18 papers on costs- effectiveness, time to return to work, quality of life and pain associated with endoscopic Totally Extra Peritoneal (TEP) repair and Trans Abdominal Preperitoneal Procedure (TAPP) versus open hernia repair (mesh and plug). It was shown that the endoscopic approach clearly benefits Quality of Life (QoL), with less postoperative pain and earlier return to work. Patient-centered outcomes favored endoscopic over open hernia repair at the expense of hospital budgets, although the overall costs to society for endoscopic repair do not need to be higher and in fact may be even lower due to lower indirect costs.

Because many surgeons adopted the endoscopic TEP approach, this technique was compared with open mesh or sutured repair in a qualitative analysis of 23 randomized trials in **Chapter 3**. The TEP repair required significantly more operative time than the open methods and the procedure involved greater expenses for hospitals, but appeared to be cost effective from a society's perspective. Hospital stay was shorter and significantly fewer workdays were lost after TEP with no differences in recurrence rate, therefore making TEP favorable over open repair in a patient's perspective.

The randomized controlled trial (RCT) 'LEVEL-trial' was designed to compare the most common endoscopic with the most common open mesh hernia repair: TEP vs. Lichtenstein with the hypothesis that TEP will decrease postoperative pain. In this multicenter RCT, presented in **Chapter 4**, 660 patients were randomized to TEP and Lichtenstein repair. Patients operated with TEP had more adverse events during surgery, but less postoperative pain. Length of hospital stay was similar although patients recovered faster to daily activities after TEP and returned to work quicker. Quality of life measured with EuroQol at 4 weeks was similar for both interventions. At 1 year, comparable incidences of chronic postoperative inguinal pain (CPIP) (25 vs. 29%) and recurrence (3.8% vs. 3.0%) respectively for TEP and Lichtenstein were seen with less impairment of sensibility in the groin area after TEP. Recurrence rates for TEP were higher if operated by an inexperienced surgeon. For Lichtenstein these differences were not found. Direct (hospital-) costs were higher for TEP, although total societal costs at 1 year were comparable. Therefore from a patient perspective, TEP is recommended if performed by an experienced surgeon.

In **Chapter 5** a letter in reaction to the published randomized controlled LEVEL-trial is presented on what endoscopic repair should be preferred: TEP or TAPP. Only length of stay was shorter for TEP presented in a single RCT. No differences between TAPP and TEP were seen in terms of length of operation, hematomas, time to return to usual activities and hernia recurrence. Non-RCT studies suggested an increased number of port-site hernias and visceral injuries, associated with TAPP rather than TEP. Therefore the Dutch guideline on inguinal hernia repair prefers TEP over TAPP.

The long term results of the LEVEL trial presented in **Chapter 6** showed that after 5 year follow up, incidence of CPIP was lower after TEP versus Lichtenstein (15 vs 28%). Incidence of hernia recurrence in the long term was comparable for the two procedures. The difference in incidence of recurrence after TEP, if operated by an experienced surgeon was still apparent. Sensibility disorders in the groin were seen more often after Lichtenstein. Patient satisfaction with the surgical procedure was higher after TEP, and additionally these patients were also more satisfied with their operative scars.

In **Chapter 7** a letter is presented regarding the use of local anesthetics for the Lichtenstein technique. The Dutch guidelines do not recommend either kind of anesthesia for Lichtenstein. The use of local anesthetics for the Lichtenstein technique should be advocated, because the literature describes less pain shortly after the operation in the group treated with local anesthesia and total operating time was shorter in comparison to spinal anesthesia. Furthermore, urinary retention and overnight admissions for the spinal anesthesia group were more often observed.

PART 3   RISK FACTORS ON CHRONIC POSTOPERATIVE INGUINAL PAIN

Because of the high incidence of chronic postoperative inguinal pain (CPIP) found in the LEVEL-trial, we focused in **Part 3** on this most frequent complication of tension-free inguinal hernia repair. Studies on risk factors on CPIP are presented together with a score-chart to predict patient's individual risk on CPIP.

