Lichtenstein versus Onstep for inguinal hernia repair: protocol for a double-blinded randomised trial

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ABSTRACT

INTRODUCTION: Inguinal hernia is a common condition that affects millions of people world-wide every year. In Denmark (population of 5.5 million), more than 10,000 repairs of inguinal hernias are performed annually. The optimal surgical procedure for mesh placement and fixation is still being debated because of long-term complications such as persisting pain and impairment of sexual function. The Onstep approach is a newer type of groin hernia repair with promising preliminary results in terms of very few cases of chronic pain and recurrences. This protocol describes a randomised clinical trial the objective of which is to evaluate chronic pain and sexual dysfunction after inguinal hernia repair using the Lichtenstein repair compared with the Onstep approach.

MATERIAL AND METHODS: The study is designed as a two-arm blinded multicentre, randomised clinical trial, currently involving five centres in Denmark and with ongoing recruitment. The plan is to recruit a total of 282 patients (Lichtenstein, n = 141 and Onstep, n = 141) and to perform one-year follow-ups. Follow-up will be done by clinical examination, phone interviews and questionnaires.

DISCUSSION: This study will be the first randomised clinical trial to compare the Lichtenstein repair with the Onstep technique. The results are important in order to guide further research and clinical guidelines for inguinal hernia repair.

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TRIAL REGISTRATION: NCT01753219 (clinicaltrials.gov)

Inguinal hernia is a common condition that affects millions of people world-wide every year. In Denmark (population of 5.5 million), more than 10,000 repairs of inguinal hernias are performed annually. The consensus is that repair of a groin hernia should be performed with a mesh in which either the Lichtenstein method or a laparoscopic approach is deployed [1, 2]; however, the optimal surgical procedure for mesh placement and fixation remains a debated issue because of long-term complications such as persisting pain and impairment of sexual function. It has been reported that up to 11-17% of patients are affected by chronic pain in a way that interferes with their daily activities one year after initial repair [3, 4]. Besides chronic pain, impairment of sexual function can also be a problem following Lichtenstein repair; and it has been reported to affect up to 6.5% of male patients [5].

The Onstep approach is a more recent type of groin hernia repair [6] with promising preliminary results in terms of very few cases of chronic pain and recurrences [6]. However, the data are still limited to those presented by two highly experienced surgeons. The proposed study is therefore conducted with the objective to compare chronic pain and sexual dysfunction after inguinal hernia repair between the Lichtenstein approach and the Onstep approach. The trial is currently ongoing.

MATERIAL AND METHODS

Study design

This study is designed as a two-armed, blinded multicentre randomised clinical trial, currently involving five centres in Denmark. The plan is to recruit a total of 282 patients and to perform one-year follow-ups.

Study population

Patients are assessed for inclusion (**Table 1**) when they visit the outpatient clinic at the participating centres. After inclusion, the patient will be booked for elective hernia repair with a surgeon capable of performing both the Lichtenstein and the Onstep procedure

Randomisation and blinding

On the day of surgery (Day 0), the surgeon will open an opaque envelope (when the patient is sleeping) with the randomisation code allocating the patient to either Lichtenstein or Onstep. The randomisation lists was generated using randomization.com and opaque envelopes with the allocation were created by an independent person.

The person doing the telephone interview will be blinded as will the investigators handling questionnaires and data management. The patient will be blinded, but will be informed about allocation after 12 months of follow-up or if they wish to withdraw from the study.

Surgeons

To mitigate any learning curve effect, all patients in this study will be operated on by surgeons experienced in performing hernia repair and who have performed a minimum of ten Onstep procedures and 40 Lichtenstein procedures [7].The minimum of ten Onstep procedures

PROTOCOL ARTICLE

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TABLE 1

Inclusion and exclusion criteria.