In **Chapter 8** the results of a meta-analysis whether the mesh is the cause of CPIP are presented. Our hypothesis, that incidence of CPIP is higher after Lichtenstein compared to Shouldice or Bassini repair, because of the mesh used in Lichtenstein, could not be confirmed by the meta-analysis of 5 randomized controlled trials. However, because the incidence of CPIP after Lichtenstein found in other literature is higher compared to Shouldice, additional research on the mesh as a cause of CPIP is warranted.

In **Chapter 9**, the effect of age on CPIP in adult patients was studied with data of the LEVEL-trial after 1 year follow up. Patient's age at time of surgery was inversely correlated a

higher risk of CPIP. Younger and middle-aged patients also had more frequently preoperative pain and intensity of pain was higher during the first 3 post-operative days. Indirect type hernias were observed more often in younger patients, however were not related to CPIP nor to surgical technique.

In **Chapter 10** eight predictors of CPIP were identified by analysing data of the LEVEL-trial of 1 year follow up: 1) age, 2) preoperative pain, 3) bilateral hernia, 4) ASA-classification, 5) low level of surgical experience, 6) conversion, 7) postoperative pain (after 1 and 3 days, 1 and 4 weeks) and 8) sensibility disorders in the groin six weeks postoperatively. Based on multivariable modelling, the strongest predictors for CPIP were: younger age, preoperative pain, bilateral hernia and ASA classification. A score chart for prediction of CPIP was created with these 4 preoperative risk factors for CPIP. The predicted risk on CPIP, 1 year after surgery varies between 16% if the patient has none of the aforementioned risk factors and 52% if all four risk factors are present. Insight in risk factors could contribute in avoiding CPIP. The score chart provides a more individualised risk of CPIP after inguinal hernia surgery.

CHAPTER 12

Future perspectives

Future Perspectives

In 1890 Bassini wrote: "*Considering all that is written about the radical treatment of the inguinal hernia repair up until now, it can be somewhat risky to try to publish more about this subject*". Since then, otherwise has been proved, today almost 14.000 publications are found on PubMed on 'inguinal hernia'. And still, more research is needed on this intriguing and challenging subject.

The risk on hernia incarceration in adults is not an indication for surgical repair since this risk is only 0.2% per year. Therefore other aspects related to the patient's inguinal hernia, like pain, discomfort or maybe cosmetic aspects should be considered in the decision for surgical correction. Because of the high risk on Chronic Postoperative Inguinal Pain (CPIP), individual preoperative risk factors on CPIP such as age, as has been described in the thesis, should also be taken into account (Chapter 9). The crossover rate for asymptomatic or minimal symptomatic hernias in a watchful waiting trial was 62% for patients below age 65. Most patients crossed over because they developed more pain. The effect of watch full waiting on CPIP, especially in younger patients should be studied.

The recommendation of the European Hernia Society Guidelines (EHSG) state that Lichtenstein or endoscopic repair should be the procedure of choice for both primary unilateral and bilateral inguinal hernias; however with the footnote that endoscopic repair should only be performed if expertise is available. The results published in this thesis validate this, because more recurrences were seen if TEP surgery was performed by an unexperienced surgeon (Chapter 4 and 5). Moreover from a patient's perspective TEP performed by an experienced surgeon is preferred over Lichtenstein, because of less acute postoperative pain, faster recovery, less absence from work and less CPIP, with higher patient satisfaction with the surgical procedure and cosmesis. In this respect the excellent performance of dedicated inguinal hernia centers should be further explored as a potential future paradigm of inguinal hernia surgery. The learning curve for performing adequate endoscopic inguinal hernia repair is known to be longer than for Lichtenstein. Adequate patient selection to minimize risks for infrequent but serious complications during the learning curve was previously suggested in the guidelines. Innovation in technology will allow future surgical residents to study on anatomy and to practice their skills to overcome the learning curve not on real patients but on virtual dissection tables and virtual ORs with virtual 3-D patients using augmented reality. A whole new area on clinical research is out there.

Little is still known on all of the aspects of CPIP. In his thesis several risk factors on CPIP like young age and preoperative inguinal pain are mentioned. Knowing the patient's risk factors is important to inform patients on their individual risk on CPIP. From prevention of

CPIP patients would benefit even more. Digital national/international registration on CPIP and mathematical analysis of Big data could possibly play a role in this.

The influence of the mesh on CPIP is still on debate. The guidelines mention that the risk of chronic pain after hernia repair with mesh is less than after non mesh repair. The meta-analysis presented in this thesis on Lichtenstein (mesh) vs. Shouldice (non-mesh) could not confirm the mesh being the cause of CPIP. However, because the incidence of CPIP after Lichtenstein found in other literature is higher compared to Shouldice; further research is needed on new-materials for light weight/large pore meshes, fixation methods or 3-D printing of meshes for individualized optimal fit. Tailor-made meshes should be developed with not only optimal individual anatomical, but also biological fit. This could be done by incubating patient's immune system related blood cells with different mesh specimens, to preoperatively assess patient specific inflammatory reaction. Even more challenging would be to investigate bioengineering-related possibilities on changing DNA to revitalize the inadequate connective tissue in the inguinal area to avoid surgical correction and thereby CPIP.

In the future, surgical techniques could be enhanced by 3D laparoscopy, robotic surgery and augmented reality. Better recognition of the anatomy or even visualization of the inguinal nerves with augmented reality would lead to better tissue handling with less collateral damage. All these new developments could benefit outcomes on inguinal hernia repair and should be investigated.

Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (WHO). Healthcare for our future inguinal hernia patient will become more individualized and safer by new technologies deriving from the digital revolution and all efforts should be undertaken to optimize outcomes on all aspects of health. A new era of inguinal hernia surgery is about to commence: the patient centered era.

APPENDICES

Nederlandse samenvatting

DEEL I   INTRODUCTIE

Deel 1 van dit proefschrift bevat een historisch overzicht over liesbreuk chirurgie. Tevens worden de doelstellingen en een overzicht van het proefschrift beschreven.

DEEL 2   LIESBREUKOPERATIE: CHIRURGISCHE BENADERING

Hoofdstuk 2 presenteert een review gebaseerd op 18 artikelen over kosten, postoperatief herstel, tijd tot werkhervatting, Kwaliteit van Leven (KvL) en pijn geassocieerd met endoscopische Totaal Extra Peritoneale (TEP) procedure en de Trans Abdominale Preperitoneale Procedure (TAPP) versus open correctie van een liesbreuk (chirurgische mat en plug). Er werd aangetoond dat de endoscopische benadering hogere directe kosten met zich meebrengt, maar betere KvL geeft door minder postoperatieve pijn en sneller postoperatief herstel en minder verlies van productiviteit. Dit leidt daarom tot lagere indirecte kosten. De endoscopische benadering heeft dus betere patiënt gerelateerde uitkomsten, maar lijkt minder gunstig voor het budget van de ziekenhuizen. Echter, door de lagere indirecte kosten kunnen de totale maatschappelijke kosten echter lager zijn.

Omdat veel chirurgen de TEP gingen toepassen, werd deze techniek vergeleken met diverse open benaderingen in een kwalitatieve analyse van 23 gerandomiseerde studies in **Hoofdstuk 3**. TEP vereiste meer operatietijd dan een open correctie en bracht hogere kosten voor het ziekenhuis met zich mee, maar bleek kosteneffectief vanuit een maatschappelijk perspectief. Verblijf in het ziekenhuis was korter en er was minder ziekteverzuim na TEP met een gelijke recidief kans, daardoor heeft TEP in het perspectief van de patiënt de voorkeur.

De prospectief gerandomiseerde multicenter 'LEVEL'-studie werd ontworpen om de meest toegepaste endoscopische benadering van liesbreukcorrectie met mat te vergelijken met de gouden standaard open benadering: TEP vs. Lichtenstein, met als hypothese dat TEP tot minder postoperatieve pijn zal leiden. In deze multicenter studie, gepresenteerd in **Hoofdstuk 4**, werden 660 patiënten gerandomiseerd voor TEP en Lichtenstein. Patiënten geopereerd met TEP hadden meer complicaties tijdens de operatie, maar een vergelijkbare opnameduur en minder postoperatieve pijn. Het postoperatief herstel was sneller na TEP en deze patiëntengroep had ook minder ziekteverzuim. Kwaliteit van Leven, gemeten met EuroQol 4 weken na de operatie was vergelijkbaar voor beide ingrepen. Na 1 jaar werden vergelijkbare incidenties van 'chronic postoperative inguinal pain' (CPIP) (25% vs. 29%) en recidieven (3.8% vs. 3.0%) respectievelijk voor TEP en Lichtenstein gezien, met minder sensibiliteitsstoornissen in de lies na TEP. Echter, er bleek een hogere kans op een recidief