Inclusion criteria
Male patients more than 18 years of age
Primary groin hernia that requires surgical intervention
Eligible for procedure performed under general anaesthesia
Exclusion criteria
Incarcerated or irreducible hernia
Other abdominal hernias being operated at the same time or such surgery was planned for the follow-up period
Emergency procedures
ASA score more than three
Previous surgery that impaired the sensation in the groin area
Local (site of surgery) or systemic infection
Unable to understand Danish, written and spoken
BMI > 40 kg/m^2 or BMI < 20 kg/m^2
Daily intake of alcohol > 5 U, 1 U = 12 g pure alcohol
Known disease that impairs central or peripheral nerve function
Concurrent malignant disease
Impairment of cognitive function (e.g. dementia)
Chronic pain that requires daily medication
Mental disorder that requires medication

ASA = American Society of Anesthesiologists.

has been set in accordance with experience from the co-ordinating department.

Surgical technique

In this study, both the Onstep and the Lichtenstein procedure will be performed in general anaesthesia. The Onstep procedure is done through a four-centimetre horizontal incision cranially to the pubic bone and laterally to the midline. The subcutaneous tissue is dissected until the fascia of the external oblique is reached. The fascia is incised and the space between the external and internal oblique muscle is dissected digitally until the spermatic cord is identified and can be mobilised. The space of Retzius is entered digitally under the transversalis fascia and a sterile gauze is inserted into the space in order to perform blunt dissection. The sterile gauze is removed and the mesh is placed partly preperitoneally and partly between the two muscle layers. The external fascia is closed with sutures and the skin is closed with staples [6].

The Lichtenstein procedure is performed according to guidelines published by the Danish Hernia Database [1]. In this group, the skin is also closed with staples.

Outcomes

During follow-up, the participants will be seen at the outpatient clinic on Day 10, contacted by phone on Day 30, and questionnaires will be sent six and twelve months post-operatively, see **Figure 1**.

Both the primary and the secondary endpoints in this study are patient-centred and will be assessed using the following questionnaires: activity assessment scale (AAS) [8], pain-related impairment of function (PIF) [5], visual analogue scale (VAS) [9], Carolinas Comfort Scale (CCS) [10] and the inguinal pain questionnaire (IPQ) [11].

The primary endpoints in this study are:

A. Proportion of patients with substantial pain-related impairment of function at the six-month follow-up (defined as an AAS > 8.3 [12, 13]).
B. Proportion of patients with pain that impairs daily function at the 12-month follow-up.
C. Proportion of patients with pain-related impairment of sexual function at six and twelve months of follow-up in the age group 18-40 years of age, as well as the whole study population (PIF).
D. Early post-operative pain measured by VAS.

The secondary endpoints of this study are:

– Cut-to-suture time (minutes) and proportion of patients with peroperative complications.
– Post-operative length of hospital stay (days or hours).
– Time to return to normal daily activities.
– Late (> 10 days after surgery) pain (VAS), amount and type of pain medication, recurrence and proportion of patients with complications related to the procedure (urinary retention, haematoma, seroma, ischaemic orchitis, infection).
– Patients' pain assessed with the IPQ.
– Patients' comfort assessed by CCS.

Sample size calculation

Four sample size calculations have been performed to ensure that the study has power to cover all of the four primary endpoints. The sample size calculations were done using SPSS Sample Power version 3:

A. Pain-related impairment of function at six-month follow-up

It was previously reported that the rate of substantial pain-related impairment of function six months after Lichtenstein treatment was 16% [13]. A rate of substantial pain-related impairment of function six months after Onstep treatment was 0% in the only available cohort trial from the inventors of the technique [6]. However, we expect a slightly higher level of undesirable outcomes, and the expected value for pain-related impairment is therefore set to 4%. Since this is considered the most important primary outcome, the beta is set to 10%. With an effect size of 12% and a two-sided alpha of 5%, the sample size needed will be two groups of 130 patients each.

Due to possible dropouts, 11 patients will be added

in each group which is considered a safe estimate based on previously published randomised controlled trials studying the same disease on the same population [14, 15]. This gives a total of 282 patients.

B. Pain at one-year follow-up

The results from a recently published randomised controlled trial (RCT) showed that 12.9% of patients operated with the Lichtenstein procedure experienced moderate to severe pain (VAS 4-10) one year after operation [4]. In the Onstep group, it is expected that the proportions of patients with pain will diminish from six months to one year post-operatively. We therefore expect that 3% of patients in the Onstep group will experience moderate to severe pain at the one-year follow-up. This gives an effect-size of 10%. With alpha set to 5% and beta at 20%, the sample size needed will be two groups of 115 patients, corresponding to a total of 230 patients. This sample is smaller than the required sample for the outcome A and therefore we do not need to increase sample size to clarify this outcome.

C. Sample size for sexual dysfunction

In a cohort of 1,224 patients with an observation time of 1.4-1.7 years, pain during sexual activity after primary hernia repair (Lichtenstein technique) was found in 20.8% of patients in the age group of 18-40 years [5]. We expect (new) pain during sexual activity to occur in no more than 3% of patients in the Onstep group one year after their operation. With alpha set at 5% and beta at 20%, the sample size needed will be two groups of 55 patients. The study includes 282 patients. We expect that this will be enough to achieve two groups of 55 patients under the age of 40 years for analysis of sexual dysfunction.

D. Early post-operative pain

Twenty-four hours after surgery, patients operated by the Lichtenstein technique had a mean score on the VAS of 34.2 mm with a standard deviation of 11.85 mm [16]. The early post-operative pain has not yet been investigated following Onstep repair. However, a 30% reduction in the mean VAS score between the Onstep and the Lichtenstein group was considered a minimal, relevant difference. With an alpha of 5% and a beta of 20%, this lead to sample size needed of two groups of 22 patients and therefore this outcome should be covered by the included population.

Statistical analysis

Data will be analysed using both parametric and non-parametric statistics depending on the distribution of the data. A p-value ≤ 0.05 is considered significant. In the scientific publications, we plan to report data after both per-protocol as well as intention-to-treat analyses.

Analysis of the AAS questionnaires will be done in the following manner. The proportion of patients with substantial impairment of function (defined as an AAS-score > 8.3) in both groups will be compared using the χ^2-test. Furthermore, a confidence interval (CI) for the difference will be calculated. The mean and standard deviation will also be calculated for the two groups' AAS overall score, and a comparison will be done by using the t-test. Since the AAS questionnaire can be divided into sub-scales for sedentary, ambulatory and work/exercise activities, the scores on these subscales will also be analysed by mean and standard deviation, and they will be compared using a t-test.

The level of pain will be assessed at the one-year follow-up by using the VAS. A χ^2-test will be done to compare the proportion of patients experiencing moderate to severe pain in the two groups. Furthermore, the two groups will be compared by calculating the mean and standard deviation for the VAS score at the one-year follow-up. When the patient is at rest on Day 1 (24 hours after surgery) mean and standard deviation of VAS scores will be calculated, and the groups will be compared using the t-test. In addition, the analysis of VAS scores on Days 1, 2, 3 and 10 will be done by summarising the data for each patient as the area under the curve (AUC) and analysed as described by Matthews et al [17]. Furthermore, the daily reported VAS for Days 2, 3 and 10 will be analysed and compared using a t-test on the mean and standard deviation for each group on each day.

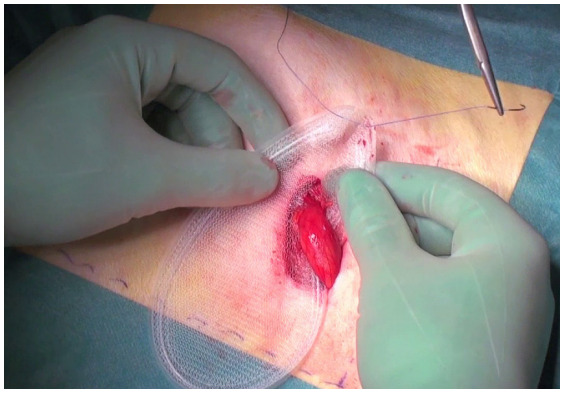
The proportion of patients in the two groups experiencing (new) pain during sexual activities will be compared using a χ^2-test. Furthermore, the questionnaire regarding sexual dysfunction following inguinal hernia repair contains a list of subscales and questions which will also be compared using non-parametric statistics.