indien TEP was uitgevoerd door een onervaren chirurg. Voor Lichtenstein werden deze verschillen niet gevonden. Directe (ziekenhuis-) kosten waren hoger voor TEP, hoewel de totale maatschappelijke kosten na 1 jaar vergelijkbaar waren. Daarom wordt vanuit het perspectief van de patiënt TEP aanbevolen, indien uitgevoerd door een ervaren chirurg.

In **Hoofdstuk 5** wordt een letter to the editor gepresenteerd over de geprefereerde endoscopische liesbreukcorrectie: TEP of TAPP. Eén gerandomiseerde studie laat een kortere ziekenhuisopname zien voor TEP. Er werden geen verschillen gezien tussen TEP en TAPP gezien in termen van operatieduur, hematomen, postoperatief herstel en hernia recidieven. Niet-gerandomiseerde studies suggereerden een verhoogd aantal port-site hernia's en viscerale letsels, geassocieerd met TAPP. Daarom verkiest de Nederlandse richtlijn TEP boven TAPP.

De lange termijn resultaten van de LEVEL-studie gepresenteerd in **Hoofdstuk 6** toonden aan dat na 5 jaar follow-up, de incidentie van CPIP na TEP lager was dan na Lichtenstein (15 versus 28%). Het aantal recidief hernia's op lange termijn was vergelijkbaar voor de twee procedures, waarbij nog steeds gezien werd dat de incidentie recidieven na TEP hoger was indien de TEP was uitgevoerd door een onervaren chirurg. Sensibiliteitsstoornissen in de lies werden vaker gezien na Lichtenstein. De patiënttevredenheid met de operatie was hoger na TEP en deze patiëntengroep was ook meer tevreden met zijn littekens.

Hoofdstuk 7 betreft een letter to the editor met betrekking tot het gebruik van lokale anesthesie bij de Lichtenstein-techniek. De Nederlandse richtlijn bevat geen aanbeveling voor een vorm van anesthesie voor de Lichtenstein procedure. Het gebruik van lokale anesthesie voor de Lichtenstein-techniek dient echter te worden aanbevolen, omdat in de literatuur postoperatief minder pijn en kortere operatietijd werd gezien in de groep behandeld met lokale anesthesie. Tevens werd meer urineretentie en een langere opnameduur waargenomen in de spinale anesthesie groep.

DEEL 3   RISICOFACTOREN VOOR CHRONISCHE POSTOPERATIEVE PIJN IN DE LIES

Vanwege de hoge incidentie CPIP in de LEVEL-studie, richtten we ons in **deel 3** op deze veel voorkomende complicatie. Studies naar risicofactoren op CPIP worden gepresenteerd samen met een scorelijst om individueel risico van patiënten op CPIP te voorspellen.

In **Hoofdstuk 8** worden resultaten gepresenteerd van een meta-analyse waarbij we onderzocht hebben of de chirurgische mat de oorzaak van CPIP is. Onze hypothese hierbij was, dat de incidentie van CPIP hoger is na Lichtenstein dan na een Shouldice of Bassini operatie, vanwege de gebruikte chirurgische mat. Dit kon echter niet worden bevestigd in de meta-analyse van 5 gerandomiseerde studies. Omdat de incidentie van CPIP na Lichtenstein in andere literatuur hoger is dan na Shouldice, is nader onderzoek naar de mat als een oorzaak van CPIP noodzakelijk.