FIGURE 1

Overview of questionnaires used in the study.

	Time	Questionnaires	VAS	AAS	IPQ	PIF	CCS
Local participating centre	Preoperative		SA	SA		SA	
	Day of surgery		SA/CI				
	Post-operative day	1	SA				
	Post-operative day	2	SA				
	Post-operative day	3	SA				
	Post-operative day	10	CI	SA			
Herlev Hospital (coordinating centre)	Post-operative day	30	PH				
	Post-operative day	180	SA	SA	SA	SA	SA
	Post-operative day	360	SA	SA	SA	SA	SA

AAS = activity assessment scale; CCS = Carolina Comfort Scale; CI = clinical interview; IPQ = inguinal pain questionnaire; PH = phone interview; PIF = pain-related impairment of sexual function; SA = self-administered; VAS = visual analogue scale measuring pain.



Fitting of the Polysoft hernia patch around the spermatic cord during the Onstep procedure.

Ethics and trial registration

This study does not involve an increased risk for any participants compared with standard treatment. All personal information will be handled according to Danish law, and therefore this study is ethically justifiable.

This study has been approved by the Danish Data Protection Agency, HEH-2013-006 and by the ethics committee (H-3-2012-175). This study is registered at clinicaltrials.gov: NCT01753219. Both negative, positive and inconclusive results will be published.

Funding

The study is funded in part by Bard Europe. Bard will not have influence on the execution of the project or the publication of the results.

DISCUSSION

This protocol describes the first randomised clinical trial comparing Lichtenstein and Onstep repair of inguinal hernia. The trial is currently ongoing, but no data analysis has been conducted yet.

The preliminary post-operative results of the Onstep procedure are based on 693 patients operated in two surgical centres [6]. This single-arm observational study reported a complication rate of 1% at the one-year follow-up. Early complications were found among 0.7% of the patients, primarily in the form of seroma, haematoma and wound infection. At the six-month follow-up, four patients (0.6%) reported residual pain, and in three of these the non-absorbable deployment ring in the mesh was removed by a subsequent small surgical procedure. At the 12-month follow-up, the pain of the last patient had become negligible; thus, no patients had pain at the 12-month follow-up. The study also investigated recurrence and found five recurrences within the first two months (four in women), yielding a recurrence rate of 0.7%. So far, sexual function after the Onstep procedure has not been investigated.

Patients operated using Lichtenstein repair generally have a higher risk of chronic pain. In a prospective study, 16% of patients had substantial pain-related impairment of function at a six-month follow-up, and 6.1% reported moderate or severe pain (nummeric rating scale (NRS) ≥ 4) [13]. Substantial pain during sexual activity was found among 6.5% of male patients receiving Lichtenstein repair in the age group of 18-40 year-olds [5]. The crude reoperation rate after Lichtenstein repair is reported to be 1% [18].

When performing an RCT, the risks and benefits for the participants have to be taken into account. The available evidence regarding the Onstep procedure suggests that, in terms of chronic pain, it may be superior or at least comparable to the Lichtenstein procedure. However, this is based on a non-randomised series of patients operated by two expert surgeons, and the Lichtenstein data are from a larger group of surgeons. In terms of recurrence, the two procedures seem to be comparable. The literature on the Onstep procedure indicates no increased risk of any complication compared with the Lichtenstein procedure.

In conclusion, a randomised controlled trial investigating chronic pain and sexual dysfunction after inguinal hernia repair using the Lichtenstein repair compared with the Onstep approach is both ethically justifiable and needed before the Onstep technique can be implemented into routine daily practice.

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