In **Hoofdstuk 9**, werd het effect van leeftijd op CPIP bij volwassen onderzocht met data van de LEVEL-studie na 1 jaar follow-up. De leeftijd van de patiënt was omgekeerd evenredig gerelateerd met een hoger risico op CPIP. Patiënten met jonge en middelbare leeftijd hadden vaker preoperatief pijn en de pijn-intensiteit was hoger gedurende de eerste drie postoperatieve dagen in vergelijking met oudere patiënten. Jonge patiënten hadden vaker indirecte liesbreuken, maar het type breuk en ook chirurgische techniek bleek niet gerelateerd aan CPIP.

In **Hoofdstuk 10** werden acht voorspellers van CPIP geïdentificeerd door analyse van data van de LEVEL-studie: 1) leeftijd, 2) preoperatieve pijn, 3) bilaterale hernia, 4) ASA-classificatie, 5) weinig chirurgische ervaring, 6) conversie, 7) postoperatieve pijn (na 1 en 3 dagen, 1 en 4 weken) en 8) sensibiliteitsstoornissen in de lies 6 weken na de operatie. Met multivariabele modellering, werden de sterkste voorspellers van CPIP gevonden: jonge leeftijd, preoperatieve pijn, bilaterale hernia en ASA classificatie. Een scorelijst voor predictie van CPIP werd gemaakt met deze vier preoperatieve risicofactoren. Het voorspelde risico op CPIP, 1 jaar na de operatie, varieert tussen 16% indien de patiënt geen van bovengenoemde risicofactoren heeft en 52% indien alle 4 de risicofactoren aanwezig zijn. Inzicht in risicofactoren zou kunnen bijdragen aan het voorkomen van CPIP. De scorelijst geeft een meer geïndividualiseerde risicoschatting op CPIP na liesbreuk chirurgie voor gebruik op de polikliniek.

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'If you want to go fast, go alone. If you want to go far, go together.'
(African saying)

En zo is het gegaan.

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"How do you spell 'love'?" - Piglet
"You don't spell it...you feel it." - Pooh
– A.A. Milne

Curriculum Vitae

Hester Langeveld werd geboren op 30 april 1975 in Deventer, waarna ze haar jeugd doorbracht in het Brabantse Uden met haar ouders en broer Aernout. In 1993 haalde zij haar VWO diploma aan het Baarnsch Lyceum te Baarn. Datzelfde jaar is zij gestart met de studie Vormgeving en Communicatie aan de Ichthus Hogeschool (tegenwoordig Hogeschool Inholland) te Rotterdam.

Twee jaar later besloot zij geneeskunde te gaan studeren aan de Erasmus Universiteit. Hiertoe behaalde zij deelcertificaten natuurkunde en scheikunde aan het James Boswell Instituut te Utrecht. In 2002 studeerde zij cum laude af en is zij haar medische carrière gestart als vrijwilliger op de spoedeisende hulp van Centro de Salud Comunal Jac de Wit in Guatemala City, Guatemala. In 2003 begon zij als ANIOS chirurgie in het Erasmus MC waar zij vervolgens in 2004 coördinator werd van verschillende gerandomiseerd klinische trials, waaronder de 'LEVEL' trial (Prof.dr. H.J. Bonjer) waarmee de basis werd gelegd voor dit proefschrift.

Haar opleiding tot chirurg volgde zij in het Reinier de Graaf Ziekenhuis te Delft (Prof. dr. L.P.S. Stassen en Dr. M. v.d. Elst) en het Erasmus MC te Rotterdam (Prof.dr. J.N.M. IJzermans) met als aandachtsgebied GE/ laparoscopie. Tijdens haar stage in het Sophia kinderziekenhuis te Rotterdam heeft zij haar passie voor de kinderchirurgie ontdekt. Als jonge klare chirurg is zij met haar echtgenoot Jurg en hun kinderen Thijn en Flore, zes maanden naar Zuid Afrika gegaan om in het Red Cross War Memorial Childrens Hospital te Kaapstad, te participeren in de kliniek en onderzoek te verrichten naar abdominaal letsel door kindermishandeling (Prof.dr. S. van As en Prof.dr. A. Numanoglu). Terug in Rotterdam is zij na 6 maanden 'chirurgie bij kinderen' nu werkzaam als fellow kinderchirurgie in het Erasmus MC-Sophia (Drs. G.C. Madern).

"It always seems impossible until it's done."

Nelson Mandela